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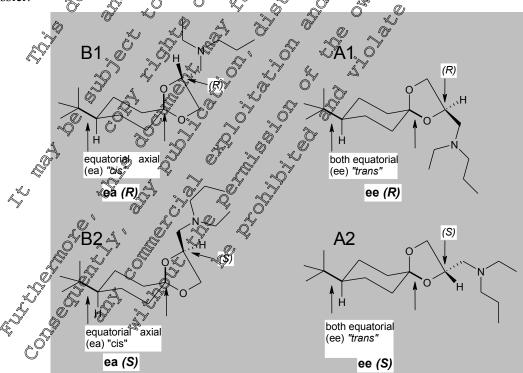
CA 7 FATE AND BEHAVIOUR IN THE ENVIRONMENT

Spiroxamine was included in Annex I to Council Directive 91/414/EEC in 1999 (Directive 1999/7) EC. Entry into Force on 1 September 1999). This Supplementary Dossier contains data which were not submitted at the time of the Annex I inclusion and first renewalof spiroxamine order Council Directive 91/414/EEC and which were therefore not evaluated during the EU review and first renewal. However, all studies submitted for the first approval and subsequent first renewal of spiroxamine have also been summarised according to current guidance and included in the dossier. Where studies meet relevant validity criteria, new robust study summaries have been provided in the appropriate dossier section. However, where studies do not meet relevant validity criteria and are not considered acceptable, less detailed summaries have been provided alongside discussions of study deficiencies. All relied upon study reports are submitted in Document K for this second renewal of approval dossier or in Document K for the previous Annex I inclusion and first renewal sybmissions.

All data which were already submitted by Bayer A@ (former Bayer CropScience) for the Annex I inclusion and first renewal under Council Directive 91/414/EC are contained in the drag Re-Assessment Report (RAR) 2010 and its revised RAR 2017, and are included in the Baseline Dossier provided by Bayer AG.

Relevant information for classification as detailed in the "Combined Draft Reneval) Assessment Report prepared according to Regulation (EC) N° 1107/2009 and Proposal for Harmonised Classification and Labelling (CLH, Report) according to Regulation (EC) N° 1272/2008 – Volume 1, Level 2" is provided in Document NY, Sections 8.2 and 8.3, and highlighted in light grey

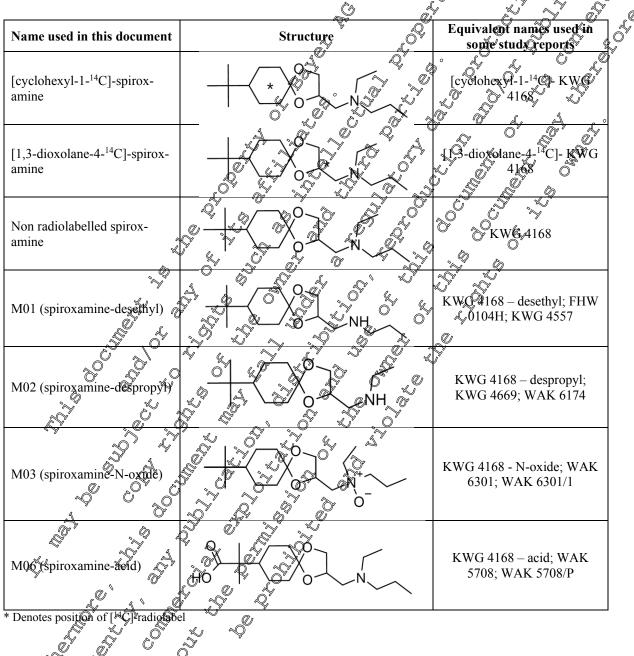
Spiroxamine consists of four isomer's (two diastereomer's each with its corresponding two enantiomers which are in a 1:1 ratio) as shown in the schematic below. The isomer nomenclature presented in some historical documentation may differ with respect to the AB and corresponding trans/cis notation as a result of a discrepance in referencing, which is discussed in detail in position paper M-761468-01-1 (see CA 1.7/01). It is recommended that the stereo assignments depicted here together with the A and B notation should be used exclusively going forward to ensure contrauity of information throughout the dossier.





This document reviews the fate and behaviour in the environment, including additional data and the appropriate risk assessments, for spiroxamine.

The structures of the active substance spiroxamine and of all associated metabolites are presented in the N3 document. A full copy of the N3 document is provided in Appendix 1 for reference only. Subject to investigate the fate and behaviour of spiroxamine have been performed with [cxclohexyl-1-¹⁴C]-spirox-amine, [1,3-dioxolane-4-¹⁴C]-spiroxamine radiolabelled or non-radiolabelled (with or without formula-tion) test substance. The structure of spiroxamine and the radiolabel positions is summarised below.



Details of the iderature search undertaken can be found in M-CA Section 9. If a relevant, scientifically peer-feviewed, open literature reference has been identified for spiroxamine or its major metabolites, it has been discussed within the relevant data point.



CA 7.1 Fate and behaviour in soil

Previously, information on the aerobic route of degradation of spiroxamine was obtained from studies performed with spiroxamine radiolabelled in either the cyclohexyl or dioxolane position (KCA 7.1.1.1/01 (<u>M-006135-01-1</u>); KCA 7.1.1.1/02 (<u>M-006141-01-1</u>); KCA 7.1.1.1/04 (<u>M-006048-01-1</u>)) (<u>M-006094-01-1</u>)). An additional study (KCA 7.1.1.1/03 (<u>M-006094-01-1</u>)) is also included for completeness but is not relied on for endpoint setting. Although conducted some years ago, these legacy studies are considered fully adequate for defining the rate and route of degradation of spiroxamine in soil.

The route of degradation of spiroxamine was consistent in all studies and driven via de-alkylation of the amine moiety and/or oxidation reactions of the alkyl chains resulting in identification of the soil metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide, please see Figure 7.1-1). Ultimately, spiroxamine was mineralized with up to 50% applied radioactivity (AR) being observed as CO_2 and bound residue of approximately 20% AR. M01 (spiroxamine-desethyl) was observed in all soils with a maximum occurrence of 8.5% in the Montreim 3 soil (KCA 741.1.1/02 (<u>M-006141-01-1</u>)). M02 (spiroxamine-despropyl) was found at lower overall percentages than M01 (spiroxamine-desethyl), but was still observed in all studies with a maximum formation of 5.8% AR with the highest formation typically occurring close to study end M03 (spiroxamine-N-oxide) was found only >5% AR in the wolf range soil (KCA 7.1.1.1/02 (<u>M-006141-01-1</u>)). Other minor metabolites were found in the studies of which no single component accounted for >3.5% AR, which included M06 (spiroxamine-desethyl), M011 (spiroxamine-desethyl-acid), M12 (spiroxamine-despropyl acid) and M15 (spiroxamine-desethyl-acid), M011 (spiroxamine-desethyl-acid), M12 (spiroxamine-despropyl acid) and M15 (spiroxamine-ketone). Overall, the tate and behaviour of spiroxamine-despropyl acid) and M15 (spiroxamine-ketone). Overall, the tate and behaviour of spiroxamine-described in the historical studies submitted in the previous renewal.

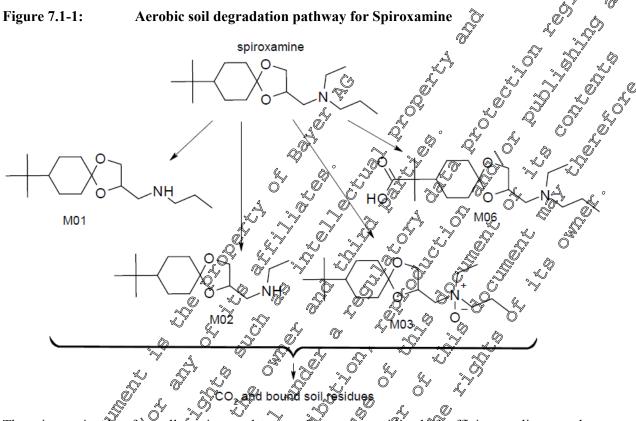
In order to clearly define the potential for stereochemical interconversion or stereochemical specific degradation, a new aerobic route study was conducted in four soils (KCA $\frac{1}{7}$ 1.1.606 (M-762349-01-1))) taking into consideration the stereochemistry guidance (EPSA, 2019). In this new study, quantification of spiroxamine and metabolites occurred using both chiral and achiral methods, with only the achiral results available at the point of stomission but will be submitted as part of the top-up submission or soon as completed.

However, considering the achirul analysis (i.e. analysis for total spiroxamine), we see a consistent picture of spiroxamine degradation with the metabolism profile previously reported in the legacy studies. The degradation of [4 C-cyctohexyl]-spiroxamine degraded ultimately to CO₂ and bound residue with the formation of the delevant metabolites M01. (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) then tiffed as major soft metabolites. M01 (spiroxamine-desethyl) was seen at a maximum formation O 12% ÅR in the Longwoods soil, and at levels >5% observed in all other soils. Likewise, M02 (spiroxamine-despropyl) was also observed in all soils >5% with a maximum observed value of 9.2% ÅR in the Longwoods soil whilst M03 (spiroxamine-N-oxide) was consistently observed in all four soils but was only found >5% ÅR in the Longwoods soil with a maximum observation of 7.2% ÅR. The only notable new observation versus the previous evaluation was that of M06 (spiroxamine-acid), previously M06 was observed only at a maximum of 3.5% (in KCA 7.1.1.1/01 (M-006135-01-1))) the most recent data show M06 at a maximum of 5.3% ÅR at the final time point in the Refesol-02Å soil thus triggering further evaluation and risk assessment. A number of additional minor metabolites were observed, but drese were not characterised due to their low levels in all soils.

In conclusion, from the studies submitted to support the route of degradation of spiroxamine, studies conducted on parent adiolabelled in the cyclohexyl or dioxolane positions fully define the behaviour of the active substance. Spiroxamine is degraded by de-alkylation of the amine moiety with further oxidation reactions of side chains, forming the relevant metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) which are thus considered in the definition of residue for soil. The observation of M06 (spiroxamine-acid) at the final timepoint of the aerobic degradation of Refesol-02A >5% (KCA 7.1.1.1/06 (M-762349-01-1)) is a new

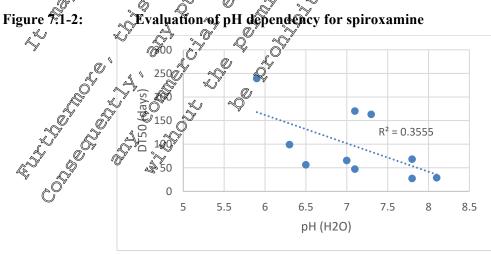


observation as this metabolite had only previously been observed at a maximum %AR of 3.5% (KCA 7.1.1.1/01 (M-006135-01-1)). No other metabolites were observed at concentrations approaching 5% and it can be considered that the route of degradation of spiroxamine has been fully characterised.



The spiroxamine data from all previous and new studies were considered of sufficient quality to evaluate degradation kinetics, and the kinetic evaluation was conducted in accordance to FOCUS (2014) and normalised using a Q_{10} of 2.58 (EFSA 2007). The spiro samine persistence DT₅₀ values ranged from 7.2 to 142 days and DT₉₀ values ranged from 80.9 to 696 days (KCA //1.2.1.1/09 (M-763139-01-1)). The persistence followed biphasic kinetics and the worst case DT₅₀/DT₉₀ was subsequently used to assess spiroxamine accumulation. The geometric mean of the model ing DT₅₀ values was calculated to be 75.4 days, with the acceptable model fits demonstrating biphasic behaviour. The outcome of the chiral analysis of spiroxamine degradation is ongoing at time of submission and will be provided, along with a definition of any Uncertainty Factor (UFOn Doc N5, at a later date.

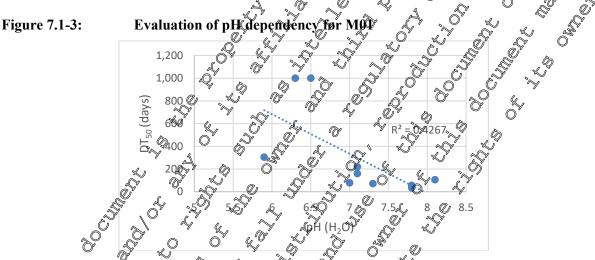
An assessment of pH dependence of spirexamine degradation in the laboratory is presented below:



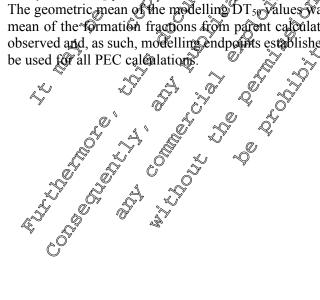


As shown, a potential weak relationship between soil DT_{50} and pH was observed ($R^2 = 0.356$), but evaluation using the German decision input tree did not conclude that the data demonstrated a statistically significant pH dependence and recommended the use of the geomean DT_{50} value in modelling estimates. As such, no pH dependency has been included in the risk assessment.

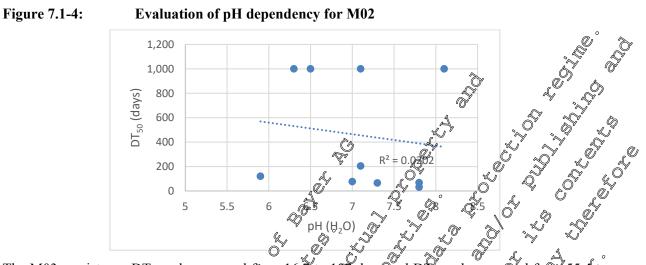
The DT₅₀ values for M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyb, M03 (spiroxamine-desethyl) oxide) and M06 (spiroxamine-acid) have also been determined from these parent studies where the metabolite was observed at levels sufficient for a kinetic evaluation (KCA 7.1.2,1.1/09 (M-765139,M-1)). M01 (spiroxamine-desethyl) persistence DT₅₀ values ranged from 28.9 to 555 days and DT₆₀ value ranged from 95.8 to >1,000 days. The observation of DT₅₀ ersistence endpoints for M01 of 60 days triggers a requirement to investigate the degradation in the field. The geometric mean of the modelling DT₅₀ values was found to be 160 days, with the arithmetic mean of the formation fractions from parent determined as 0.183. Evaluation of pH dependency was impacted by having only 2 acidic soils of which 2 evaluations resulted in default endpoints of 1000 days. As such pH dependency was not established and modelling endpoints, established from the geomean of the aerobic fab studies, will be used for PEC calculations.



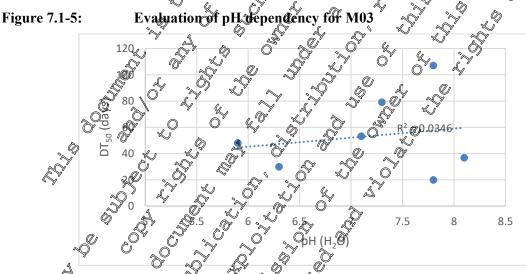
The M02 persistence DT_{50} values ranged from 26.6 to 1,000 days FOCUS default) and DT_{90} values ranged from 88.2 to 3,520 days (FOCUS default) a number of soils did not have acceptable fits for M02 which resulted in the assignment of the FOCUS default of 1,000 days as the persistence endpoint as a conservative approach (KCA 7.1.21.1/09 (M-263139-01-1)). Once again, the observation of $DT_{50persistence}$ endpoints for M02 60 days triggers a requirement to investigate degradation in the field. The geometric mean of the formation fractions from parent calculated as 0.139. No evidence of pH dependence was observed and, as such, modelling DT_{50} with the geomean of the acrobic lab studies will be used for all PEC calculations.







The M03 persistence DT_{50} values ranged from 167 to 107 days and DT_{90} values ranged from 554 to 358 days. All study data included a clear decline phase allowing for an accurate determination of persistence DT_{50} , with only two soils yielding $DT_{30 persistence} > 60$ days. As such, the requirement for a field study on M03 is triggered, although the risk assessment has been finalised considering only lab data. The geometric mean of the modelling DT_{30} values was 46.4 days and the arithmetric mean of the formation fractions from parent was 0.149. No evidence of pH dependence was observed and modelling endpoints established from the geometric for the aerobic lab studies will be used for all PEC calculations.



Acceptable fitting could only be performed for persistence endpoints in one soil for M06 resulting in the assignment of a number of default values. The persistence DT_{50} values, therefore, ranged 49.6 days to 1,000 days whils DT_{90} values was 166 days to 3,320 days. The geometric mean of modelling DT_{50} values was calculated at 479.6 days. The formation fraction from parent was 0.0947. A specific rate study to define the appropriate DT_{90} for 4066 is currently ongoing but for this assessment, the conservative M06 endpoints identified in KCA 7.1.2.5.1/09 (M-763139-01-1) are used to provide an initial investigation into 406. This will be refined upon completion of the M06 rate study and assessment of the data by FOCLS kinetics (2014). The current data package did not adequately define whether a field study was required for M06 as a reliable fit could only be established for a single soil. No evaluation of pH dependency could be conducted.

In conclusion, the large number of studies performed on spiroxamine allows for a clear definition of the degradative behaviour of spiroxamine for the purposes of conducting a risk assessment. Spiroxamine consistently follows biphasic kinetics resulting in a number of studies giving DT₅₀ persistence values



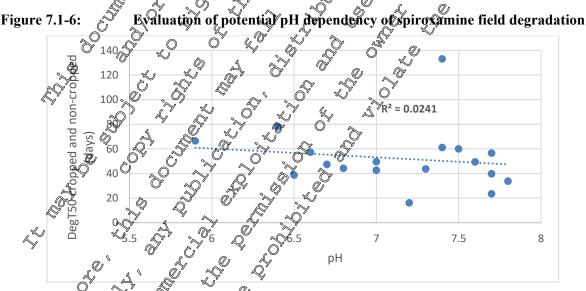
>60 days and as such the requirement to assess spiroxamine degradation in the field is triggered. Modelling endpoints for spiroxamine, M01, M02, M03 and M06 were successfully established for the purposes of conducting a risk assessment, with no pH dependency observed and the endpoints based on the geomean of all data points. Field studies are triggered for M01, M02, M03 and potentially for M06. In order to provide further information on the degradation of M06, a laboratory study on the rate of degradation of M06 (spiroxamine-acid) is currently in progress to allow a further refinement of the degradation the risk assessment:

• Rate of degradation of M06 (spiroxamine-acid) in 3 soils.

Nevertheless, the large number of studies on spiroxamine fully define the route of piroxamine dation under aerobic conditions in soil and this pathway is presented in Figure 7.1.

In order to address potential spiroxamine persistence, a number of field dissipation studies, which have previously been reviewed and accepted, have been further considered for an assessment of persistence and derivation of modelling endpoints of spiroxamine M01 and M02. No new field studies have been performed. In total, 18 valid field dissipation trials were conducted across 5 studies (KCA 7 \pm 2.2.1/01 (M-006116-01-1); KCA 7.1.2.2.1/02 (M-006126-01-1), KCA 7.1.2.2.1/03 (M-006127-02-1); KCA 7.1.2.2.1/04 (M-006128-01-1) & KCA 7.1.2.2.1/05 (M-006129-01-4)) conducted in representative agricultural fields across the EU. These dissipation trials followed the "legacy" design and as such were either applied to bare soil (without exclusion of surface processes) or applied to cropsed plots. For an assessment of persistence, a kinetic analysis to determine DTs and DT₉₀ values for comparison with relevant study triggers and persistence eriteria was performed using non-normalised data, in accordance with the flowcharts for persistence/trigger endpoints provided by FOCUS (2014). The spiroxamine persistence/trigger DT₅₀ values ranged from 05 to 59.6 days and DT₉₀ values ranged from 43.5 to 433 days. The modelled field persistence DP₅₀ values were all \leq 60 days and as such spiroxamine was classified as non-persistent.

An evaluation of pH dependency of spiroxamine degradation in the field is presented below:



As outlined in the previous evaluation, we pH dependency was noted for the field degradation of spiroxamine, and as such a geomean $\text{PegT}_{50,\text{matrix}}$ was applied in the risk assessment.

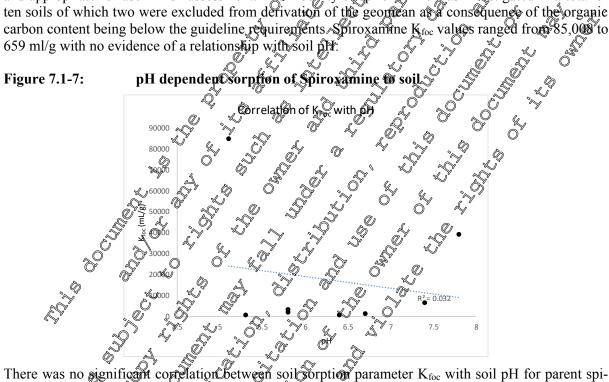
M01 persistence/trigger DT₅₀ values ranged from 17.8 to 223 days and DT₉₀ values ranged from 59 to 742 days whilst M02 persistence/trigger DT₅₀ values ranged from 21 to 161 days and DT₉₀ values ranged from 69.6 to 533 days. Overall, both metabolites were considered persistent in soil.

To determine DegT_{50, matrix} values for spiroxamine, a kinetic assessment was performed following the flowcharts for calculating modelling endpoints provided by EFSA (2014), and using data that have been



normalised to reference conditions (20°C and pF 2 soil moisture content) and subject to time step normalisation procedures. These endpoints were used for the selection of an appropriate modelling value for use with regulatory Predicted Environmental Concentration (PEC) models. Modelling DegT_{50 matrix} values (at 20°C and pF 2) ranged from 23.4 to 78 days, with a geometric mean of 43.8 days. Overall the rate of degradation of spiroxamine in the field appeared faster than degradation in the lab studies, and this was confirmed through an evaluation using the EFSA DegT_{50 matrix} endpoint selector resulting in the selection of the DegT_{50 matrix} endpoint as the appropriate modelling endpoint for groundwater and surface water for spiroxamine.

The mobility in soil of spiroxamine and its degradation products relevant for assessment was studied by batch equilibrium tests on a variety of different soils. The adsorption and desorption of spiroxamine has been investigated in two studies (KCA 7.1.3.1.1/01 and KCA 7.1.3.6.1/02) which were evaluated during the previous EU review. Following a review of the tudy reliability using the EOSA 106 checklist v2 0, it can be concluded that the adsorption endpoints from these two batch equilibrium studies are retable and appropriate for use in risk assessment. The mobility of spiroxamine was investigated in a total of ten soils of which two were excluded from derivation of the georetical as a consequence of the organic carbon content being below the guideline requirements. Spiroxamine K_{foc} values ranged from 85,008 to 659 ml/g with no evidence of a relationship with soil phy.



There was no significant correlation between soil orption parameter K_{foc} with soil pH for parent spiroxamine (R² 0.032), therefore no pH dependence was concluded. The study data indicated that the two clay soils gave very high sorption estimates tadicating that the binding of spiroxamine to clays was significant, potentially mediated via binding to charged sites on the clay. Sorption to non-clay soils yielded K_{foc} values ranging from 659 to 6477 mL g and these interactions were considered to be mediated via soil organic matter. Considering the importance of the two sorption mechanisms, an overall geomean of the data has been used for modelling purposes to reflect both aspects of spiroxamine sorption behaviour. Overall, spiroxamine exhibits low mobility in soil according to the McCall mobility classification. No information on the individual sportive behaviour of the spiroxamine isomers was determined.

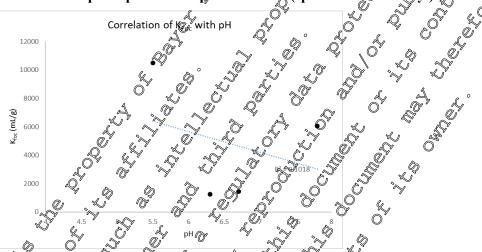
The adsorption and desorption of metabolites of spiroxamine have been investigated in three studies (KCA7.1.3.42/01 to KCA7.1.3.1.1/03) which were evaluated during the previous EU review. Sorption of Xi01, M02 and M03 was measured in four soil types and the outcome of the studies reviewed for reliability using the EFSA 106 checklist v2.0. It was concluded that despite some minor deviations the outcome of the adsorption/desorption studies were reliable and suitable for use in risk assessment. Some differences between the calculated K foc values and those reported were noted, but this was attributed to



the use of averages in the original calculations. Since differences were minor, for consistency the reported values from the report were used in the risk assessment.

Adsorption of M01 was investigated in 4 different soils with K_{foc} ranging from 1237 to 1051 C/kg (KCA 7.1.3.1.2/01 (M-006084-01-1)). Adsorption was shown to be generally correlated with organic carbon content, and M01 (spiroxamine-desethyl) exhibits medium to immobile phobility in soft according to the McCall mobility classification. As part of the risk assessment, potential relationships between pH and sorption were investigated:

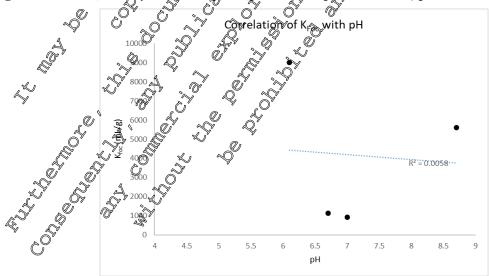




No significant correlation was observed between soil sorption parameter K_{foc} with soil pH for M01 (spiroxamine-desethyl) (R²=0.102) therefore no pH dependence was concluded. The geomean of the four soils was considered appropriate for use in the risk assessment as previously concluded (EFSA Journal (2010);8(10):1710)).

Adsorption of M02 was investigated in 4 different soils with K& ranging from 916.7 to 8993.6 L/Kg (KCA 7.1.3.1.2/02 (M-006086-01-1)). Adsorption was shown to be generally correlated with organic carbon content, and M02 (spirovamine despropri) exhibits medium to immobile mobility in soil according to the McCall mobility classification. As part of the risk assessment, potential pH dependency was investigated:



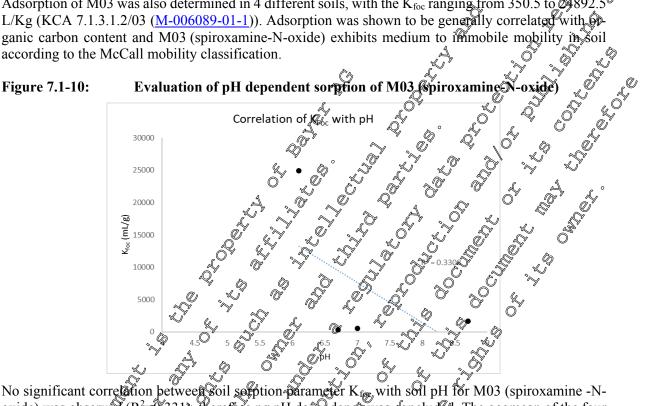


No significant correlation between soil sorption parameter K_{foc} with soil pH for M02 (spiroxamine-



despropyl) was observed ($R^2=0.005$), therefore no pH dependence was concluded. The geomean of the four soils was thus considered appropriate for use in the risk assessment as previously concluded (EESA Journal (2010);8(10):1719)).

Adsorption of M03 was also determined in 4 different soils, with the K_{foc} ranging from 350.5 to 24892.5° L/Kg (KCA 7.1.3.1.2/03 (M-006089-01-1)). Adsorption was shown to be generally correlated with Ω ganic carbon content and M03 (spiroxamine-N-oxide) exhibits medium to immobile mobility in soil according to the McCall mobility classification.



No significant correlation between soil sorption parameter Kip, with soil pH for M03 (spiroxamine -Noxide) was observed (R²-0.331), therefore no pH dependence was concluded. The geomean of the four soils was thus considered appropriate for use in the tisk assessment as previous concluded (EFSA Jour-. ₹ nal (2010);8(10):1712).

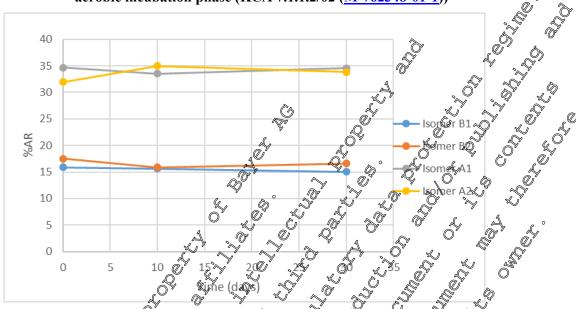
One further study is being conducted to provide soil Sorption properties for metabolite M06 (spiroxamine-active) and will be provided as soon as available. As such, in order to provide a basis for the risk assessment, an estimated Kin value of 3.2 Kg for M06 for usern the preliminary risk assessment was obtained from KocWIN. This will be updated upon completion of the M06 OECD106 study.

The high sorption displayed by spirovamine and its metabolites is reflected in the outcome of column leaching studies investigating the leaching behaviour of aged residue of spiroxamine in soil. These studies demonstrated that in sol column studies, aged residues of spiroxamine did not significantly leach to the column percolate with only 0.2 % K being found in the leachate. The major residue in this leachate was found to be M03 (N-oxide) representing only 0.03% of the applied radioactivity in column leachates. Overall, leaching behaviour or spiro amine (including individual isomers) or its major soil metabolités is not envisaged.

In addition to consideration of aerobic degradation, the rate and route of degradation of spiroxamine, including potential changes in the stereoisomer composition, was investigated in a single anaerobic soil. Following a period of in abatic of 30 days under aerobic conditions, the degradation of spiroxamine proceeded via the aerobic path ar in Figure 7.1-1, with formation of M01 (spiroxamine-desethyl), M02 (spiroxamine, espropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) to >3% AR prior to flooding the vessel During the anaerobic (flooded) phase, almost no further degradation of spiroxamine or the metabolites occurred, although levels of M06 (spiroxamine-acid) increased slightly from 4.7 to 9.9% AR? Analysis of spiroxamine using chiral methods also demonstrated that, under anaerobic conditions, the relative proportions of each isomer did not change significantly during either the aerobic or anaerobic phases (see Figure 7.1-11 and 12).

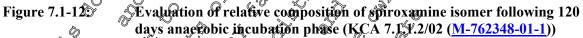


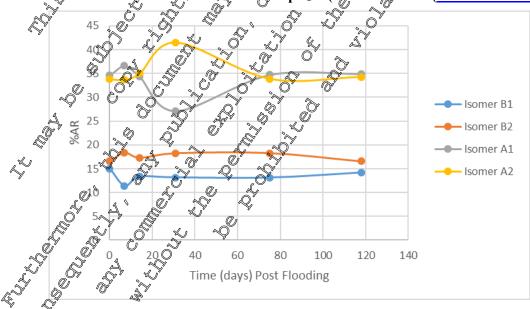
Figure 7.1-11:Evaluation of relative composition of spiroxamine isomer following 30 days
aerobic incubation phase (KCA 7.1.1.2/02 (M-762348-01-1))



From the chiral analysis of the aerobic phase, no evidence of a change in stereoisomer ratio was observed indicating that for the 30 days aerobic incubation, isomer specific degradation or interconversion was not observed. As outlined, the study data from KCA 7.1.1.1/06 (v_1 -762349-0)-1) is being analysed using chiral techniques to provide for ther information on potential changes in spiroxanine isomer ratios and to define whether an isomer Uncertainty Factor preds to be applied.

Considering the anacrobic (the oded phase, no significant changes in stereoisomer composition were noted between the start and end of the theoded phase as such, no isomer UF has been considered on the basis of this analysis.





It was noted that a single time point (31 Days Post Flooding) demonstrated a significant change in %se for isomers A1 and A2, but this was not considered sufficient justification of an UF (EFSA, 2019). However, it is not clear that the change at 31 DPF is reliable, and that the performance of the method performance is essential in order to identify, reliably, the relatively small changes needed to trigger a



significant %se. As such, the analytical methodology is being revised for some studies and this has delayed the submission of this data. The data will be submitted at top-up or as soon as it is available.

Finally, a soil photolysis study is presented, which confirms that soil photodegradation is not a spinificant process for spiroxamine with an estimated photolytic DT_{50} of approximately 119 days (KCA 7.1.1.3/01 (M-006150-01-1)). During the conduct of the study, M01 (spiroxamine-desethyl) and M02 (spiroxamine-despropyl) were identified as relevant metabolites as they are being observed >5% at two consecutive time points with the maximum formation being 9.1 and 6.1% AR respectivels. In addition, M03 (spiroxamine-N-oxide) was observed at 6.2% AR but not >5% at two consecutive time points whilst M15 (spiroxamine-ketone) was observed at 2.7% AR. Other minor metabolites, including M05, were observed but not > 1.7% AR. Considering the DT_{50} for photologis, it is likely that a combination of this slow rate with movement from the soil surface renders the process of photolysis as insignificant, with aerobic degradation the major soil degradation mechanism.

CA 7.1.1 Route of degradation in soil

Use of plant protection products containing the active substance piroxamine will potentially result in contact with soil, therefore the route of degradation in soil of the active substance under aerobic, maerobic and sunlight conditions is considered under Points CA7.1.1.6 (aerobic), CA 7.1.12 (anaerobic) and CA 7.1.1.3 (soil photolysis) in laboratory studies according to the data requirements laid down in Commission Regulation (EU) No 283/2013

In accordance with the data requirements defined by EC Regulation 283/2013, for soil degradation studies included under Point CA 70.1, metabolites are considered major if they exceed 10% AR at a single timepoint or exceed 5% AR on two consecutive sampling intervals or exceed 5% AR and are rising at the end of the study. If metabolites do noet any of these criteria, they are considered minor and are not included as part of the definition of reside for that comparament.

 \bigcirc

Overview:

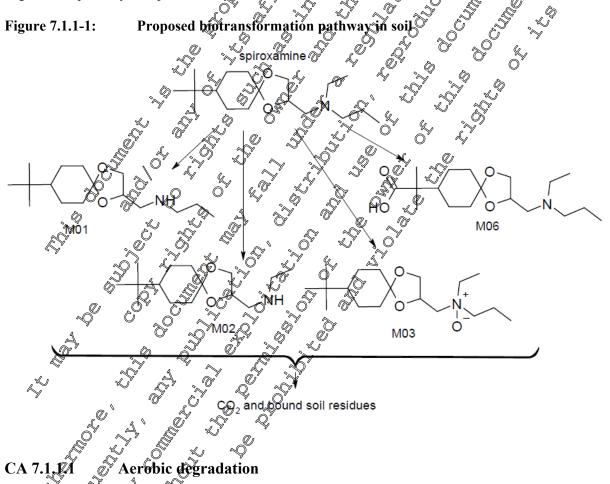
The route of spirovamine degradation in soil has been assessed for derobic degradation in six studies of which 5 were previously evaluated in the last EU feview. A single new study has been conducted to address the new data requirements (EFSA, 2019). In aerobic soil, spirovamine degraded ultimately to CO_2 and bound residue with the formation of a number of metabolites; M01 (spirovamine-desethyl), M02 (spirovamine-despropyl), M03 (spirovamine-N-oxide) and M06 (spirovamine-acid) present as major metabolites. The major soil metabolite was identified M01 (spirovamine-desethyl) and was seen at a maximum formation of 12% AR in the Longwoods soil, and Levels >5% AR in all other soils. Likewise, M02 (spirovamine despropyl) was also observed in all soils >5% with a maximum observed value of 9.2% AR in the Longwoods soil. M03 (spirovamine-N-oxide) was consistently observed in all four soils but was only found >5% AR (seen at two consecutive timepoints) in the Longwoods soil with a maximum observation of 7.2% AR. However, M06 (spirovamine-acid), previously observed but always at low levels, was observed at >5% AR in the fund timepoint in the Refesol-02A soil, triggering further evaluation and risk assessment. No other metabolite was identified at >5% AR.

The active substance spirovamine contains two stereogenic centres and therefore the new aerobic soil degradation study was established to include an investigation in accordance with the requirements of EFSA 2019. The active substance spirovampe and the associated environmental metabolites each have 4 possible isomers (except for metabolite M03 (spirovamine-N-oxide) which has three stereogenic centres and hence eight possible isomers). To simplify the analytical challenge associated with separation of so many components, the approach adopted in the new study was to quantify separate isomers only for parent spirovamine and to address any possible change in isomeric composition of metabolites by incorporating a word-case UF (Uncertainty Factor) in the environmental risk assessment. The outcome of the chiral analysis of spirovamine degradation is ongoing at time of submission and will be provided, along with a definition of the UF in Doc N5, in a top up submission. The achiral analysis in this study has been completed and the interim study report (KCA 7.1.1.1/06 (M-762349-01-1)) presents the outcome of this analysis and the achiral study data has been considered in this evaluation.



In addition to consideration of aerobic degradation, the rate and route of degradation of spiroxamine, and potential changes in the stereoisomer composition, was investigated in a single anaerobic soil (KCA 7.1.1.2/02 (M-762348-01-1)). Following a period of incubation of 30 days under aerobic conditions, the metabolic profile observed was similar to that previously reported in the aerobic studies (with formation of M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) to >3% AR). During the anaerobic phase, almost no further degradation of spiroxamine or the metabolites occurred, although levels of M06 (spiroxamine-acid) increased from 4.7 to 9.9% AR. Analysis of spiroxamine using chiral methods also demonstrated that under anaerobic conditions the relative proportions of each isomer did not change significantly.

Further, a soil photolysis study is presented to confirm that soil photodegradation is not considered significant for spiroxamine with estimated photolytic D_{250} s of approximately 119 days (KCA 7 (1.3/04) (M-006150-01-1)). During the conduct of the study, M01 (spiroxamine-deserbyl) and M02 (spiroxamine-despropyl) were identified as relevant metabolites being observed at >5% on two consecutive timepoints with the maximum formation being 9.1 and 6.1% AR respectively. In addition, M03 (spiroxamine-N-oxide) was observed at 6.2% AR but not 5% at two consecutive timepoints. M15 (spiroxamine-ketone) was observed at 2.7% AR and other minor metabolites, including M05, were also observed but not > 1.7% AR. On the basis of this study, soil photolysis was not considered a significant degradation pathway for spiroxamine.



In view of the proposed use pattern for spiroxamine, as a post-emergence spray applied fungicide for application to cereal's cross and vines, potential exposure to aerobic conditions in soil is envisaged. The degradation of spiroxamine in aerobic soil has been investigated in five studies (KCA 7.1.1.1/01 to KCA 7.1.1.105) all of which were evaluated during the previous EU review. In addition, one new study has



Sub- stance	Report refer- ence	Document no.	Test material used	Comment
Spirox- amine	KCA 7.1.1.1/01; KCA 7.1.2.1.1/01	<u>M-006135-01-1</u>	[cyclohexyl-1- ¹⁴ C]-spiroxamine	Submitted for first approval of spi- roxamine 1999. Reviewed under
Spirox- amine	KCA 7.1.1.1/02; KCA 7.1.2.1.1/02	<u>M-006141-01-1</u>	[cyclohexyl-1- ¹⁴ C]-spiroxamine	UP. Considered valid and accepta-
Spirox- amine	KCA 7.1.1.1/03; KCA 7.1.2.1.1/03	<u>M-006096-01-1</u>	n Cao	
Spirox- amine	KCA 7.1.1.1/04; KCA 7.1.2.1.1/04	<u>M-006148-01-1</u>	[cyclohexyl-1- ¹⁴ C]-spiroxamineC	
Spirox- amine	KCA 7.1.1.1/05; KCA 7.1.2.1.1/05	<u>M-303803-01-1</u>	91,3-dioxolane-4- ¹⁴ C]-spiroxatorne	UP Considered wild and acceptad
Spirox- amine	KCA 7.1.1.1/06; KCA 7.1.2.1.1/08	<u>M-762349-01-</u>	[&yclohexyl-1- [C]-spipoxamir@	Nevodata not yet reviewed under
.a. not appli	icable		X X X	

been conducted, mainly to address the new requirements of EFSA, 2019¹.

The aerobic degradation of spiroxamine in soft has been investigated in stotal of six andies a 20°C. Some supplemental studies are additionally provided under Point KCAS7.1.2.5.1 but these studies do not indicate the formation of any further major metabolites. Previously evaluated studies have been conducted using both [cyclohexy]-1-14C] spiroxamine and [1,97dioxolane-4,94C]-piroxamine and show a consistent degradation pathway throughout the studies and very intle to no separation of the two possible radiolabelling positions. Therefore, the new aerobic soil degradation study was conducted using [cyclohexyl-1-¹⁴C]-spiroxaanine only.

A number of minor deviations are reported for the investigation of bound residue the studies evaluated previously, but considering the extensive extraction schemes employed in KCA 7.1.1.1/05 (M-303803-01-1) and KCA 7.1 (1/06 (M-76 2) 49-0 1) these minor deviations are considered insignificant for the understanding of the behaviour of spiroxamine in soil. The metabolic profile of spiroxamine degradation in KCA 7.1.1 106 (MO62349-01-1) validates the observations of the previous studies, with the confirmation of the major metabolites as M01 (desthey spiroxamine M02, despropyl-spiroxamine) and M03 (spiroxamine-N-oxide) confirmed, and the additional recognition of M06 (spiroxamine-acid) as a major metabolite as a consequence of a single soil having M06 3% at the final timepoint. Overall, it can be considered that the studies provided outline the rate and route of spiroxamine degradation in aerobic soils.

The active substance sport ampre contains two stereogenic centres and the new aerobic soil degradation study was set up to include an investigation in accordance with the requirements of EFSA 2019¹. The active substance spiroxamme and the associated environmental metabolites each have 4 possible isomers (except for metabolite MQ3 (spire amine N-oxide) which was three stereogenic centres and hence eight possible isomers). To simplify the analytical of allenge associated with separation of so many components, the approach adopted in the new dudy was to quantify separate isomers only for parent spiroxamine and to address any possible change in immeric composition of metabolites in environmental residues by incorporating a worst-case LOF (Uppertainty Factor) in the relevant environmental risk assessments. The outcome of the chiral adalysis of spiroxamine degradation is ongoing at time of submission and will be provided, along with a defunction of the UF in Doc N5, as part of a top up submissiont at a later date The achiral analysis has been completed and as such the interim study report (KCA 7.1.1.1/06

EFSA (2019). Guidance of EFSA on risk assessments for active substances of plant protection products that have stereoisomers as components or impurities and for transformation products of active substances that may have stereoisomers. EFSA Journal 2019;17(8):5804, 33 pp.



(M-762349-01-1)) presents the outcome of this analysis and the data has been considered in this evaluation.

New studies, not previou	usly evaluated
	usly evaluated
Data Point:	KCA 7.1.1.1/06
Report Author:	
Report Year:	
Report Title:	[14C]-spiroxamine: Route and rate of degradation in four soils under aerobic con-
	ditions at 20°C - Interim report
Report No:	VC/19/055
Document No:	<u>M-762349-01-1</u>
Guideline(s) followed in	(EU) No. 283/2013(EC) 6. 1107/2009
study:	OECD 307 (2002) (200
Deviations from current test guideline:	None Of Contraction of An Andrew
Previous evaluation:	No, not previously submitted
GLP/Officially recog-	Yes, conducted under GLP Officially recognised testing facilities S
nised testing facilities:	
Acceptability/Reliability:	Yes of the state o
Executive Summary	

Now studios not providually avaluated

A. The route and rate of degradation of spirovarnine was investigated in four European soils (Longwoods, sandy loam; Refesol-02-A, silt loam; Refesol-03-G, clay loam; Speyer 6S, clay) under laboratory aerobic conditions. Soil samples (100 g dw³) were reated with [cvclohexyl-1-4C]-spiroxamine (radiochemical purity 99.6%) at a prominal application rate of 20 mg/kg soil dry weight (reported as equivalent to 750 g/ha assuming mixing depth of 2 fcm and soil density of 1.9 g/cm³, otherwise equivalent to 1500 g/ha assuming a mixing depth of 5 cm) and incupated (20°C, 5F 2) for 120 days in the dark.

Duplicate treated samples of each soft were removed for analysis after 0, 3, 7, 14, 30, 44, 59, 80, 97 and 120 days of incubation. Soil samples were extracted your times at from temperature with acetonitrile/water/35% ammonia solution 80/20/1 v/6v, by addition of solvent, vigorous mechanical shaking and centralingation. Sold extracts were analysed, without concentration, primarily by reverse phase HPLC. Confirmatory analysis was conducted by normal-phase FLC on selected samples. Degradation products were also sonfirmed using LC-MS on selected samples.

The material balances ranged from 92 to 105.1% of appred radioactivity (% AR) indicating a complete mass balance. The amounts of unextractable adjoactivity increased to a maximum 16.9% AR by DAT 120. Mineralisation to carbon diocide was a major pathway, steadily increasing throughout the study to a maximum of 16.3 to 59.9% AR by DAT 120. No significant levels of organic volatiles were observe

Following application of government of a government of parent in the soil extracts of the Longwoods soil decreased from 101.2% AR at DAT 0 to 5.8% AR by the end of the study at DAT 120. The amount of parent in the soil extracts of the Refesol-02-A, Refesol-03-G and Speyer 6S soils decreased from 102.2 5.4 and 99.4% AR at DAT 0 to 50.6, 55.1 and 56.0% AR respectively by the end of the study at DAT 120 DT₅₀ values for the degradation of spiroxamine were calculated in the report, however@a re-evaluation of the degradation kinetics in accordance with FOCUS guidance document of degradation Ainetics (FOCUS 2014), was performed in the report presented under point KCA 7.1.2 1.1/09 (<u>M-76) 39-01+1</u>).

Degradation of [cyclohexyl-1-14C]-spiroxamine was accompanied by the formation of 4 major metabolites: M01 (spiroxamine-desethyl, maximum 12.0% AR), M02 (spiroxamine-despropyl, maximum 9.2% AR), M03 (spiroxamine-N-oxide, maximum 7.2% AR) and M06 (spiroxamine-acid, maximum 5.3% AR). Some other metabolites were detected typically <1% AR but all <5% AR.



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Additional work is currently being conducted on the chiral analysis of the samples for parent spiroxamine. This work will be submitted in the final report for the study (currently report included is an interim report) and will be supplied as part of a top up submission (estimate August 2021).

A Contraction of the contraction I. **Materials and Methods** A. Materials 1. Test Items [cyclohexyl-1-¹⁴C]-spiroxamine * Denotes post Specific Activity: Radiochemical Purity: 2. Test System (soil)

The study was performed using four test soils accharacterise on Ø

		· * *	<u>, , , , , , , , , , , , , , , , , , , </u>	
Parameter	<u>A</u>			
Soil Designation	: Dongwoods	Refesol-02-A	Referent-03-G	Speyer 6S
Geographic Location & O'			4	
Geographic Location		Northenine, 🛪	© Worthrhine,	Sieb- eldingen,
	Quatery,	Westphalia B	Westphalia ^B	Rheinland- Pfalz ^B
Country 9 Textural Classification (USDA)	UK UK	Germany	Germany	Germany
Textural Classification (SDA S	Sandsoloam	Silt-Joam	Clay loam	Clay
Country Classification (USDA) Textural Classification (USDA) Sand [50 - 2000 µm]	N No NTO	<u>م</u> ۲۱6	30	18
Silt [2 – 50 µm]	Ø 38 Ø [™]	66	40	28
Sand $[50 - 2000 \ \mu m]$ Silt $[2 - 50 \ \mu m]$ Clay $[< 2 \ \mu m]$ pH in H ₂ O (1; 1) (%)		18	30	54
pH ~ C ~ ~ ~				
in H ₂ O (1:)		7.1	5.9	7.3
in 0.01 M CaCl ₂ (1:1)	67 7.80 7 7.80 7 7.5	6.7	5.6	7.1
Organic Matter (%)	2.4	1.7	7.6	2.8
Organic Carbon (%)	S 1.4	1.0	4.4	1.6
Cation Exchange Capacity (mee 100 g)	11.3	11.4	12.7	19.8
Water Holding Capacity (g HSO per 400g dry soil) pF 2.0 (00 bar, www.)	\$			
pF 2.0 (00 bar, www)	20.0	35.9	41.1	30.7
pF 2.5(0.33 ba) w/w (3)	11.0	19.9	30.0	25.7
$\frac{pF 2.5}{\sqrt{9.33}} (0.33 \text{ bg} + w/w - 9) = \frac{1}{\sqrt{9}} = \frac{1}{\sqrt{9}}$				

Ő Table CA 7.1.1.1-1: Physico-chemical properties of test soil



Parameter	Soil							
Soil Designation:	Longwoods	Refesol-02-A	Refesol-03-G	Speyer 65 °				
Soil Microbial Biomass (mg org C/100 g soil)			*	speyer va				
Initial, DAT 0	31.8 (2.3)	17.3 (1.7)	4802(1.1)	32,4 (2.0)				
Final, 100 DAT 120	29.2 (2.1)	12.4 (1.2)	35.2 (0.8)	23.3 (1.5)				

* Calculated by multiplying organic carbon content by 1.724 (not reported)

A Biomass as a percentage of organic carbon content provide in parentheses B Location known free of pesticide use for ≥ 3 years and used with 3 months from sampling.

The test soils were handled in accordance with ISO 18400-102 and 105 prior to t

B. Study Design

1. Experimental Conditions

Tests were performed in flow through system consisting of glass dasks each containing 100 g soil and attached to an ethylene glycol trap to collect organic votatiles followed by two potensium bydroxide traps (2M) to collect carbon dioxide.

Soil samples (100 g) (prepared within $\frac{1}{2}$ months of sampling) were pre-acclimatised to the inclustion conditions (dark, 20°C and pF 2 moisture content) for 5-4 days before application of the test substance. The study was conducted at a concentration of 2.0 mg/kg dry weight of soil (reported as equivalent to 750 g/ha assuming a mixing depth of 2.5 cm and soil density of 4.5 g/cm, otherwise equivalent to 1500 g/ha assuming a mixing depth of 5 cm). Application of [cyclohexyl-1-¹⁴C]-spirovamine in a solvent (acetonitrile, <170 µL) was made to the soil surface. Soil samples were lightly agitated after application to aid distribution throughout the soil and to allow solvent evaporation. Soil moisture was maintained by addition of water (every *ca*, 3 weeks).

Additional samples for each soil were treated with an equivalent amount of black solvent only to monitor microbial activity at the beginning and end of the incubation period.

2. Sampling

Duplicate samples for each soil were removed for analysis after 0, 9, 7, 14, 30, 44, 59, 80, 97 and 120 days of incubation. Untreated samples were analysed for biomass at the beginning and end of the experiment.

3. Analytical Proceedures

Soil samples were extracted four times at room temperature with acetonitrile/water/35% ammonia solution 80/20/1 v/s/v, by addition of solvent, vigorous mechanical shaking and centrifugation. Radioactivity in extracts was determined by liquid scintillation counting (LSC). Soil extracts were analysed (without concentration) by HPEC with radio detection. Degradation products were identified by comparison of the retention times of reference standards. Confirmatory analysis using an alternative technique was conducted by TLC with co-chromatography against reference items on selected samples. Degradation products were also confirmed using LCAIS on selected samples.

Volatile radioactivity in volatile traps was quantified by LSC. Carbon dioxide in the potassium hydroxide traps was confirmed by barium carbonate precipitation.

Following homogen isation, non-extractable residues (NER) in extracted soils were determined by combustion

Additionally soil extracts were separately analysed using a chiral HPLC method. This work is on-going and will be submitted in the final report for the study (currently interim) as soon as possible

4. Determination of degradation kinetics

The degradation kinetics of data within this report are subject of a separate modelling study. DT_{50} and DT_{90} values for the degradation of spiroxamine and its metabolites have been re-calculated from the



reported data following the recommendations of the FOCUS work group (FOCUS 2014²). Full details are provided in the report under point KCA 7.1.2.1.1/09 (M-763139-01-1).

II. **Results and Discussion**

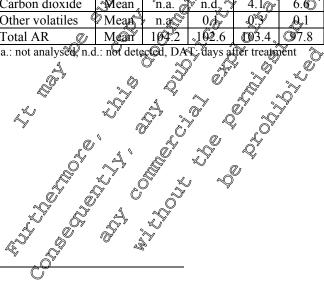
A. Data

The distribution and characterisation of radioactivity for the test soils incubated at 20°C follo plication of [cyclohexyl-1-¹⁴C]-spiroxamine are summarised in Table CA 7-1.1-2 to Table 5.

	un	der aero	odic coi	altions		q	Ŵ,	Ro [°]	k V	, × č	ĵ "O
Commonwel	Rep-			6	of Inc	ubation	time (D	AT)	$\frac{1}{\sqrt{0}}$	<i>b</i>	Ű
Compound	licate	0	3	7 "	[♥] 14, °	30,0	44~>>	59 0	89	\$ 97	×120
	Α	101.8	80.6	658	516	325	20.5	5.7	\$3.0	6.7 4	5.5
Spiroxamine	В	100.6	82.7	67.6	5 3.5	28.9		Õ16.8	10.8		° 6.Q°
	Mean	101.2	81.6	66.7	√52.6 [^]	30.7	[∞] 22.0∆	16	11.9	7 .	<u>z</u> s
M01 (spirox-	Α	1.6	6.1	/ 8.1	11.2,>	112	127	95 5	6.4	\$.0	3.5
amine desethyl)	В	1.1	4.8	8.₽	10.6	10 % 2	A.I.8	ر 9.7		§°4.1 [©]	3.4
annine desettiyi)	Mean	1.3	59.4 °	8.4	"	9	©12.0			4,62	3.4
M02 (spirox-	Α	0.8	Q4.2	6.6	8.1	10.20	8.2	6	5:0	\$3,6	2.2
amine despro-	В	0.6	4.3	6.7	8.2	87	83	0:0	3 .0	, <u>3</u> .1	2.3
pyl)	Mean	0,%	4.3∕	6,6	<u>89</u> 2	~ 9 .2	8.2	6.9	°5.0 °	[♥] 3.3	2.2
N02 (Α	n.d.	\$6.0	ð.1	∮7.2 <i>(</i>	⊳ 5.6 <i>×</i>	\$ 5.8°	* 4 <u>,</u> 9©	2,8	2.8	1.5
M03 (spirox-	B 🗞	Q1.2	© 5.1 🗞	6.7	7.2	7.0	5,9	A.	3,Ĩ	1.8	1.5
amine N-oxide)	Mean	^୭ 0.6₄	5.5 [×] & 4	69	70	63	<u>چ</u> 5.9	¥4.5	\$2.9	2.3	1.5
MOC (minut	A.	nze.	۸,Ă	1.9	A.2 .	×2.2 (€2.4	/ 4.2 N	1.0	1.7	2.0
M06 (spirox- amine acid)	B	n.d.	<u>پ</u> 1.3	1.8 *	ື 3.2 ລັ	3.8	2.4	3.6	2.1	2.8	1.9
amme aciu)	ÁMean ()"n.d.	1.4	1.8	3,20	3.0	25A	" " 9.9	1.5	2.3	2.0
Total other me-	Mean	n.d.	J.	B .6	£1.9	5.4	\$ ⁷ 1.5	ل ^ک ^{0.9}	n.d.	n.d.	n.d.
Total extracta- ble radioactivity	Mean	, 101.8	99.94	, 94.	84.0	65.3	5159	42.6	28.1	19.6	14.9
Non-extractable radioactivity	Mean	~QA	2.7	\$ ^{4.9}	97.1	10.2	©_13.7	14.0	16.1	16.2	16.6
Carbon dioxide	Mean	n.a.	» n.d.	4.1	6.	26.3	37.4	47.1	57.6	66.3	69.9
Other volatiles	Mean	n.a	0	Q.Y	Q.1	.4	0.1	0.2	0.4	0.3	0.2
Total AR	Mean	104.2	s102.6	Ø3.4 、	0 7.8	Ør02.3	103.2	103.8	102.2	102.3	101.6

Table CA 7.1.1.1-2: Degradation of [cyclohexyl-1-14C]-spiroxamme at 20°C in Long under aerobic conditions [%/AR]

n.a.: not analysed, n.d.: not detected, DAT; days after treatment



2 FOCUS (2014). Generic guidance for estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU registration. Version 1.1 (18-Dec-2014).



	un	ider aer	obic co	ndition	s [% A	RJ					a,°	
с I	Rep-				Inc	ubation	time (D	AT)				
Compound	licate	0	3	7	14	30	44	59	80	97	ُنِّ 120	0°
	Α	103.0	96.5	88.8	85.1	75.2	66.6	66.7 🦼	65.0	54.6 [@]	50 D	1
Spiroxamine	В	102.1	97.4	89.3	80.1	76.5	67.0	64.10	61.6	54.6	50,6	
	Mean	102.5	97.0	89.0	82.6	75.9	66.8	65 4	63.3	54.6 54.6	\$ 0.6	Ô
M01 (anirow	Α	0.7	1.9	3.5	4.2	6.9	7.2	£ 6.9	7.2	≫10.3 %		
M01 (spirox- amine desethyl)	В	0.0	1.9	3.0	4.6	0 .7	8.8	¢*7.3	7.1	9.87	8.0	
amme desetnyt)	Mean	0.3	1.9	3.3	4.4	[°] 6.8	8.05	7.1	J.Z	101	<u>Ø</u> .1	Ő
M02 (spirox-	Α	0.0	1.7	2.9	3.	5.5	4.7	5.8	<u>4</u> .4	G .7	07.2 Å	
amine despro-	В	0.7	1.5	3.1	3.9	3.8	° 3 ∕.5	ر م \$.9	6.3	6.4	7.0	ĺ
pyl)	Mean	0.3	1.6	3.0	\$3.5	4.7 🧖	≯ 5.1₀	5.9	≶ <u>5</u> .¥	6,6	24	
MO2 (anirow	Α	n.d.	1.3	3.3 🌾	3.20	° 2.85	4. 4 /	4.9	Ĵ.	°~3y.8	≪ Å .2	
M03 (spirox- amine N-oxide)	В	n.d.	1.2	3.10 [°]	3.8	2,7	<u>31</u>	Ø .4	@3 .4	4.0 🧸	2.3 。	
amme N-0xide)	Mean	n.d.	1.2	3.2	@ .3	ØŽ.8	Q3.8	⁰ 3.8	3.4 〇	× 3.20°	334 2017	
MOG (anirow	Α	n.d.	n.d.	M.1 🕷	[≫1.0~	≥ 3.1	4.4	2.40°	2,4	4.2	Q 7	
M06 (spirox- amine acid)	В	n.d.	n.d. 🧷	0.4~	3.00	2.6	20	3,7	Q.8	4 .2	4 .9	
amme actu)	Mean	n.d.	n.đ	Q.7×	20	~Q29	3.4	Č3.0	2.6	4.2	5.3	
Total other me-	Mean	n.d.	Q.d.	0.3	n.d.	n.d.		n.dÔ	n.d	.0.2	n.d.	
tabolites		n.u.	St.u.	6 Q	n.u.)		0.0		<u> </u>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	n.u.	
Total extracta-	Mean		101.7	Ĩ O	95.9	Ű	Ø7.6	Ŏ,	8	₩_		
ble radioactiv-		103.2	101.7	99,5	95.9	92.9	(287 .6	85.2	81.8 C) [°] 79.5	75.3	
ity		<i>b</i>		S ^O	Û	°°			<u>Č</u>			
Non-extractable	Mean	×0.5 4	2.4	3.2	4.4	4.4×	6.4	55	×.9	7.8	7.2	
radioactivity	Mas	n	02	1.6	2 .0	v ^≫7.1	9.6 §		15.2	17.8	20.5	•
Carbon dioxide	Mean	0	97.4 29.d.	1.6 n.d.				√ 12.6 [°] ^ n.d. √			20.5	-
Other volatiles	Mean	_n.a. ∩03.7°≉			≫n.d. 1049	<u>7 n.d.</u> 10 4 5	n.d.	n.d. *	0.1	0.1	0.1	
Total AR	. ≪synean	mru3./*	Խ/104. <i>2</i> %	1044	04 ❤	1 1 U41/20	10/%/6	∣ມ⊯⊿າ	103.0	105.1	103.1	1

 Table CA 7.1.1.1-3:
 Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C in Refesol-02-A soil under aerobic conditions [% AR]

 Total AR
 Mean
 Model
 <

	_0				- 0	The second se					
	Rep-			Q° ?	^O Inc	ubation	time (D	AT)			
Compound	Acate	اي 0`∛∾	3 🔍	P`7 ≪	14 🖗	30	44	59	80	97	120
Č	A 🔬	95.6®	86:30	80.4	77.9	70: 5	69.4	66.7	66.4	56.8	54.9
Spiroxamine	BÔ	9532	85.7	76.6	\$3.8	\$1.3	67.0	66.3	64.8	58.7	55.4
	Mean	\$ 3.4	`^\$6.0 ∧	78.5 🌶		[©] 71.4	68.2	66.5	65.6	57.7	55.1
.4	A	J 3.2 ~℃	[≫] 5.0 €	6.2 6.7	6.	8.1	7.3	8.9	7.7	10.4	9.7
M01 (desethyl)	B	3.20	56	<u>6</u> .7	<u>,</u> 5 9	7.9	9.2	8.7	8.2	10.2	10.7
	Mean	3.2	~5.2	6.5	6.0	8.0	8.2	8.8	7.9	10.3	10.2
<i>"</i> «	Ň		@ ⁵ .3	D″5.6 🛸	¥ 4.7	6.0	6.6	6.6	5.4	7.9	7.0
M02 (despropyl)	B	2.3	4.8	5.	5.5	5.4	6.5	5.6	5.5	7.1	6.1
, O	[∾] Mean	2.6	_5 <u>9</u> 4	55	5.1	5.7	6.5	6.1	5.4	7.5	6.5
A A	Â	5.6	× A.0	¥ .1	3.9	5.2	3.6	3.8	2.5	4.1	3.3
M03 (N-oxide)	<u>кув</u>	2.0 ₁	4.5	4.0	4.6	3.7	3.7	3.5	2.6	3.4	3.3
	Mear	1.80	4.3 *	4.1	4.3	4.4	3.6	3.7	2.6	3.7	3.3
. S 2	A	"p.g.	n.d.	0.6	3.5	1.6	1.6	1.3	2.3	2.5	3.2
M06 (acid)	B.	Kn.d.	n.d.	0.5	3.7	2.1	2.1	2.1	2.9	2.0	2.5
M06 (acid)	Mean	[≫] n.d.	n.d.	0.6	3.6	1.8	1.8	1.7	2.6	2.2	2.8
Total other me- tabolites	Mean	n.d.	n.d.	0.1	n.d.	0.9	n.d.	n.d.	n.d.	n.d.	0.4
Total extractable radioactivity	Mean	103.1	n.d.	95.2	95.4	92.2	88.4	86.8	84.1	81.5	78.4



Commound	Rep-				Inc	ubation	time (D	AT)			
Compound	licate	0	3	7	14	30	44	59	80	97	120 °
Non-extractable radioactivity	Mean	1.2	3.5	4.5	5.6	5.6	7.2	7.0	7.6	9.0	\$.8 \$
Carbon dioxide	Mean	n.a.	n.d.	1.6	3.1	5.8	7.5	9.5 '	<u>}</u> 11.2	13.7	16.3
Other volatiles	Mean	n.a.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d S	n.d.	n.d.	n.d.
Total AR	Mean	104.3	104.1	101.3	104.1	103.6	103.2	103.3	103.3	1,03.5	103.5

n.a.: not analysed, n.d.: not detected, DAT: days after treatment

n.a.: not analysed, n.d.: no	t detected, DAT: days after treatment	Ĉ4	L'AND		
		Auron .			
Table CA 7.1.1.1-5:	Degradation of [cyclohexyl-1	^{Ty} C]-spiroxa	amine at 20°C	in Speyer	6S goril
	under aerobic conditions [%	AKJ ^	¥ 6' 6¥	' <u>4</u>	l l

					-07'			<u>?</u> .C	<u>, o'</u>	, 	
Compound	Rep-				lnç	ubation	time 🍽	AT)		. «	Ś
Compound	licate	0	3	7 😽	14	30	4 4	\$ \$	~ \$ 0	≫9 7	[×] 120
	Α	98.6	94.2	91.1	\$8.9	80.2	<u></u> ØŽ.9 '	73.1	©70.2 🗸	🖌 59.4	, 55.6 °
Spiroxamine	В	99.5	93.6	م 1.7 ب	@87.3∝		∛74.2₄	72.0	69.6 ⁰	60	503
	Mean	99.1	93.9 🔊	91.4	⁷ 88.∱≫	82,0	750	72,8	69.9	59.8	\$6.0
	Α	1.7	3.10°	342	3.4	A,I	L \$.5	≴ 5.5	A.7	©7.2 (ວີ 5.7
M01 (desethyl)	В	1.9	DI V	3/3	.	\$ 3.6	@ ⁵ .3	© 5.5 ≰	5.1	5.8	6.0
	Mean	1.8	Å 3 .1	3.3	³ 3.7	3.8	5.40	5.8	4,9	<u></u> 6∜5	5.9
	Α	1.4	[∞] 2.4 ¢	2.6	2.4 ^{0°}	3.0) 2.5	307	Å.	3.5	3.0	4.1
M02 (despropyl)	В	1,25	23	3.0	267	2.5	<u>\$</u> .2	3.7	°3.5 ≥	🖌 5.7	3.6
	Mean	¥Å.	¢ 2.3	2.8	£ 2.5	3.0 🖌	3.5	9 4.1 ₀	3.5	5.3	3.9
	А	©1.4 ($\frac{2.1}{2.1}$	2.4	1.7	3.4	2;	3.0/	29	4.3	4.3
M03 (N-oxide)	B 🌾	1.0	2.1 🖗	2,3	2,6/	nQt.	3.8	×3.0	2.3	3.3	3.7
	Mean	1.Q**	22	<u>D</u> 3	@ .2	Q.7	\$~3.2 _€	3.0 %	₽ 2.6	3.8	4.0
	X	n.d.	n.d.	©0.3 ू	S 1.5 🕺		3.30	2.4√	3.1	3.4	4.1
M06 (acid)	B A	∮n.d _^	≫n.d, ∧	0.4	140	3,00	4.3	Z,5	2.8	3.5	4.3
é	Mean	n.d	n.d.	Ø.3 ¹	Ĩ.	<u>3</u> r3	Ø .8	\$ 2.9	2.9	3.5	4.2
Total other me-O tabolites	Mean	. Dd.	Q.d.	\$0.7	0.6) n.d.	n.d	0.3	n.d.	n.d.	0.1
Total extractable radioactivity	Mean	103 4	101	\$ <u>~</u>	98.6	9 9 .5	. 9 9 .8	88.4	83.8	78.9	74.1
Non-extractable radioactivity	Mean		\$2.1	² .6 2.6	∀ 3.5¢	3.6	5.2	4.6	5.8	7.8	7.4
Carbon dioxide	Mean	n.a.	n.d k	0,60	1.6	66	7.5	10.0	14.2	17.3	17.6
Other volatiles	Mean	n a.	p.e.	în≱d.	19.d.	A.d.	0.1	n.d.	n.d.	0.1	0.1
Total AR	Mean	194.3	°4\$04.1∧	\$ 04.1%		103.1	103.7	103.1	103.8	104.1	99.2

n.a.: not analysed, n.d.: not detected, DAT. days after treatment ŵ

B. Material Balance, 🤇

Mass balances ranged from 101.6 to 1040, 103 b to 105.1, 101.3 to 104.3 and 99.2 to 104.3% AR for the Longwoods, Refesol 2-A, Refesol 3-G and Speyer 6S soils, respectively.

C. Extractable and Non-Expactable Residues

Extractable adioactivity declined most significantly in the Longwoods soil. For this soil extractable radioactivity decreased from 100.8% AR at DAT 0 to 14.9% AR by DAT 120. Non-extractable residues (NER) for the bongwoods soft increased from 0.4% AR at DAT 0 to 16.9% AR by DAT 120. Further investigation of NER showed the majority of the applied radioactivity associated with the humin fraction 🄊 Å Ô

Extracta Re radioactivity for the three remaining soils declined more steadily and comprised 103.2, 103.1 and 103.4% AR at DAT 0 and declined to 75.3, 78.4 and 74.1% AR by DAT 120 for the Refesol-02-A, Refesol-03-G and Speyer 6S soils, respectively. Non-extractable residues (NER) for these soils increased from 0.5, 1.2 and 0.9% AR at DAT 0 to maximums of 7.8, 9.0 and 7.8% AR at



DAT 97 and then declined to 7.2, 8.8 and 7.4% AR by DAT 120, respectively.

D. Volatile Radioactivity

Levels of ¹⁴C-carbon dioxide formed in the Longwoods soil increased during incubation to 69.2% AR by DAT 120. Levels of ¹⁴C-carbon dioxide formed for the three remaining soils ranged from 16.3 to 20.3% AR by DAT 120. Other volatile radioactivity was $\leq 0.4\%$ AR for all soils at all time points.

E. Degradation of Parent Compound

Following application of [cyclohexyl-1-¹⁴C]-spiroxamine the amount of parent in the soil extracts of the Longwoods soil decreased from 101.2% AR at DAT 0 to 5.8% AR by the end of the study at DAT 120. The amount of parent in the soil extracts of the Refesol Q2-A, Refesol 93-G and Spoyer 6% soils decreased from 102.2, 95.4 and 99.1% AR at DAT 0 to 50.6, \$5.1 and 56.0% AR by the end of the study at DAT 120.

Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine was accompanied by the formation of the degradation products M01 (spiroxamine-desethyl), M02 (spiroxamine-desproper), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid). M01 was detected at a maximum of 12.0% AR at DAT 44 in the Longwoods soil and maximums ranging from 6.5 to 10.3% AR at DAT 97 in the other soils. M02 was detected at a maximum of 9.2% AR at DAT 30 in the Longwoods soil and maximums fanging from 5.3 to 75% AR around DAT 97-120 in the other soils M03 was detected at a maximum of 7.2% AR at DAT 14 in the Longwoods soil and maximums of 7.2% AR at DAT 14 in the Longwoods soil and maximum of 7.2% AR at DAT 14 in the Longwoods soil and maximum of 7.2% AR at DAT 14 in the Longwoods soil and maximum of 7.2% AR at DAT 14 in the Longwoods soil and maximum of 3.9% AR at DAT 59 in the Longwoods soil and maximums ranging from 3.6 to 5.3% AR between at DAT 14-120 in the other soils. Some other metabolites were detected typically <1% AR but all \$5% AR

F. Degradation Kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.1.2.1.1/09 (M-763 ϕ 9-01-1).

G. Isomers of Parent Compound

Additional work is being conducted on the chiral analysis of the samples for parent spiroxamine. This work will provide the quantified amounts of each individual isomer of spiroxamine in all samples. This work will be submitted in the final report of this study (currently the is interim) as soon as possible.

 \bigcirc

M. Conclusions

Spiroxamine degraded in soil under derobic conditions (20°C, pF 2) with 5.8% of applied radioactivity remaining as parent compound in the Longwoods soil at DAT 120 and with 50.6 to 56.0% of applied radioactivity remaining as parent compound in the other three soils. The amounts of unextractable radioactivity for creased to 16.9% AR by DAT 120 in one soil but remained <10% AR in the other three soils. Mineralisation to carbon dioxide was a mator pathway, steadily increasing to 69.9% AR in one soil and comprised 16.3 to 20.3% AR in the other three soils. No significant levels of organic volatiles were observed. The metabolic pathways involved de alkylation of the amine moiety to form metabolites: M01 (spiroxamine-desethyl, maximum 12.0% AR) and M02 (spiroxamine-despropyl, maximum 9.2% AR); oxidation of the amine moiety to form metabolite M03 (spiroxamine-N-oxide, maximum 7.2% AR); oxidation of a methyl group to form M00 (spiroxamine-acid, maximum 5.3% AR).

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in the report presented under point KCA 7.1.2.1.1/09 ($\underline{M-763139-01-1}$).



Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) OECD 307 (required guideline). The study is consi ered valid to assess the aerobic degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in soil.

Existing studies, previously evaluated

ered valid to assess the a	erobic degradation of [cyclohexyl-1- ¹⁴ C]-spiroxamine in soil.
Existing studies, previo	usly evaluated
Data Point:	KCA 7.1.1.1/01
Report Author:	
Report Year:	
Report Title:	Aerobic degradation of KWG 4168 in BBA soil 2.2 0 A
Report No:	PF4027
Document No:	<u>M-006135-01-1</u>
Guideline(s) followed in	BBA: Part IV, 4, 18BA Part IV, 4-1
study:	
Deviations from current	Yes (refer befow) Some min@ deviation(s) not relevant for the reliability of the study (described in study summary)
test guideline:	Some min@ deviation(s) not relevant for the reliability of the study (described in
	study supprinary) "
Previous evaluation:	ves, evaluated and accepted a the second sec
	DAR (1997), RAR (2010), BAR (2017)
GLP/Officially recog-	DAR (1997), RAR (2010), RAR (2017) Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q

Executive Summary

The route and rate addegradation of spiro samine was investigated in one European soil (BBA 2.2, loamy sand) under laboratory verobic conditions. Sold samples (100 g dw) were treated with [cyclohexyl-1-¹⁴C]-spiroxamine (radiochemical purity >99%) at an application rate of 0.766 mg/kg soil dry weight (equivalent to 575 g ha assuming 5 cm depth and 1.50 cm³ Soil depsity) and incubated (20°C, 40% MWHC) for 100 days in the dark

Single treated sample overe to noved for analysis after 0, 4, 3*, 9, 14*, 30*, 59 and 100* days of incubation (except for intervalsmarked* when duplicate samples avere taken). Soil samples were extracted three times at room temperature and er agitation using acetopitrile for 30 minutes, and once using water. Soil extracts were analyzed, without concentration, primarily by normal phase TLC. Confirmatory analysis was conducted by reverse-phase TLC.

The material balances ranged from 994 to 101.5% of applied radioactivity (% AR). The amounts of unextractable radioactivity increased to 18.5% AR by DAT 100. No significant levels of organic volatiles were observed. Mineralisation to carbon dioxide was a major pathway, steadily increasing throughout the study, and accounted for 29.9% of by OAT 100.

After 100 days probic degradation, spiroxamine degraded to 40.1% AR. A DT₅₀ value for the degradation of spiroxanine was calculated in the report, however, a re-evaluation of the degradation kinetics in accordance with FQCUS midance document on degradation kinetics (2014), was performed in the report presented upder point KCA 7.1.2.1.1/09 (M-763139-01-1).

Two major metabolites were observed formed by de-alkylation of the amine moiety: M01 (spiroxaminedesetsyl, maximum 5.6% AR); M02 (spiroxamine-despropyl, maximum 5.6% AR). Additional minor metabolites observed were M03 (spiroxamine-N-oxide, maximum 3.3% of AR); M06 (spiroxamineacid, maximum 3.5% AR). No other metabolites were observed >1.8% AR.



I. **Materials and Methods**

A. Materials

1. Test Items

[cyclohexyl-1-¹⁴C]-spiroxamine

^{*} Denotes position of 2.59 MBang >99% 491 at

2. Test Soil

Specific Activity:

Radiochemical Purity:

.1 6. No soil history is The study was performed using one test soil as the available.

Table CA 7.1.1.1-6:	Physico-chemical	properties	of test	soft
	T hysico chemica	bi ob ci cico	- Contraction	SX.

	<i>\\</i>	
Parameter 🔍	Q	Sol & Sol
Soil Designation		BBA 2.2
Geographic Location		Spexer, Rhinehand-Papatinate
City		A ^N AV ANDEVEL NIIIIEIAIIU-FASALIIIAIE
Geographic Location City Country Textural Classification (USDA) Sand [50 - 2000 µm] Silt [2 - 50 µm]		Contrary and Contr
Textural Classification (USDA)		Loamy sand
Sand [50 - 2000 am]	(%)	N 3 3 0 890
Silt [2 – 50 μm 0 0 0		۲ <u>ک</u> <u>۲</u> 13.0
Clay $[< 2 \mu m]$ O^{*} \checkmark O	(%) *	13.0 13.0 13.0 13.0 13.0 13.0 13.0
pH N N		
in H ₂ QQT:1)	L. L.	6.3 4 4 4 5 5.5
Clay [< 2 µm] 0 4 6 pH 7 7 in H ₂ QQT:1) in 0.01M CaCl ₂ (1:40 4 7	′_~°	\$\$ \$\$ \$\$ 5.5
pH in H ₂ QQU:1) in 0.01M CaCl ₂ (1:40 Organic Matter (%) Organic Carbon (%)*		2.15 2.15 1.25
Organic Carbog (%)* O		1.25
Cation Exchange Capacity (preq/100)	() Q	10.0 No.
Maximum Water Holding Capacity (g	Ho per	17.67
100g dressoil)	, Å	
Cation Exchange Capacity (meq/100) Maximum Water Holding Capacity (g 100g dr soil) Soil Microbial Biomass (mg organice Initial untreated (0 DAT)	(kg s@A)	10.0 17.67 256 211
Initial, untreated (0 DAT)		256 J
Final, untreated (100 DAT)	ça ça	_
Initial, untreated (100 DAT)		201

* Calculated by multiplying organic carbon content by 1.724 (not reported)

B. Study Design

1. Experimental Conditions

Tests were performed in sealed static systems consisting of glass flasks each containing 100 g soil with solid traps of oil-coated (2% paraffin oil in hexane) quartz glass wool for sorption of volatile organic compounds and soda lime for absorption of evolved carbon dioxide.

The study was conducted at a concentration of approximately 0.766 mg/kg dry weight of soil. The test



concentration was based on a field rate of 750 g a.s./ha assuming 10 cm soil depth and 1.0 g/cm³ soil density (note - this is equivalent to a field rate of 575 g a.s./ha, assuming a mixing depth of 5 cm and a soil density of 1.5 g/cm³). Application of the re-purified [cyclohexyl-1-¹⁴C]-spiroxamine in solvent acetonitrile) was made to a subsample of soil, which was then added to the bulk soil and mixed thorage hly after solvent evaporation, for 1.5 hours before use in the experiment. After mixing, samples 100 g dry weight equivalent of soil was weighed into incubation vessels. Soil moisture was adjusted at 40% MWHC, at the time of application (i.e. no pre-acclimatisation), and maintained during inerbation with periodic additions of water (30 days). The soil samples were incubated at a temperature of 20° under aerobic conditions.

Two untreated samples were incubated alongside test systems at under the same conditions to monitor microbial activity at the beginning and end of the study.

2. Sampling

Prior to opening the sealed static incubation vessels other for sampling or maintenance of moisture, possibly volatile components were flushed into the trap attachment by introducing water saturated air (10 mins). Single treated samples were removed for analysis after 0, 1, 3*, 7, 14*, 30*, 59 and 100* days of incubation (except for intervals marked * when duplicate samples were taken).

Untreated microbial biomass samples were analysed at the beginning and end of the experiment. Additionally, the biomass in treated soil was analysed at the end of the experiments

3. Analytical Procedures

Soil samples were extracted three times at toom temperature under agitation using aceonitrile and once using water (30 mins each), Liquid extracts were separated by centrifugation, filtered and radio-assayed by Liquid Scintillation Counting (LSC) directly. Extracted soil debris and filter papers were air-dried and analysed by combustion LSC. Ô

C against reference standards using two meth-Aliquots of combined soil extracts were analysed by TL ods: Ô \bigcirc

- Normal phase Silica gel plates and an acetonitrile water: 25% aromonia (80:18:2, v/v/v) solvent system

- Reverse phase: RP018 plates with two solvent systems (used sequentially in 1 dimension):

hexane:dictioromenane propyl alcompl:25% ammonia (30:70:10:2, v/v/v/v) and a satunated tank system (developed until solvent front at 14 cm)

ii) chloroform:ethyl alcohol (50.50 v/v) and arQunsaturated tank system (developed until solvent Ċ front at 7°cm)

The TLC plates were evaluated using a mear analyser to determine the quantities of radiolabelled test substance and its degradation products Ľ

Volatile adioactivity in volatile traps was determined by LSC (organic volatiles were extracted using ethyl acetate and aliquots quantified by LSC; ¹⁴CO₂ was liberated from soda lime through addition of 18% (w/w) hydrochloric and absorbed by a suitable cocktail and quantified by LSC).

4. Determination of degradation kinetics

The degradation kinetics of data within this report are subject of a separate modelling study. DT₅₀ and DT₉₀ values for the degradation of spiroxamine and its metabolites have been re-calculated from the reported data following the reported data following the reported data following the reported data following the reported data for th are provided up in the report under point KCA 7.1.2.1.1/09 (M-763139-01-1).

II. **Results and Discussion**

A. Data

The distribution and characterisation of radioactivity for the test soil incubated at 20°C following application of [¹⁴C]-spiroxamine are summarized in Table CA 7.1.1.1-7. Mean values are used for replicate



ð

samples.

	condition			Jxamme	III DDA	2.2 SUII à	.u 20 € u	liuer aer	S S	F
	D I /	Incubation time (DAT)]	
Compound	Replicate	0	1	3	7	14	30	5.9		
	А	89.4	88.5	85.1	78.9	74.2	58.3	×48.8 ×	¢¥0.5 🔬	Ş.
Spiroxamine	В	-	-	83.8	þ -	72,3	61.7	× - ^	40	_
	Mean	89.4	88.5	84,5	78.9	A3.3	60.0	48.8	40.3	Ó
	А	n.d.	0.7	. ACĂ	2.3	✓ 4.1 °	40	5.2	° ⁰ 5.4	×
M01 (spirox- amine-desethyl)	В	-	-	o ⁻¹ .7		3	Q.3	6 ⁷ - &	5.6	
unine desetilyi)	Mean	n.d.	0.7	1,6.	203	8.9	▶ 5.0	7.2	<u>s</u> a i	
M02 (spirox-	Α	n.d.	n.d	Ø .6	×1.1	2.50	3,55	5.2	5.4	_
amine-despro-	В	-	A	@`0.7_@		2.0	~ -	ó ^v - ₂ 0	⁹ 5.6	
pyl)	Mean	n.d. 🦼	n.d	0.7	۵) ا	2.6 👡	Q [™] 3.5≪	5.2 \$	\$5	
MO2 (minor	Α	n.d	0,7×	L.1	×1.5 🔬	D 1.9	46	Q.9	© 1.6	
M03 (spirox- amine-N-oxide)	В			\$ ⁷ 1.5		139	<u>\$</u> 2.0	Ç - Q	1.8	
	Mean	-@j.d. ⊘	0.7	13,	A9.5	01.9	° 3.3	1:25	1.7	
	A	0 n.d.∜	n.do	ard.	Ø0.8 Č	¥ 1.6℃	25	\$3.5	3.1	
M06 (spirox- amine-acid)	В	4		n.d.	× -L	<u>,1</u> .3	<u>گ</u> 2.9	° -	3.1	
unine uera)	Mean	On.d.	∑n.d. n≪a	n.d.	0.8	~\$1.6	× 2.6	3.5	3.1	
Unknown	Mean 🚄	1.0	nat	@.d.	∂ [©] n.d. _©	n.d.	8	0.3	0.4	
Total extracta- ble radioactiv- ity	Mean a grant and a grant a gra	20.4 X	©89.9 < >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>	88.0	84.6	83.2	76.1	66.9	59.1	
Non-extractable residue ^A	De Mean	Š	£ 00.5	¢12.0	12	13.0	14.8	17.0	18.5	
¹⁴ C-Carbon & oxide incluiding other votatiles ^B	Mean (n.a	0.7		2.8 2.8	¥ 4.9	9.0	15.2	21.9	
Total radioac- tivity	Mean	2900.0°		100.5	100.0	101.1	99.9	99.1	99.5	

Table CA 7.1.1.1-7:	Degradation of [¹⁴ C]-spiroxamine in BBA 2.2 soil at 20°C under	aerobje	6
	conditions [% AR]	1 A	

n.a.: not analysed, n.d.: not retected DAT: days after treatment, LOD, 0.1% AR All values expressed as percentage of applied radioactivity. (% AR)

- Value includes recovery from paper filters used in contribugation of extracts А
- Other valatile radioactivity was 50.1% AR В

B. Material Balance

O Recoveries of initial radioactivity range@from 99.1 to 101.5%. Values presented are % of initial recovery at time = 0 rather than % applied radioactivity. This is not considered to have had any impact on the 0 Ø study conclusions. 4 L.

C. Extractable and Non Extractable Residues

Total extractable radioactivity decreased from 90.4% AR at 0 DAT to 59.1% AR by DAT 100. The total of non-extractable residues (NER) increased from 9.6% AR at DAT 0 to 18.5% AR by the end of the study) (DAT 100). Š

D. Volatie Radioactivity

Levels of ¹⁴C-carbon dioxide formed increased to 21.9% AR by DAT 100. Other volatile radioactivity was < 0.1% AR at all timepoints.



E. Degradation of Parent Compound

Following application of [¹⁴C]-spiroxamine in BBA 2.2 soil, the amount of parent in the total soil@xtracts decreased from a maximum of 89.4% at 0 DAT to 40.1% AR by 100 DAT. In addition to parent & material, two major metabolites were observed. M01 (spiroxamine-desethyl) increased over the course of the incubation period, and accounted for a maximum of 8.1% of applied radioactivity at 400 DAP. M02 (spiroxamine-despropyl) was detected at a maximum of 5.6% of applied radioactivity at 100 DAT. Other metabolites observed were: M03 (spiroxamine-N-oxide) was detected at a maximum of 23% of applied radioactivity at DAT 30 and declined to 1.7% AP by DAT 100 M06 (spiroxamine-avid) was detected at a maximum of 3.5% of applied radioactivity at DAT 5 and declined to 3 A R by DAT 100. No other metabolites were observed >1.8% AR.

F. Degradation kinetics

Srt presented under point 45 Degradation rates determined in the report are superseded by the 7.1.2.1.1/09 (M-763139-01-1). K,

Conclusions III. «

Spiroxamine degraded in BBA 2.2 soils under serobic conditions at 20°C, with 40/1% of the applied radioactivity remaining as parent compound after 100 days. The amounts of unexpactable radioactivity increased to 18.5% AR by DAT 100, Do significant evels of organic volatiles were observed throughout the study. Mineralisation to carbon dioxide was a major pathway, steadily increasing throughout the study, and accounted for 21.9% AR by PAT 100. The primary metabolic pathway involved de-alkylation of the amine moiety to form two major metabolites MOR (spiroxamine-desethyl, maximum 8.1% AR) and M02 (spiroxamine desproppi, maximum 5.6% AR). Additional minor metabolites observed were M03 (spiroxamine-Noxide maximum 3.3% of AR) and M06 (spiroxamine-acid, maximum 3.5% AR).

A re-evaluation of the degradation Kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed by the report presented under point KCA 7, 1.2.1.1/09 (M-763139-01-<u>1</u>).

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013

The study was conducted to study guideline(s) BBA: Part IV, 4-1 (similar to current required guideline, with only minoralifferences). The study is considered valid to assess the aerobic degradation of [cy-

At which and a start of the sta



Data Point:	KCA 7.1.1.1/02
Report Author:	
Report Year:	1995
Report Title:	Aerobic degradation and metabolism of KWG 4168 in soil
Report No:	PF4034
Document No:	<u>M-006141-01-1</u>
Guideline(s) followed in study:	BBA: Part IV, 4-1
Deviations from current test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the refability of the midy (described in study summary)
Previous evaluation:	DAR (1997), RAR (2010) RAR (2017) The degradation rates of spiroxamine (1997), and (2008)) were included in the following survey (1997) and (2008)) were
GLP/Officially recog-	
nised testing facilities:	Yes, conducted under GLP Officially recognised lesting facilities
Acceptability/Reliability:	Yes y y y y y y y y

Executive Summary

The route and rate of degradation of spiroxamine was investigated in two European and one US soil (Laacherhof/silt loam, Monheim 3/sardy loam and Howe/sandy loam, respectively) under laboratory aerobic conditions. Soil samples (100 g dry weight) were treated with [cyclohexyl-1-CC]-spiroxamine (radiochemical purity >99%) at an application rate of 0.5mg/kg soil (courselent to 375 g a.s./ha assuming 5 cm soil depth and 1.5 g/cm³ soil density) and incubated at 20°C and $\geq 40\%$ Maximum Water Holding Capacity, MWHC (except \downarrow S soil incubated at 20°C and $\geq 40\%$ Maximum Water Holding Capacity, MWHC (except \downarrow S soil incubated at 20°C and $\geq 40\%$ MWHC) for 100 days in the dark.

Duplicate (Laacherbor) of singlicate (Monheim 3 and Howe) samples were removed for analysis after 0, 1, 3, 7, 14, 30,60, and 100 days of incubation. Solf samples were extracted three times at room temperature under agitation using acetonitrile of 30 minutes, and once under reflux for 6 hours, also using acetonitrile. Liquid extracts were radio-assayed by Liquid Scmtillation Counting (LSC) directly. Extracted soil debris was at dried and analysed by combustion LSC Liquid extracts were analysed and quantified by normal phase TC and quantitatively confirmed by reverse-phase HPLC (selected samples). Metabolite identity was also confirmed by reverse-phase HPLC (selected samples).

The material balances ranged from 94.8 to 98.0% AR in Laacherhof soil, 95.0 to 97.5% AR in Monheim 3 soil and 93.6 to 90.5% AR in Howe soil. Levels of NER increased to maximum levels of 17.0 to 23.9% AR by DAT 30-100 and Subsequently declined in some soils. Mineralization to carbon dioxide was a major pathway, demonstrated by the high amount of radioactivity recovered in the volatile traps for all soils (maximum of 44.6% AR in Laacherhof, 30.5% AR in Monheim 3 and 35.2% AR for Howe by the end of the study). No significant levels of organic volatiles were observed.

After 100 days incubation at 20 °C, [1 C]-spiroxamine degraded to 14.3% of the radioactivity applied in Laacherhof soil, to 22.4% in Monheim 3 soil, and to 24.9% in Howe soil. A re-evaluation of the degradation kinetics in accordance with FOCLS guidance document on degradation kinetics (2014) was performed in the report presented under point KCA 7.1.2.1.1/09 (<u>M-763139-01-1</u>).

The primary metabolic pathway involved de-alkylation of the amine moiety to form two major metabolites M01 (piroxanine-desproyl) maximum 8.8% of AR in Monheim 3 soil) and M02 (spiroxamine-desproyl) maximum 5.8% AR in Monheim 3 soil). Additional minor metabolites observed were M03 (spiroxanine-N-oxide, maximum 2.5% AR in Laacherhof soil only) M06 (spiroxamine-acid, maximum 1.6% of AR in Laacherhof soil) and M07 (spiroxamine-hydroxy acid, maximum 0.2% AR in Laacherhof soil).



I. **Materials and Methods**

A. Materials

1. Test Items

Table CA 7.1.1.1-8:	Physico-chemical	properties of	testsoil
---------------------	------------------	---------------	----------

A. Materials			° r
l. Test Items			
[cyclohexyl-1-14C]-spiroxamine			
		O"	
A. Materials I. Test Items [cyclohexyl-1- ¹⁴ C]-spiroxamine Specific Activity: Radiochemical Purity: 2. Test Soil The study was performed using three s available. Table CA 7.1.1.1-8: Physico-chemical Parameter Soil Designation Geographic Location City Country Textural Classification (USDA) Sand [50 - 2000 μ m] (%) Silt [2 - 50 μ m] (%)	+ (*)	N N	
	* Denotes position of	[¹⁴ C]madiolabel	
Specific Activity	2 59 MBaying		
Radiochemical Purity:	>99% (MPL C)		
Radioenenieur Funty.			' & A L'
Tost Soil		S A O	
The study was performed using three	test soils as characteriz	ed in Fable OA 7.187.	1-8. No soil history
	8 8 D		
Cable CA 7.1.1.1-8: Physico-Chemical	ical properties of test	wil Q ⁴ ⁷ 7	
Parameter 🖏 🐇		Soil 2	<u>~</u>
Soil Designation	& Karacherhof	Monheim 3	Howe
Geographic Location			
City		^O M ⊚ heim √	Howe
Country	German	German	Indiana, USA
Textural Classification (USDA)	Silt Joan	Sandy	Sandy loam
Sand [50 - 2000 µm] (%) O	6.9	58.2	65.5
Silt $[2 - 500 \text{ gm}]$ (%)	A 5751.1 8 0	31.0	26.3
Silt [2 – 50 g m] (%) Clay [< 2 m] (%) pH in H ₂ O (1:1)		10.8	8.2
DH A A A		3 Y	
in H ₂ O (1:1)	\$ 8.1 O [*]	e.5	7.1
in H ₂ O (1:1) in CaCl ₂ (1:1) Organic Matter (%) * \bigcirc	× 72, ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	6.3	6.8
Organic Matter (%) *	<u> </u>		1.87
Organic Carbon (%)	2 0.9 0°	1.98	1.09
Cation Exchange Capacity (meg 100 g)	<u> </u>	10.0	10.0
Water Holding Capacity (g HoO per 190 dry goll)	0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9 0.9		
40% of maximum		16.6	11.3
750/ - 61/21		-	13.7
	- × -	-	13.7
Soil Microbia Biomas (mor /kg soil)	¢.		
Soil Microbian Biomass (mgC/kg soil)		257	285
Soil Microbia Biomass (mcC/kg soil) Initial, unfreated CDAT	307	257 202	285 250
Soil Microbia Biomass (mgC/kg soil)		257 202 246	285 250 347

* Calculated by multiplying organic carbon content by 1.724 (not reported)



B. Study Design

1. Experimental Conditions

Tests were performed in sealed static systems consisting of glass flasks each containing 100 g sont (dryweight) with solid traps of oil-coated (2% paraffin oil in hexane) quartz glass wool for sorption of ganic volatiles and soda lime for adsorption of evolved carbon dioxide.

The study was conducted at a concentration of approximately 0.5 mg/kg dry weight of foil. The test concentration was based on a field rate of 750 g a.s./ha assuming a 10 cm soil depth and 1.5 g/cm³ soil density (note – this is equivalent to 375 g a.s./ha assuming 5 cm soil depth and 1.5 g/cm³ soil density). Application of [¹⁴C]-spiroxamine, dissolved in acetonitrile/triethylamine (100/0.5 v/v), was made to a 0 subsample of each soil, which was then added to the fulk soil and poxed thoroughly, after solvent evap oration, for 2 hours before use in the experiment. After mixing, 100 g dry weight equivalent of soil vas weighed into incubation vessels. Soil moisture was adjusted to 40% MWHC at the time of application i.e. no pre-acclimatisation (75% of 1/3 bar for Howe soil, equivalent to 48% MWHC) and maintained at this level during incubation with periodic additions of vater (30 days). The soil samples were incubated at a temperature of $20 \pm 2^{\circ}$ C under actions.

Additional samples in Laacherhof soil treated with 10 and 400 for increased application rates were prepared with 500 g soil and incubated under the same conditions as test vessels only for use in identification of parent spiroxamine and metabolities.

Two treated (applied at the same rate) and two untreated son samples were incobated alongside test systems under the same conditions to monitor microbial activity at the beginning and end of the study.

2. Sampling

Prior to opening the sealed static incubation ressels, either for sampling or manitenance of moisture, possibly volatile components were thished into the trap attachment by introducing water saturated air (10 mins). Test samples (duplicates for Latcherhof soil, single samples for Monheim 3 and Howe soils) were removed for malysis after 0, 1, 3, 0, 14, 30, 60 and 100 days of incubation.

Treated and untreated pricrobial biomass samples were analysed at the beginning and end of the experiment for each soil.

3. Analytical Procedures

Soil samples were extracted three times at room temperature under agitation with acetonitrile for 30 minutes. Liquid extracts were radio-assaved by Liquid Scintillation Counting (LSC) directly. Extracted soil debris was an dried and analysed by combustion LSC Soil NER was further refluxed for 6 hours with acetonitrile and quantified by LSC separately

The combined room temperature soil expracts were analysed (without any prior work-up or concentration) by TFC against reference standards using the main primary (normal phase) method below:

- Silica gel plates and an acetonitrile water 25% ammonia (either i) 320:18:2, v/v/v or ii) 80:18:2, $\sqrt[4]{v/v/v}$ solvent system $\sqrt[6]{v/v/v}$

Quantitative confirmatory analysis was conducted using the following reverse phase TLC method:

- RP-16 plates with two solvent systems (used sequentially in 1 dimension):
 - n-hexane.dichloromethane:2-propyl alcohol:25% ammonia (30:70:10:2, v/v/v) and a saturated tank system (developed until solvent front at 14 cm)
- $\sqrt{}$ choroform ethyl alcohol (50:50 v/v) and an unsaturated tank system (developed until solvent front at 6 cm)

The NER reflux extracts were analysed separately, however, the methodology used is unclear.

The TLC plates were evaluated using a linear analyser to determine the quantities of radiolabelled test



substance and its degradation products. Confirmatory analysis of soil extracts to determine parent spiroxamine levels was also conducted by reverse-phase HPLC against reference standards with a LiChrosphere 100 RP-18 column and mobile phase of 20% water (with 0.09% o-phosphoric acid and \$3% triethylamine) and 80% acetonitrile (isocratic).

Additional soil samples, treated at x10 and x100 application rates, were analysed as follows:

- for isolation of metabolites M01 and M02: soil samples treated at the x10 rate were expected with acetonitrile after DAT 69 and 71, respectively. Soil extracts were concentrated under vace uum and analysed using the normal phase TLC pronary analytical method using solvent system i). The radioactive substance corresponding to the reference standards were extracted from the silica gel with acetonitrile.
- for isolation of metabolites M03 and M06 poil samples treated in the 2000 rate were extracted with acetonitrile after DAT 16 and 10, respectively. Soil expacts were concentrated (servent evaporated at ambient temperature) and analysed using the normal phase ALC primary analytical method using solvent system ii). The radioactive subvance corresponding to the reference standards were extracted from the silica gel with acetomerile (plus methanol) and emanolatespectively.

The isolates above were then analysee by GC MS against authentie reference standards to confirm metabolite identity and structure.

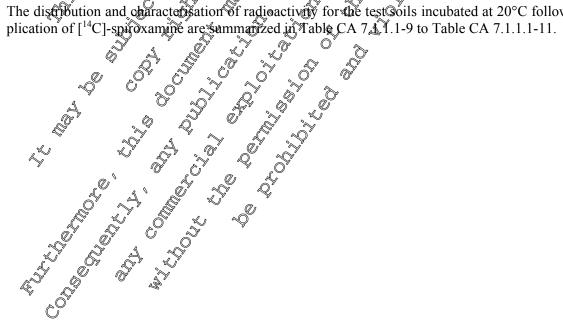
Volatile radioactivity in volatile traps was extracted using ethyl acethe and aliquots quantified by LSC. ¹⁴CO₂ was liberated from sode time through addition of 18% (w/w/hydrochlori@acid and absorbed by a suitable cocktail and quantified by LSC Identity of ¹⁴₄CO₂ was further confirmed by conversion to ¹⁴C]-benzoic acid by means of the Griggard reaction. Ċ

4. Determination of degradation kinetics

The degradation kingings of data within this reperir are subject of a separate modelling study. DT₅₀ and DT₉₀ values for the degradation of spiroxamine and is metabolites have been re-calculated from the reported data following the recommendations of the FOCUS work group (FOCUS 2014²). Full details are provided in the provided in the provided point KCA 7.12.1.1/0 (<u>M-33139-01-1</u>).

, Results and Discussion

The distribution and characterisation of radioactivery for the testooils incubated at 20°C following ap-





C	ondition	is [% AF	k j						Ø)°	
	Repli-			In	cubation	time (DA	.T)		- Contraction of the second se	S
Compound	cate	0	1	3	7	14	39	60) 100	0*
	Α	75.3	71.3	67.8	61.1	47.8	#1.0	28.1 🖗	150	
Spiroxamine	В	76.3	72.2	66.5	60.2	52.2	41.5	2	A.3	Ô
	Mean	75.8	71.8	67.2	60.7	50 0	41.3	_°2¥8.8_°	¥14.7	j"
	Α	0.5	1.4	2.9	4.4	ŢĹŽ	6.0	7.3	7,2	L.
M01 (spiroxamine-de- sethyl)	В	0.7	1.4	2.9	4.3	Ő Š .7	6.1	60	Ø.0	O'
settiyi)	Mean	0.6	1.4	<u>2</u> .9	4.4 <i>"</i> Q	6.5 °	¢.)	7.0	° 7.1 °	1 V
	Α	0.4	1.0 🗸	1.9	2.7	<u>_</u> \$6	\$.9 ∖	O″4.9©	5.0	
M02 (spiroxamine- despropyl)	В	0.7	1.0	læ§°	<u>3.8</u>	ير 3.6	3.80	4.3	\$5 .7	
despropyry	Mean	0.6	1.9	× 9.9	2.8	3:60	309	£4.6 A	ء , 5.7	
	Α	0.7	<u>,</u> 9.8 ∽	0°1.4	1.78	2.4	£\$2.1	0 ⁻ 1.8	18	
M03 (spiroxamine-N-ox-ide)	В	0.8	0.9	13	P.7	\$ 2.5 °	1.8	k]	¥.9	
	Mean	0.80	0.9	,≪¥.4 , , (¢1.7 👟	2.5	26	A.8	© _{1.9}	
	Α	40 .1	00.2	∀ [™] 1.1 [≪]	1.6/	<u>~</u> 2	<u>کُ</u> 1.0	0.6	0.7	
M06 (spiroxamine-acid)	В	₹0.1 ¢		10	<u>6</u> 6	⁰ 1.6	0.50	0.3	0.7	
	Mean	n.ð.	0.2	Ø ř .1 ,	¢ 1.6	1,4	Ì.	0 .5	0.7	
M11 (A	\$0 .1	×0.1	<0.↓ _⊘	0.1	×9.1	Q0.1	0.1	< 0.1	
M11 (spiroxamine-de- sethyl acid)	₅ _≫ B	Q.1 ¢	-<0,£ x0,£ x0,1,5 x0,1,5	< 0 ,1	0.1	€0.1~€	0.2	0.1	< 0.1	
settiyi deld)	Mean	n.¢	ŋŋd.	SH.d. 🔪	0.1%	n.d.	S OF	0.1	n.d.	
Ambient extract	_0"	J.7	@75.2 _	74.3	71.2	63.9	\$4.0	42.6	30.0	
Total extractable radioac- tivity	ó ^s - ż	977.7 ²	7 5 .2	\$29.3	371.2 ¢	\$ 63.9 *	54.0	42.6	30.0	
Non-extractable Padioac tivity (including refluto	\$ \$	0 © ^{17.1}	20.6	1954	29.6	×J2.1	26.3	22.9	20.2	
and filter papers) A				~ ×		<i>b</i> r				
Reflux extract	- 5	2:9	8 .7	6 x	<u>* 6.70</u> ″	6.7	7.7	4.9	1.9	
¹⁴ C-Carbon dioxide in cluding other volations ^A	47 1	Sn.a. S	0 [×] 1.0 [×]	30	5.7 5.7	9.4	17.6	31.2	44.6	
Total radioactivity	r - S	94.8	96.8	~96 .7 🦨	97.4	95.4	97.9	96.7	94.7	

 Table CA 7.1.1.1-9:
 Degradation of [14C]-spiroxamine in Laacherhof soil at 20°C under aerobic conditions [% AR]

n.a.: not analysee n.d.: not detected above OD, DAT: days after treatment, LOD: 0.1% AR A Max filter paper value of S%AR B Other volatile radioactivity was 0.1%AR

A 7.1.1.1-19 Degradation of [140]-spice amine in Monheim 3 soil at 20°C under aerobic conditions [% AR] Table C

Compound of a s			/ I	ncubation	time (DA	T)		
Compound			3	7	14	30	60	100
Spiroxamine 2	72	7 9.5	71.5	65.0	57.7	43.6	34.3	27.4
M01 (spinoxamine-desethyl)	0 .6	0.9	1.7	3.9	5.8	6.9	8.8	7.7
M02 (spiroxannine-despro-		0.7	1.1	2.3	3.4	4.6	5.8	5.4
mbient extract	73.9	75.9	75.7	73.5	69.2	57.9	53.5	43.5
Total extractable radioactiv- ity	73.9	75.9	75.7	73.5	69.2	57.9	53.5	43.5



Commonia	Incubation time (DAT)											
Compound	0	1	3	7	14	30	60	10 0 ,°				
Reflux extract	7.0	5.9	6.8	5.7	7.2	6.6	3.5	, <u>3</u> 9				
Non-extractable radioactivity (including reflux and filter papers) ^A	21.7	20.8	19.1	20.4	21.5	24	21.4	21.00 21.00				
¹⁴ C-Carbon dioxide includ- ing other volatiles ^B	n.a.	0.8	1.9	3.6	6.5	12.5	24,22	26.6				
Total radioactivity	95.6	97.5	96.7	1 97.5	97	95.1	096.1	94.				

n.a.: not analysed, n.d.: not detected above LOD, DAT: days after reatment, LOD 9.1% AR

A Max filter paper value of 2.2%AR

B Other volatile radioactivity was <0.1%AR

Table CA 7.1.1.1-11: Degradation of [14C]-spiroxantine in Howe soil at 20°C under aerobic con-

ditio	ns [% A	AK]			0.0	, ·U	ô i	7 4°
Commoned		K)	L 🐔	ncubation	time (DA	Ţ)Ô ^Ÿ «	,	<u> </u>
Compound	0		ې ۲ 🖉	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u></u> <u> </u>	چ 30	60	ð 100
Spiroxamine	75.1	071.5	68:9	6 4.5	\$7.9°	4 3 Å	3 4.1 g	24.9
M01 (spiroxamine-desethyl)	0.6	0.5	1.2	2.1	2.0	م 3.5	Ĵ [™] 3.9 [≪]	3.4
M02 (spiroxamine-despro- pyl)	S CA	×.4	® 0.7	Q.8	Q1.5	2.50	\$\$%9	2.6
Ambient extract	76.1	73.5 ⁰	72/.3	@69.8	65.6	\$3.6	4 5.6	34.8
Total extractable radioactive	761	73.5	\$ ⁷ 72.3	<u>6</u> 88	65.6	53.6	45.6	34.8
Reflux extract	©3.9 _~	3.4 ₀	¢,3	×1.0 ⁽	6.2	×6.3	2.8	1.4
Non-extractable radioactivity (including reflux and filter papers) ^A	24,7 0		22.4	2452	26.5 °	Ø 31.7	25.5	23.6
¹⁴ C-Carbon dioxide invlud- ing other volatiles ^B	n.a.Q	046 26	ð.5	2.9	\$.4	12.2	22.9	35.2
Total radioactivity	Ø 7.2	§96.9	96	×96.9	© [♥] 97.5	97.5	94.0	93.6

n.a.: not analysed, n.d.: ap detegted above LOD, DAT: days after reatment LOD: 0.1% AR

A Max filter paper alue of 1.7%AB

B Other volatile adioactivity was 0.1% AR

B. Material Balance

Material balances ranged from \$9.8 to \$7.9% &R in Paacherhof soil, 95.0 to 97.5% AR in Monheim 3 soil and \$9.6 to 97.5% &R in Howe soil.

C. Extractable and Non-Extractable Residues

For samples of Laacherhof soil total extractable radioactivity decreased from 77.7% AR at DAT 0 to 30.0% AR by DAT 100. The total of nonextractable residues (NER) increased from 17.1% AR at DAT 0 to 20.0% AR by the end of the study (DAT 100).

For samples of Monheim 3 soiDtotal extractable radioactivity decreased from 73.9% AR at 0 DAT to 43.5% AR after 100 days incubation. NER was 21.7% AR on DAT 0 and showed a slight overall decrease to 21.6% AR by DAT 100.

For samples of Howe soil total extractable radioactivity decreased from 76.1% AR at DAT 0 to 34.8% AR after 100 days of incubation. NER was 21.1% AR at 0 DAT and increased to 23.6% AR by DAT 100.



D. Volatile Radioactivity

Levels of ¹⁴C-carbon dioxide increased to 44.6, 30.5 and 35.2% AR for the Laacherhof, Monheim 3 ond Howe soils, respectively. Other volatile radioactivity was < 0.1% AR at all timepoints for all soils

E. Degradation of Parent Compound

Following application of [¹⁴C]-spiroxamine in Laacherhof soil, the amount of parent in the total soil extracts decreased from a maximum of 75.8% AR at DAT 0 to 14.7% AR by DAT 100 in addition to parent material, M01 (spiroxamine-desethyl), M02 (spiroxamine-desethyl), M03 (spiroxamine-N-oxide), M06 (spiroxamine-acid) and M11 (spiroxamine-desethyl acid) were detected. Evels of M01^{em} creased over the course of the incubation period, and accounted for a maximum of 7.1% of applied or radioactivity at DAT 100. M02 was detected at a maximum of 5.5% of applied radioactivity at DAT 100. M02 was detected at a maximum of 5.5% of applied radioactivity at DAT 4. M06 was detected at a maximum of 1.6% at DAT 7. Metabolite M11 was detected at a maximum of 0.2% at DAT 30.

Following application of [¹⁴C]-spiroxamine in Monterim 3 soil, the amount of parent in the total soil extracts decreased from 72.3% at DAT 0 to 27.4% AR by DAT 100. In addition to parent material, M01 (spiroxamine-desethyl) and M02 (spiroxamine-despropyl) were detected. Levels of M01 increased over the course of the incubation period and accounted for a maximum of 8.8% of applied radioactivity at DAT 60. M02 increased to a maximum of 5.8% of applied radioactivity at DAT 60.

Following application of $[^{14}C]$ -spiroxamine in Howe soil, the amount of parent in the total soil extracts decreased from 75.1% at DAT 0 to 24.9% AR by DAT 100 in addition to parent material, M01 (spiroxamine-desethyl) and M02 (spiroxamine-desprop d) were detected. Levels of M01 increased over the course of the incubation period and accounted for a maximum of 3.9% of applied radioactivity at DAT 60. M02 was detected at a maximum of 3.9% of applied radioactivity at DAT 60.

Analysis of the reflux extracts (containing a maximum 7.7% AR in Laacherhof soil) seems to have been conducted separately and were reported to comprise mostly M15 (spire amine ketone) without providing full details. The report postulated that M15 was formed from parent spiroxamine during the reflux process.

F. Degradation kinetics

Degradation rates determined in the report are superseded by the peport presented under point KCA 7.1.2.1.1(9) (M-76313(01-1))

ЦŔ

Conclusions

Spiroxamine degraded in Laacherhof Monherm 3 and Howe soils under aerobic conditions at 20°C, with 14.7%, 27.4% and 24.9% of the applied radioactivity remaining as parent compound in these respective soils after 100 days. The amounts of unextractable radioactivity increased to an overall maximum of 31.7% AR by DAT 30 in Howe soil and subsequently declined to 23.6% AR by DAT 100. No significant levels of organic volatiles were observed in the study. Mineralisation to carbon dioxide was a significant pathway, steadily increasing throughout the study in all soils, accounting for an overall maximum of 44.6% AR in Caacherhof soil after 100 days. The primary metabolic pathway involved dealkylation of the amine moiety to form two najor metabolites, M01 (spiroxamine-desethyl, maximum 8.8% of AR in Monheim 3 soil) and M02 (spiroxamine-despropyl, maximum 5.8% AR in Monheim 3 soil). Additional minor metabolites observed were M03 (spiroxamine-N-oxide, maximum 2.5% AR in Laacherhof soil only) M06 (spiroxamine-acid, maximum 1.6% of AR in Laacherhof soil) and M11 (spiroxamine-desethyl acid, maximum 0.2% AR in Laacherhof soil).

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in the report presented under point KCA 7.1.2.1.1/09 ($\underline{M-763139-01-1}$).



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Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) BBA: Part IV, 4-1 (similar to required guideline) minor differences). The study is considered valid to assess the aerobic degradation of [cyclohex] $^{-14}$ n spiroxamine in soil.

Data Point:	KCA 7.1.1.1/03
Report Author:	
Report Year:	
Report Title:	[Cyclohexyl-1-14C] KWG 4168 residues in following cross 6 6
Report No:	$PF4043 \qquad \qquad$
Document No:	<u>M-006096-01-1</u>
Guideline(s) followed in	US EPA §165-1 Contined accumulation studies on rotational crops, 1983
study:	
Deviations from current	Yes. A A A A A
test guideline:	Yes. OECD 502 guideline (January 2007) requires three plant-back-intervals for spe-
	ceeding crops ² the appress interval set 2/0 to 365 days to represent stops sown
	the follow the veal was not conducted in the study a study of the stud
Previous evaluation:	yes, evaluated and accepted
	D/R(1)//, R/R(2010), R/R(2010))
GLP/Officially recog-	Yes Conducted under GLP Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	yes y y y y y

Executive Summary

A full summary of this study is provided under Point KQA 6.6.191. The study is also referenced at this location as potentially containing belevant information (i.e. information of the degradation of the active substance in soil). The study was also previously provided under the location and, therefore is provided for completenes. However, the study does not fulfil modern requirements and was not previously used ×,° of setting of endpoints and is therefore not addressed further.

Assessment and conclusion by applicant

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to address a different data requirement, but potentially contains information relevant to Point KCA 7, 10.1. The study is provided for completeness only and considered supple-

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How we have a study is proved to the study is



Data Point:	KCA 7.1.1.1/04
Report Author:	
Report Year:	1997
Report Title:	Degradation and metabolism of KWG 4168 in soil aerobic soil metabolism
Report No:	PF4274
Document No:	<u>M-006148-01-1</u>
Guideline(s) followed in	US EPA Pesticide Assessment Guidelines, Subdivision N § 162-1: Aerobic sol
study:	metabolism studies (1982)
Deviations from current test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the reliability of the study (described if a
_	study summary)
Previous evaluation:	yes, evaluated and accepted RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GQP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes O' O A A
Examples Summany	

Executive Summary

The route and rate of degradation of spiroxamine was investigated in one US soil (Wolf Ranch a loam) under laboratory aerobic conditions soil samples (100 g c w³) were treated with [cyclohexyl-1-¹⁴C]-spiroxamine (radiochemical purity 99%) and application rate of 0.89 mg/kg soil (equivalent to a single application of 668 g a.s./ha assuming 5 cm soil depth and 1.56 cm³ soil density) and incubated at 20°C and 75% of 1/3rd bar moisture (equivalent to 48% MWHC) for 360 days in the dark.

Duplicate samples were removed for analysis after 0, 1, 2, 7, 14, 20, 58, 90, 120, 181, 269 and 360 days of incubation. Soil samples were extracted three times at room temperature under agitation using acetonitrile for 30 minutes, and once using a Sox Fec extraction system for 1 hour, using boiling methanol. Liquid extracts were radio-assayed by Liquid Scintillation Counting (LSC) directly. Extracted soil debris was air-dried and analysed by combustion LSC. Liquid extracts were analysed and quantified by normal phase TLC and quantitatively confirmed by Toverse phase TLC. Levels of parent spiroxamine were also confirmed by GC/MS and metabolite identity was confirmed by Isolation and HPLC-MS/MS.

The material balances ranged from 95.1 to 100.5% AR devels of NER increased to maximum levels of 19.7% AR by DAT 360. Mineralization to carbon dioxide was a major pathway, demonstrated by the high amount of radioactivity becovered in the volative trans for all soils (maximum of 53.5% AR by the end of the study). No significant levels of organic volatiles were observed.

After 360 days incubation at 20 %, [¹⁴C] spiro amine degraded to 12.0% of the radioactivity applied. A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) was performed in the report presented under point KCA 7.1.2.1.1/09 (M-763139-01-1).

Two major soil metabolites were observed via de-alkylation of the amine moiety to form metabolite M01 (spiroxamine-desethyl, maximum 6.1% AR) and oxidation of the tertiary amine to form metabolite M03 (spiroxamine-Noxide, maximum 7% AR). Other minor metabolites observed were M02 (spiroxamine-despropyl, maximum 4.2% AR) and M06 (spiroxamine-acid), M11 (spiroxamine-desethyl acid), M12 (spiroxamine-despropyl acid) and M15 (spiroxamine-ketone) all observed at levels <1% AR.



] joadiolabel

I. **Materials and Methods**

A. Materials

1. Test Items

[cyclohexyl-1-¹⁴C]-spiroxamine

* Denotes position of 3.63 MBoong >999

2. Test Soil

Specific Activity:

Radiochemical Purity:

cA 7.1.5 1-12 No pesticide of The study was performed using one for soil as characterized in fable CA 7.1 the same chemical class was used for two years before sampling for the study °°

Table CA 7.1.1.1-12: Physico-Chemical properties of test soil

Parameter & S	The sold of the so
aus 6 0	
Geographic Location	Fosno, California
Geographic Location	Fosno, California
City Country	
Textural Classification (USDA) Sand [50 - 2000 μm] Ο (%) Ο (%) Ο	Loam
	29.7 29.7 45.1
Silt [2 – 50 gm]	
	29.7 29.7 45.1 25.2 7.8
Clay Charles Complexity Complexity	
in H ₂ O (1:1)	7 6 5 7.8 7.8
in CaCl ₂ (1:1)	8.7 1.67
pH in H ₂ O (1:1) in CaCl ₂ (1:1) Organic Matter (%) *	1.67
pH in H ₂ O (1:1) in CaCl ₂ (1:1) Organic Matte $\mathcal{U}(%)$ *	0.97 0.97 19.0
Cation Explange Capacity (meg 100 g)	19.0
Water Holding Capacity (g HeO per 190g dry soil)	
Organic Matter (%) * Organic Carbon (%) Cation Explange Capacity (meg 100 g) Water Holding Capacity (g H ₂ O per 100g dry soil). 40% of maximum Soil Microbial Bjomass (mg C/kg soil)	18.8
Soil Microbial Biomass (mg C/kg soil)	
Initial, untreated (0 DAT)	320
Cation Exchange Capacity (meg100 g) Water Holding Capacity (g H ₀ O per 190g dry soil). 40% of maximum Soil Microbial Biomass (mg C/kg soil) Initial, untreated (0 DAT) Mid point, treated (00 DAT) Mid point, treated (90 DAT) Final, attreated (360 DAT) Final, untreated (360 DAT)	290
Mid point untreased (90 DAT)	272
Final, Treated (Sto DAT)	110
Final untreated (360 DAT)	135
* Calculated by multiplying organic carbon content by 1.72	

* Calculat of by multiplying organic carbon content by 1.724 (not reported)



B. Study Design

1. Experimental Conditions

Tests were performed in sealed static systems consisting of glass flasks each containing 100 g sont (dryw weight) with solid traps of oil-coated (2% paraffin oil in hexane) quartz glass wool for sorption of organic volatiles and soda lime for adsorption of evolved carbon dioxide.

The study was conducted at a concentration of approximately 0.89 mg/kg dry weight of soil. The test concentration was based on a single application of 2 kg as /ha (field rate of four applications of 500 g a.s./ha per year) assuming a 15 cm soil depth and 1.5 g/cm³ soil density (note – this is equivalent to a single application of 668 g a.s./ha assuming 5 cm soil depth and 1.5 g/cm³ soil density). Application of \bigcirc [¹⁴C]-spiroxamine, dissolved in acetonitrile, was made to a subsample of each soil, which was then added to the bulk soil and mixed thoroughly, after solvent evaporation for 2.5 hours before use in the experiment. After mixing, 100 g dry weight equivalent of soil was weighed into incubation vessels. Soil moisture was adjusted to 75% of 1/3 bar at the time of application (i.e. to pre-acclimatisation) and maintained at this level during incubation with periodic additions of water (30 days). The soil samples were incubated at a temperature of 20 ± 1 \bigcirc under a robit conditions.

Two treated (applied at the same rate) and three untreated still samples were incobated alongside test systems under the same conditions to monitor microbial activity at the beginning, during and at the end of the study.

2. Sampling

Prior to opening the sealed static incubation vessels, either for sampling or maintenance of moisture, possibly volatile components were flushed into the trapattachment by introducing water saturated air (10 mins). Duplicate test samples were the word for analysis after 0, 1, 3, 7, 14, 30, 58, 90, 120, 181, 269 and 360 days of incubation.

Treated and untreated microbial biomass samples were analysed at 0, 90 and 360 days of incubation.

3. Analytical Procedures

Soil samples were extracted three times at ambient temperature under agitation with acetonitrile for 30 minutes and combined. Following this extraction series the remaining radioactivity in the soil was quantified by combustion. Subsequently, a second extraction was performed of the soil residue with boiling methanol for 60 minutes, and methanol rinse for a further 60 minutes, both in a SoxTec system. Soil extracts were radio assayed by Liquid Schtillation Counting (LSC). The soil residue remaining after the second soil extraction was requantified in the 1, 30, 120 and 270 days "A" replicates samples only; for the remaining samples it was calculated by difference (due to good agreement with measured values). The soil extracts from the first and second extraction procedures were analysed separately.

The combined ambient temperature soil extracts were analysed (without any prior work-up or concentration) using the main primary TLC formal phase method below against reference standards:

- Silica gel plates and an acetonitrife. water 25% ammonia (80:18:2, v/v/v) solvent system.

A quantitative confirmatory analysis was conducted using the following reverse phase TLC method:

RP-18 plates with two solvent systems (used sequentially in 1 dimension):

- nchexane dichloromethane:2 popyl alcohol:25% ammonia (30:70:10:2, v/v/v/v) and a saturated tank system (developed until solvent front at 14 cm)

 \sim chloroform chyl alcohol (50:50 v/v) and an unsaturated tank system (developed until solvent \sim from at 6 cm)

The TL Oplates were evaluated using a linear analyser to determine the quantities of radiolabelled test substance and its degradation products. Additional confirmatory analysis of soil extracts to confirm spiroxamine and metabolites by MS was also conducted on single replicates of samples from 90 DAT (spiroxamine and M03 (spiroxamine-N-oxide)) and 120 DAT (M01 (spiroxamine-desethyl) and M02



(spiroxamine-despropyl)). These samples extracts were concentrated and chromatographed using the normal phase TLC method above, excised from the TLC plate, extracted and analysed by GC/MS (spiroxamine) or HPLC/MS/MS (metabolites) to confirm identity.

Volatile radioactivity in volatile traps and polyurethane plugs was extracted using ethyl acetate and aliquots quantified by LSC. ${}^{14}CO_2$ was liberated from soda lime through addition of 18% (w/w) hydrochloric acid and absorbed by a suitable cocktail and quantified by LSC. Identity of ${}^{14}CO_2$ was further confirmed by conversion to [${}^{14}C$]-benzoic acid by means of the Grignard reaction.

4. Determination of degradation kinetics

The degradation kinetics of data within this report are subject of a sparate modelling study. DTa and \bigcirc DT₉₀ values for the degradation of spiroxamine and is metabolites have been to calculated from the reported data following the recommendations of the FOCUS work group (FOOUS 20)4²). Full details are provided in in the report under point KCA 7.12.1.1/09 (M₂₇63139,01-1)

II. Results and Discussion

A. Data

The distribution and characterisation of radioactivity for the test softs incubated at 20°C following application of [14 C]-spiroxamine is summarised in Table CA $\frac{1}{1}$.1.1.43.

Table CA 7.1.1.1-13: Degradation of [¹⁴C]-spiroxamine in Wolf Ranch soil at 20°C under aerobic conditions [% AR]

	com			ar)	"U"	ð,	Ç <u> </u>	an si	<u></u>	ð			
Compound	Rep.	\$C'	K	Ö	Å	Incu	bation	time (1	DAT)		»»		
Compound	°~	0	\mathbb{O}_1^*	<u>5</u> 3	J.	14	30	58	90	126	181	269	360
	A,	88.0	83.2	79.0°	^{\$79.3}	Ç75.3	6.3	\$50.2	40.8	330	21.5	14.7	11.9
Spiroxamine	B	8 9 .3	79.8	84,3	79.9	79.2	70.5 [©]	55.2°	40.7	34.3	21.7	12.7	12.1
	Mean	∕86.7ू	\$ 1.5	80.2	79.4	Æ.3	68.4	52.7	408	33.7	21.6	13.7	12.0
	A	n.đ.	02	0.7	¢ [≫] 1.0 _	2.5	Ĩ.7	¥.8	<u>_</u> 2	5.3	3.7	3.3	3.8
M01 (spiroxamine- desethyl)	_≪B	0 .2	Ŵ	ſ¢,Ţ	0.2	2.80	4.1	[≥] ″4.9 _∅	5.9	5.1	4.2	2.8	3.7
Č,	Mean	0.1		0.7) %.0	207	3.9	4,9	6.1	5.2	4.0	3.1	3.8
	AU	n	0.1	0.5		≫ 1.8 ^	Q2.3	3.0	4.3	3.9	2.4	2.6	2.7
M02 (spîroxamine- despropyl)	×B	°≈0.1	_0_1	0, Ç	0.4	1.8	2.3	3.4	4.0	3.9	2.9	2.2	2.8
	Mean	[≫] 0.1 ″	َ\$0.1 ∫	∕≫0.4	0.4	D.8	2.3	3.2	4.2	3.9	2.7	2.4	2.8
M02 (AS -	n	0.10	1/	1.4	2.9	\$5.0	6.2	8.0	7.3	7.4	5.6	6.6
M03 (spiroxamine- N-oxide)	B	ø.d.	'n.d.	A.S.	0,0	3.20	5.3	6.4	7.5	7.5	8.3	5.4	6.6
	Mean	- ~	0.1	9 9.5	÷٩.2	ð.i	5.2	6.3	7.8	7.4	7.9	5.5	6.6
Mode	, ÂQ	nð	n.d.	n.d	n.d	n.d.	n.d.	0.1	0.3	0.3	0.1	0.5	0.3
M06 (sphoxamine- acid) «	, ©B	_n.d.	nd.	n et.	n de	n.d.	n.d.	0.1	0.2	0.4	0.2	0.3	n.d.
	Mean	× - ×	× - ×	Q ~-	\$ -	-	-	0.1	0.3	0.4	0.2	0.4	0.2
M11 (spiroxamine-	A	n 🎝	n.d	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	0.1	0.1	0.1	n.d.
desethyl agid)	A₿	æ.d.	₩a.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.1	0.3	0.1	0.1
	Mean	- 4	> - ₹	Ş -	-	-	-	-	-	0.2	0.2	0.1	0.1
	A	nð	0.1	0.1	n.d.	n.d.	n.d.	0.1	0.1	n.d.	n.d.	0.3	0.1
M12 (spiroxamine- desprepyl acie)	₿.	ĴŶ.d.	0.1	n.d.	n.d.	n.d.	n.d.	0.1	0.3	0.2	0.2	0.2	0.2
	Mean	- 1	0.1	0.1	-	-	-	0.1	0.2	0.1	0.1	0.3	0.2
, Ox	A	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.5	n.d.	0.6	1.3	n.d.
M15 (spiroxamine- ketone)	В	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.2	n.d.	n.d.	1.3	n.d.
	Mean	-	-	-	-	-	-	-	0.4	-	0.3	1.3	-
Unknown 1	А	n.d.	n.d.	n.d.	n.d.	n.d.	0.1	0.2	0.4	0.4	1.9	0.6	0.6



Compound	Rep.					Incu	bation	time (l	Incubation time (DAT)											
Compound		0	1	3	7	14	30	58	90	120	181	269	360							
	В	n.d.	n.d.	n.d.	n.d.	n.d.	0.1	0.2	0.5	0.4	0.3	0.6	@ .6							
	Mean	-	-	-	-	-	0.1	0.2	0.5	6.4	1.1	0.6	0.6							
	А	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n§d.	nce.							
Unknown 2	В	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d	n.d.	n.d. 🖉	≫ 0.1 _≪	0.1							
Ν	Mean	-	-	-	-	-	-	-		-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Z.								
Ambient extract (in-	А	66.6	66.0	65.4	67.0	66.5	62.0	48.4	ZA2.3	36.5	26.2	19%5	1 % Å							
cluding filter pa-	В	64.4	63.8	67.2	65.6	66,5	62.1	52	42.3	37.5	26.6	A7.2	G 9.7							
pers) ^A	Mean	65.5	64.9	66.3	66.3	6.5	62.1	50.4	42.3	37,0	26.4	18.4	19.@							
Hot extract	А	21.5	17.7	15.5	150	16.0	15.4		18.3	PA.1 .	Ø.8	86	Ø							
	В	21.2	16.4	15.6	16.0%	20.6	202	17.8	16,90	′ 14.5C	×11.5	8.7 🕫	6.6							
	Mean	21.4	17.1	15.6	D15.6	Å 8.3	7.8	£7.0	126	14,3	11.7	9,2	6.7							
T (1 () 1 1	А	88.1	83.7	80.9	82.Ø	82,5	77.4	R64.5	60.6	© \$0.6	\$8 .0	29.1	26,1							
Total extractable ra- dioactivity	В	85.6	80.2	\$2.8	8¥.6	87A	829	70.0	59.2°	52. 0	¥.	, 25.9 į	26.3							
diodetivity	Mean	86.9	82.00	81.9%	81.9	84.8	*7 9.9	×67.4	5 9.9	5123	38,1	27.5	26.2							
Non-extractable ra-	А	10.7	15.9 ⁸	163	15:2	14.≸	15.9 [®]	()	A6.9	€ 8 .1 ^B	P 9.3	2₽.5 ^B	19.6							
dioactivity (includ-	В	10.2	*4 .7	¢\$7.6	₫ \$4.4	۶ ۵	129	15.0	18.0	16.6Ĉ	°19.3∛	¥20.4	19.8							
ing filter papers) A	Mean	105	15:2	16.8	14.8	À1.9	4.4	45 .7	17.6	104	19.3	21.0	19.7							
¹⁴ C-Carbon dioxide	А	ñ.a.	Q.1	0	0.0	1.9	5.04	1	19.6	Q28.5	41.3	52.4	53.8							
including other vol-	В 👡	Qn.a.	Q _{0.1}	§0.3	.9	1.9	4.9	12.0	185	29.0	40.2	51.6	53.2							
atiles ^C	Mean	n.a.	0.1	0.3	® 0.9 _≫	©1.9	5.0	£12.1	19.1	28.8	40.8	52.0	53.5							
	Â	98 .8	27.7	97,2	98.Q	98.5	98.7 [©]	92.9°	97.1	95.7	98.6	103.1	99.5							
Total radioactivity	B	y95.8	95.0 _x		96.9	\$.6	100/1	97.3	95 <i>Q</i>	97.6	97.6	97.9	99.3							
õ	Mean	97. S /	96,4	99.0	97.6 _s	98.6	ે9 9.4	95 .1	96.5	96.7	98.1	100.5	99.4							

Rep.: Replicate, p.a. not analysed o.d.: not detected above POD, DAS: days after treatment, LOD: 0.1% AR

A Max filter paper value of 18% AR
 B Other value radioactivity was max 0.2% AR for replicate Pat 58, pAT. All other timepoints were <0.1% AR.

B. Material Balance

Material balances ranged from 95 to 109.5% AR in Wolf Ranch soil.

C. Extractable and Non-Extractable Residues

For samples of Wolt Ranch soil total extractable radioactivity decreased from 86.9% AR at DAT 0 to 26.2% AR by DAT 360. The total of pon-extractable residues (NER) increased from 10.5% AR at DAT 0 to 26.2% AR by the end of the study (DAT 360).

D. Volatile Radioactivity

Levels of ¹⁴C-carbon dioxide increased to 53,5% AR at the end of the study. Other volatile radioactivity was < 0.1% AR at all timepoints, except for a single replicate at DAT 58 of 0.2% AR. This is included in the ¹⁴C-carbon dioxide values.

E. Degradation of Parent Compound

Following application of [¹⁴C]-spiroxamine in Wolf Ranch soil, the amount of parent in the total soil extracts decreased from a maximum of 86.7% AR at DAT 0 to 12.0% AR by DAT 360. In addition to parent material, M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide), M00 (spiroxamine-acid), M11 (spiroxamine-desethyl acid), M12 (spiroxamine-despropyl acid) and M15 (spiroxamine-ketone) were detected. Levels of M01 (spiroxamine-desethyl) increased over the course of the incubation period, and accounted for a maximum of 6.1% AR at DAT 90. M02 (spiroxamine-despropyl) was detected at a maximum of 4.2% AR at DAT 90. M03 (spiroxamine-N-oxide) was



detected at a maximum of 7.9% of AR at DAT 181. M06 (spiroxamine-acid) was detected at a maximum of 0.4% AR at DAT 120 (and DAT 269). M11 (spiroxamine-desethyl acid) was detected at a maximum of 0.2% AR at DAT 120 (and DAT 181). M12 (spiroxamine-despropyl acid) was detected at a maximum of 0.3% AR at DAT 269. M15 (spiroxamine-ketone) was detected at a maximum of 1.3% AR ab DAT 269.

F. Degradation kinetics

Degradation rates determined in the report are superseded by the report presented under 7.1.2.1.1/09 (M-763139-01-1).

III. Conclusions

Spiroxamine degraded in Wolf Ranch soil under aerobic conditions at 20°C, with 12.0% of the applied radioactivity remaining as parent compound after 360 days. The amounts of unextractable radioactivity increased to an overall maximum of 21.0% AR by DAT 269 and subsequently declined to 19.7% AR by DAT 360. No significant levels of organic solatiles were observed. Mineralisation to carbon dioxide was a significant pathway, steadily increasing throughout the study and accounting for an overall maximum of 53.5% AR after 360 days. The primary metabolic pathway involved de-alkylation of the amine moiety to form two major metabolites, \$101 (spiroxangine-desethyl maximum 6.1% of AR at DAT 90) and M02 (spiroxamine-despropyl, maximum 4.2% AR). An additional major metabolitic observed was M03 (spiroxamine-N-oxide, maximum 7.9% AR), formed by oxidation of the service of the servi tabolites formed include M06 (spiroxamine-acid, maximum Ø.4%, ØR), Ø11 (spiroxamine-desethyl acid, maximum 0.2% AR), M12/(spiroxamin@despropyl acid, maximum 0.3% AR) and M15 (spiroxamine-ketone, maximum 1.3% AR). m

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in the report presented under point KCAI.1.2 [1/09 (M-763139-01-<u>1</u>).

Study meets the current guidance and the requirement on 2830013, @

The study was conducted to study guideline(s) US EPA Pesticide Assessment Guidelines, Subdivision N § 162 1: Aerobic soil metabolism studies (1982) (similar to required guideline, minor differences). The study is considered valid to assess the aerobic degradation of [cyclohexyl-1-14C]-spiroxamine in

the requirements a to sees the aerobic degrada a valid to assess the aerobic degrada a vali



Data Point:	KCA 7.1.1.1/05
Report Author:	
Report Year:	2008
Report Title:	[1,3-Dioxolane-4-14C]spiroxamine: Metabolic screening for degradation path-
	ways under aerobic conditions in soil
Report No:	MEF-08/214
Document No:	<u>M-303803-01-1</u>
Guideline(s) followed in	EU 95/36/EC amending 91/414/EEC; OECD 307; SEPA, Subdivision N. Sec-
study:	tion 162-1
Deviations from current	None
test guideline:	
Previous evaluation:	yes, evaluated and accepted Q^{*}
	RAR (2010), RAR (2017) \sim
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes v v v v v A v

Executive Summary

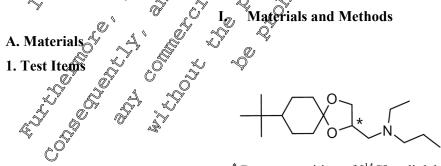
The route and rate of degradation of spiroxatnine was investigated in one European soil (HoefChen am Hohenseh, silt loam) under laborator aeropic conditions. Soil samples 0.00 g dry weight) were treated with [1,3-dioxolane-4-¹⁴C]-spiroxamine (radiochemical purity 100% at the time of application) at an application rate of 2.09 mg/kg dry weight of soil (equivalent to nominal 1500 g/m assuming 5 cm soil depth and 1.5 g/cm³ soil density) and incubated (20°C, \$5% maximum water holding capacity) for 120 days in the dark.

Duplicate samples were removed for analysis after 0, 4, 3, 7, 16, 31, 58, 88 and 120 days of incubation. Soil samples were extracted three times at room temperature under agitation using acetonitrile/water for 30 minutes, and twice under for 30 minutes, also using acetonitrile/water. Liquid extracts were analysed by reverse phase HPLC confirmed by normal phase TLC, run against reference standards to confirm metabolite identity.

The material balances ranged from 98.0 to 103 4% of applied radioactivity (% AR). Non-extractable radioactivity increased to 33.1% AR by DAT 120. No significant levels of organic volatiles were observed. Mineralisation to carbon dioxide was a major pathway, steadily increasing and accounting for 40.5% AR by DAT 120.

After 120 days incubation at 20°C, [¹⁴C] spiro amine degraded to 8.2% AR. A DT₅₀ for spiroxamine was given in the report, however, a re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) was performed in the report presented under point KCA 7.1.2.1. 909 (M²763)(99-01-1).

Two major inetabolites were observed formed by devalkylation of the amine moiety: M01 (spiroxamine-desethyl maximum 7.9% of AR); M02 (sphoxamine-despropyl, maximum 9.2% AR at DAT 31). No other metabolites were observed 32.9% AR.



* Denotes position of [¹⁴C]-radiolabel

[1,3-dioxolane-4-¹⁴C]-spiroxamine



Specific Activity:	4.09 MBq/mg	0	
Radiochemical Purity:	100% (as measured at time of application to the soils)		Ĉ

2. Test Soil

The study was performed using one test soil as characterized in Table CA 7.1.1.1-14, which had not been treated with any pesticides within the previous five years.

Parameter	roperties of test soil
Soil Designation	eoperties of test soil
Geographic Location	
City	Burscherer, North Rhine Westfalia
Country	Burschofel, North Rhine Westfalia
Textural Classification (USDA)	Silt loam & L
Sand [50 - 2000 μm]	W L W W.O C S
Textural Classification (USDA) Sand $[50 - 2000 \ \mu\text{m}]$ Silt $[2 - 50 \ \mu\text{m}]$ Clay $[< 2 \ \mu\text{m}]$ (%)	Burscheidt, North Rhine Westfalia Germany Silt lögan H.O. H.O. H.O. H.O. H.O. H.O. H.O. H.O
Clay [< 2 μm]	
pH	
in H ₂ O (1:1)	× ~ ~ ~ 7.0 &
in H ₂ O (1:1)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Organic Matter (%)*	\mathcal{A}^{*}
Organic Carbon (%)	
Cation Exchange Capacity (meq/100)g)	
Water Holding Capacity (g H ₂ O per 100g dry	
Maximum O S A	55.1 25.0
0.33 bar 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	55.1 57 57 57 55.1 55.1
Soil Macrobial Biomas (mg CRg soil)	23.0 25 25 0 25 25 0 1217
Initial, untreated (0-DAT)	
Maximum 0.33 bar Soil Microbial Biomase (mg CRg soil) Initial, untreated (0.0AT) Final, untreated (0.2 DAT) Final, solvent only (12 DAT) * Calculated formulting or graphic cathon content	682
Final, solvent only (1200AT)	<u>602</u>

* Calculated by multiplying organic carbon content by 1,524 (no reported)

B. Study Design

1. Experimental Conditions

The study was performed in static systems consisting of flasks each containing 100 g dry weight of soil attached to solic traps containing a performed in plug for adsorption of organic volatiles and soda lime for adsorption of carbon divide. Soil moisture was adjusted to 55% MWHC. Soil samples were preacclimatised to the study conditions (dark, 20°C) for 5 days prior to application of the test substance.

The study was conducted at a dominal soil concentration of 2.0 mg/kg dry weight of soil (actual study concentration was 2009 mg/kg dw). The nominal test concentration was based on a field rate of 750 g a.s./hg assuming 2.5 cm soil depth and 1.5 g/cm³ soil density (note - this is equivalent to a field rate of 1500 g a.s./ha, assuming a mixing depth of 5 cm and a soil density of 1.5 g/cm³). [¹⁴C]-spirox-amine dissolved in methanol and diluted with an equal volume of analytical grade water was applied dropwise to soil in each vessel, which were then shaken for 30 minutes to allow evaporation of solvent and mixing. Soil moisture was maintained monthly. Samples were incubated over 120 days in the dark at 20.1 \pm 0.2°C and aerobic conditions.



Two untreated samples and one sample treated with solvent only were incubated alongside test systems under the same conditions to monitor microbial biomass at the start and end of the study.

2. Sampling

Duplicate vessels were removed for analysis after 0, 1, 3, 7, 16, 31, 58, 88 and 20 days of ingulation

Untreated microbial biomass samples were analysed at the beginning and end of the experiment. The solvent treated biomass sample was analysed at the end of the experiment.

3. Analytical Procedures

Soil samples were extracted three times at room temperature under agitation using acconitrite waz ter (80:20, v/v) for 30 minutes, and twice under redux for 30 minutes, also using acetonit le/wa ter (80:20, v/v). Liquid extracts from ambient and reflux were centrifuged and combined separately, concentrated and analysed by reverse phase HPRC using a Purospher RP18e column and a gradient system using mobile phases 0.5% triethylamine in water / 0.5% triethylandine in acetonitrile (0 and 1 DAT only) or 0.05% triethylamine in water / 0.05% triethylamine in acconitrile (all other timepoints). Samples were run against reference standards for identification purposes. The effluent was passed through a UV detector (210 + 230 + 254 mm) to detect reference standards, and a radioactivity detector to determine the quantities of radiolabered test substance and its degradation products.

Confirmatory analysis was performed using TLC with silica get plates and an automated multiple development method using mobile phases of methanol +3% NKP (25%) and dichloromethane, again run against reference standards for dentification. TLC plates were evaluated using a Pineak analyser to determine the quantities of radio abelled test substance and its degradation products.

Volatile radioactivity in volatile traps was extracted using ethyl acetale and all quots quantified by LSC. ¹⁴CO₂ was liberated from soda lime through addition of 18% (w/w) hydrochloric acid. Identity of ¹⁴CO₂ was determined by conversion of [14G]-barium carlonate

4. Determination of degradation kinetics

The degradation Grinetics of data within this report are subject of a separate modelling study. DT₅₀ and DT90 values for the degradation of opiroxamine and its metabolites have been re-calculated from the reported data following the recommendations of the FOCUS work group (FOCUS 2014²). Full details are provided in in the report under point KCA9.1.2 1.1/09 (1-763 99-01-1).

A. Data

Ô The distribution and characters ation of radioactives for the test soils incubated at 20°C following ap-

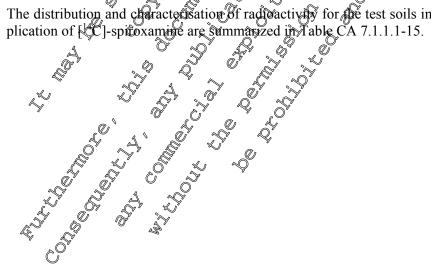




Table CA 7.1.1.1-15: Mass balance of [¹⁴ C]-spiroxamine in Hoefchen am Hohenseh soil at 2	0°C	
under aerobic conditions [% AR]	<i></i>	0

Compound	ReplicateAB	0 89.6	1	1 3	ncubat 7	ion tim 16	e (DAT 31/5>	í.		
-	A			3	7	16	24	50	00 ()	
Spiroxamine		89.6	015					58	88	120
Spiroxamine	В		81.5	64.7	55.3	42.0	29.2	22.7	129	<u>,</u> 79
		89.1	82.0	62.6	54.8	40.9	28.6		\$10.8 ×	\$ 8.6
	Mean	89.3	81.8	63.7	55.1	41.5	27.9	22 ts		8.2
	А	n.d.	n.d.	A .3	1.9	8 .8	4.6	ÛĬ	<u>J</u>	3.9
HPLC-P1	В	n.d.	n.d.	1.4	2.0		4.0 🛪	2.4	3.3	\$3.6
	Mean	n.d.	núd.	1.3	1.0	3,60	4.3	2.2	[♥] 3.4℃	3.6®
	А		0.8	2.2	2.3	@ .6	194 194	\ 0 ?2	nçal.	n@d.
HPLC-P2	В	0.6	0.9	° 2.1	2.6		¢1.3	¢0.3 %	yn.d. 1	0.2
	Mean	0.6	.0,8	2)	25	28	1.40	0.3	n.d.	0.1 。
	A	<u>}</u> 0.3 ∘,	Ø1.1 🛛	J.5	₽.3	<u>_</u> 1.1	\$ <u>7</u> .2	0.5	A.	Ŕ
HPLC-P3	B	0.2	1.0	1.4	1.8		1.1	©0.3 <u>√</u>		§0.2
	Mean	6B	K.Ø	1.34	1%6	12	12	0	0.3	0.2
	Al a Br a	@°0.4	°∕ľ.1	[≪] ¶.́.7	1.3	A.5	£.3	\$.6	<u>"</u> 04	n.d.
HPLC-P4	<u> </u>	0.40	1.20	2.36	1.4	1.7	1.4	ື 0.4	≫0.4	n.d.
	Mean	0.4	101	20	L'R	1.6	1.0	05	0.4	n.d.
	- 7)°0.4	¶√1.3 (_≫ 1.7	<i>™</i> .6	°ي.7 .	Q .8	0.5	0.4	0.4
HPLC-P5	<u> </u>	0.0	1.k	1.9	2.6	[♥] 1.2~©	¥ 1.8 🕊	J 0.5	0.3	0.5
×,	Mean	65	A.2		21	1.5	1.	0.5	0.3	0.5
	A A A A A A A A A A A A A A A A A A A	0.3	§1.2	©Ĩ.8	9.5	ðľ.4	Q.5	0.6	0.5	n.d.
HPLC-P6	<u>~~</u> * ~~	0.7	1.40	1.9		1.5 ₀	1.4	0.6	0.3	0.3
	Mean	0 15	1Ì	1.8	18	k)	1.5	0.6	0.4	0.1
M01 (spiroxamine-de		√0.3 (1.5	Q2.7	<u>4</u> .4	© ^{6.2}	7.3	8.0	6.0	3.9
sethyl)	3 8 <u>A</u>	03	1.70	2.9	4.8	6.0	7.2	7.7	4.7	4.9
	~Mean &	0.4	A \$6	28	Âø	6.1	7.2	7.9	5.3	4.4
M02 (spiroxamine-despro-		Ø.6 [%]	yn.d.	3.0	∕≫4.5	6.1	9.4	7.3	6.9	4.1
byl) combined isomer's A +	<u>B</u>	0.7	0.70	2.8	4.8	6.9	9.0	7.8	4.9	5.3
3	Mean	×0.6	.Q ≈ 7	L.9	4.7	6.6	9.2	7.5	5.9	4.8
M02 (spiroxamine- despropyl) isomer Actors)	Méan -	0.30		° 1.4	2.5	3.6	5.2	4.1	3.3	2.9
M02 (spiroxantine- despropyl) isomer B (trans) Ambiep@extract Reflue extract	[™] Mean	0.3	0.4	1.5	2.2	3.0	4.0	3.4	2.5	1.9
Ambienextract	Mean	A 4.6	71.1	55.9	54.4	50.8	45.5	36.9	25.3	19.9
Reflugextract	🎙 Mean 🧷	ľ7.9	18.4	24.1	21.3	16.7	12.5	7.1	5.3	4.6



Commoned	Darkasta	Incubation time (DAT)								
Compound	Replicate	0	1	3	7	16	31	58	88	120
Total extractable radioactiv- ity ^A	Mean	92.5	89.5	80.0	75.7	67.6	58,0	44.0	30.6	24 5 ⁴
Non-extractable radioactiv- ity	Mean	10.9	11.7	19.0	23.1	24.4	26.1	30.3	34.1	°33.1
¹⁴ C-Carbon dioxide includ- ing other volatiles ^B	Mean	n.a.	0.2	0.8	2.0	6.9	[*] 13.8	24.6	34.5	40.5%
Total radioactivity	Mean	103.3	101.3	99.7	100.9	8.9	97.9	98.8	2 99 .1	28.1

Sum of ambient and reflux extracts А В

Other volatile radioactivity was <0.1%AR

Table CA 7.1.1.1-16: Characterisation of [14C]-spiroxamine in soil after 120 aerobic conditions

	4			Of States		L.
Total bound residues (%AR)	Humin		Humic aci	2 12 U.U	Fulvic Scid	
Total bound residues (%AR)	(% of bound/residu	ies) (% of	f bound res	adues) >> ('	% of bound residues	.s)
33.9	46 .5		<u>29</u> 29		24.4	
	L O	°∼j° ¢⊘		No No		

B. Material Balance

Material balances ranged from \$8.0 to \$03.4% AR.

C. Extractable and Non-Extractable Residues

Total extractable radioactivity decreased from \$2.6% AR at DAT 0 to 24. 5% AR by DAT 120. The total of non-extractable residues (NER) increased from 10.9% AR at DAT 0 to a maximum of 34.1% AR by DAT 88 and then declined to 3.1% AR by the end of the study (DAT 20). Further characterisation of NER in a selected soil sample is possented in Table CAST.1.1, @16, the majority of applied radioactivity was associated with the humin traction."

D. Volatile Radioactivity

Levels of ¹⁴C-carbon dioxide formed ranged from 0.2% AR (DAT) to 40.5% AR (DAT 120) during incubation. Other volative radioactivity was < 0.1% AR at all timepoints.

E. Degradation of Rarent Compound

Following application of [14C]-spiroxamine the amount of papent in the total soil extracts decreased from a maximum of \$9.4% or at DAT 0 6 8.2% AR by DAT 20. In addition to parent material, two major metabolites were observed M01 (spiroxamine-desethal) accounted for a maximum of 7.9% of applied radioactivity at DAT 58 and MQ² (spiroxamine-despropyl) accounted for a maximum of 9.2% AR at DAT 31 to other metabolites were observed 2.9% AR.

F. Degradation kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.1.2.1.1/09 (<u>M</u>[@]63 <u> 9-01</u>-

"H¥.

Conclusions

Spiroxamune degraded in Hoer hen am Hohenseh soil under aerobic conditions at 20°C, with 8.2% AR remaining as parent compound after 120 days. The amount of unextractable radioactivity increased to a maximum of 4.1% AR by DAT 88 and then declined to 33.1% AR by the end of the study (DAT 120). Mineralisation to carbon dioxide was a major pathway, steadily increasing throughout the study, accounting for 40.5% AR at DAT 120. The primary metabolic pathway involved de-alkylation of the amine moiety to form M01 (spiroxamine-desethyl, maximum 7.9% AR, DAT 58), M02 (spiroxaminedespropyl, maximum 9.3% AR at DAT 31). No other metabolites were observed >2.9% AR.



A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in the report presented under point KCA 7.1.2.1.1/09 (M-763139-04-<u>1</u>).

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

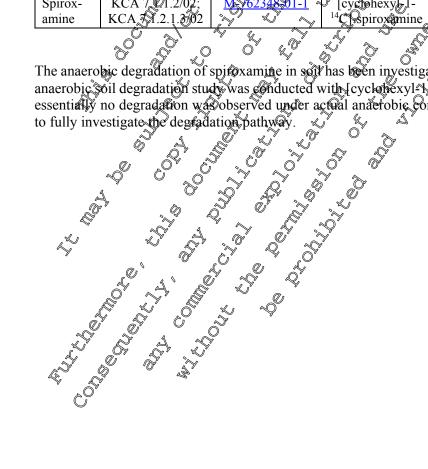
The study was conducted to study guideline(s) OECD 300 (required guideline). The study is ered valid to assess the aerobic degradation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in

CA 7.1.1.2 Anaerobic degradation

In view of the proposed use pattern for spirosamine as a post-emergence spray applied fungicide for application to cereals crops and vines, exposure to anaerobic conditions in soil is not onvisaged. However, the degradation of spiroxamine in an arobic soft has been investigated in one study a CA 7.1.1.2/01) which was evaluated during the previous EU review. As the existing study was not fully conducted according to the required study guideline, one new study has been conducted to fulfil this requirement. The new study was also conducted to address the new requirements of SFSA 2019¹.

Sub- stance	Report refer- ence	Document no	Test material for the Comment
Spirox- amine	KCA 7.1.1.2/01; KCA 7.1.2.1.3/01	<u>M409601002-1</u>	¹⁴ C]-spiroxamine ¹⁴ C]-spiroxamine ¹⁵ C]-spirox
Spirox- amine	KCA 7 21.2/02; KCA 31.2.1.202	M 762348 01-1 ~	Icyclohexyl-1- New data not yet reviewed under 14C Spirovamine UP.

The anaerobic degradation of spiroxamine in soft has been investigated in two studies at 20°C. The new anaerobic soil degradation study was conducted with [cyclobexyl_44C]-spiroxamine only, however, as essentially no degradation was observed under actual anaerobic conditions this is considered sufficient to fully investigate the degradation pathway.





Data Point:	KCA 7.1.1.2/02
Report Author:	
Report Year:	
Report Title:	[14C]-spiroxamine: Route and rate of degradation in soil under anaerobic condi- tions at 20°C
Report No:	VC/19/053
Document No:	<u>M-762348-01-1</u>
Guideline(s) followed in	Commission Regulation (EU) No. 283/2013 paccordance with Regulation (EC)
study:	No. 1107/2009
	OECD 307
Deviations from current test guideline:	None Q S S S S S S
Previous evaluation:	No, not previously submitted by a first testing facilities
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes 2 4 4 4 7 4 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7

New studies, not previously evaluated

Executive Summary

Õ The route and rate of degradation of spiroxamme was nvestigated of one European soik (Refesol-02-A, silt loam) under laboratory anaerobic conditions. Soil samples (400 g dw3) were treated with [cyclohexyl-1-14C]-spiroxamine (radiochemical purity 99.6%) at a nominal pplicatron rate of 2.0 mg/kg soil dry weight (reported as equivalent to 750 g/ha assuming a mixing depth of 2.5 cm and soil density of 1.5 g/cm³, otherwise equivalent to 1500 g/h@assunang a roxing depth of 5 cm@and incubated (20°C, pF 2) for 30 days under aerobic conditions in the dark before being flooded to a 2 cm depth of water.

Duplicate samples for each soil were removed for analysis after 0, 10 and 30 days after treatment (DAT) and for 7, 14, 31075 and 118 days post flooding (DPF). Overlying water (post flooding only) was decanted from the underlying soil and combined with acet or trile. Soil samples were extracted four times at room temperature with acetonitrile/water/35% ammonia solution \$0/20/1 v/v/v, by addition of solvent, vigorous mechanical shaking and centrifugation. The overlying water and soil extracts were combined and analysed, without or neutration, primarily by revers of hase HPLC. Confirmatory analysis was conducted by normal-phase TVC on Selected samples. Degradation products were also confirmed Ô using LC-MS on selected samples.

The material balances anged from 100.6 to 109.4% AR indicating a complete mass balance. Under the initial aerobic Conditions, the amount of mextractable radioactivity increased to 6.5% AR and mineralisation to carbon dioxide mcreased to 741-15.8% AR by DAT 30. Post flooding, unextractable radioactivity from the soil increased to 10.5% AR and mineralisation to carbon dioxide increased to 15.6% AR by DPF 118. No significant levels of organic volatiles were observed.

Following application of evclohexyl-1 C]-sproxamine, the amount of parent in the soil extracts decreased from 99,9% AR at DAT 0 t@65.7% AR by DAT 30 (time of flooding). During the flooded phase, the amount of parent in the combined overlying water and soil extracts did not change from a total of 62.2% AR at DPK to 62.6% AR at DPF 118. There was no appreciable decline during the flooded phase in the level of spiroxamine. No further kinetic evaluation was conducted, spiroxamine is stable under anaerobie conditions.

As sach, under flooded conditions degradation of [cyclohexyl-1-14C]-spiroxamine was minimal and there was no appreciable increase in the level observed of any metabolites. ć

dry-weight



I. **Materials and Methods**

A. Materials

1. Test Items

[cyclohexyl-1-¹⁴C]-spiroxamine

Denotes position of Cloadiolabel 4.26 MB (34 >9

2. Test System (soil)

Radiochemical Purity:

Specific Activity:

ve test sour was The study was performed using one test soil as characterised from the same batch as that used for study KCA .14.1/06

Table CA 7.1.1.2-1: Physico-chemical properties of test soft

0

-	<u> </u>	
Parameter		
Si	M Designation	Referrol-02#A
Geographic Location		
City	A	\mathcal{A} \mathcal{A} Northrhine, Westphan ^B
Geographic Location City Country Textural Classification (USDA Sand [50 - 2000 µm] Silt [2 – 50 µm Clay [< 2 µm]		
Textural Classification (USDA) 6 %	Silt loam
Sand [50 - 2000 µm]		
Silt [2 – 50 µm)		Silt loam Silt loam Silt loam Silt loam Silt loam Silt loam
Clay [< 2 μm]		Silt loam 5 5 5 5 5 5 5 5 5 5 5 5 5
pH NY K		× × × × × × × × × × × × × × × × × × ×
in $H_2O(U:1)$		\sim \sim \sim \sim \sim \sim \sim \sim 7.1
in 0.01M CaCl ₂ (1:40)		0 0 0 0 0 0 7.1 ↓ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
pH in H ₂ Q(T:1) in 0.01M CaCl ₂ (1:4) Organic Matter (%) Organic Carboo (%)		0.7 0.7 1.7 0.7 1.0
Organic Carbon (%)		<u> </u>
Cation Exchange Capacity	q/100/g)	11.4 x x x x x x x x x x x x x x x x x x x
Water Holding Capacity (g H20	Deper 100g dry	1.0 11.4 35.9 19.9
pF 2-0 (0.1 bar, w/w/%)		35.9
pF 2-0 (0.1 bar, w/w %) pF 2.5 (0.33 bar, w/w %) Soil Microbial Momass (mg og	O ON	0 [×] 19.9
soil) pF 2.0 (0.1 bar, w/w %) pF 2.5 (0.33 bar, w/w %) Soil Microbial Momass (mg or A Initial, DAT 0 Final, 100 DAT 20	¢ ¢C/100 g soil) ¢	
	N Y	15.2 (1.5)
Final, 100 DAT 020	0	0.49 (0.5)

* Calculated by multiplying organic carbon content by 1.724 (not reported)

A Biomass a percentage of organic carbon content provide in parentheses
 B & Location known free of persicide use for previous 3 years and used within 3 months from sampling.

The test soils were handled in accordance with ISO 18400-102 and 105 prior to use.



B. Study Design

1. Experimental Conditions

Tests were performed in flow through systems consisting of glass flasks each containing 100 g soil (dryweight) and attached to an ethylene glycol trap to collect organic volatiles followed by two potassium hydroxide traps (2M) to collect carbon dioxide.

Soil samples (100 g) were pre-acclimatised to the initial aerobic incubation conditions (dark, 20 °C and pF 2 moisture content) for 13-15 days before application of the test substance (within 3 months of sampling). The study was conducted at a concentration of 2.0 mg/kg dry weight of soil (reported as equivalent to 750 g/ha assuming a mixing depth of 2.5 cm and soil density of 1.5 g/cm³, otherwise equivalent of 1500 g/ha assuming a mixing depth of 5 cm). Application of [Syclohexyl-1, °C]-spiroxample in a solvent (acetonitrile, 201 μ L) was made to the soil surface. Soil samples were behave behave a grade of the soil and to allow solvent evaporation.

After 30 days (at the time the study was being conducted, information was available from the first few sampling intervals of the associated study KCA 7.1.1/06 (M-202349-91-1) which indicated that the degradation rate of the active substance in Reference 2.4 soil under aerobic conditions was 30 days), the soil samples were flooded to a 2 cm depth of water

Additional samples for each soil were reated with an equivalent amount of blank solven only to monitor microbial activity at the beginning and end of the incubation period.

2. Sampling

Data

Duplicate samples for each sold were removed for analysis after 6, 10 and 30 days after treatment (DAT) and for 7, 14, 31, 75 and 108 days post flooding (DPF). Untreated samples were analysed for biomass at the beginning and end of the experiment.

3. Analytical Procedures

Overlying water (post flooding only) was decanted from the underlying soil and combined with acetonitrile. Soil samples were extracted four times at room remperature with acetonitrile/water/35% ammonia solution 80/201 v/v/x by addition of solvent, vigorous mechanical shaking and centrifugation. Radioactivity in extracts was determined by liquid schullation counting (ESC). The overlying water and soil extracts were combined and analysed (without concentration) by HPLC with radio-detection. Degradation products were identified by comparison of the etention times of reference standards. Confirmatory analysis using an alternative technique was conducted by TLC with co-chromatography against reference items on selected samples begradation products were also confirmed using LC-MS on selected samples.

Volatile radioactivity in volatile it aps was quantified by LSC. Any radioactivity in the polyure thane foam bung was extracted using acetonic le and quantified by LSC. Carbon dioxide in the potassium hydroxide traps was confirmed by barfum carbonate precipitation.

Following homogenisation hon-extractable residues (NER) in extracted soils were determined by combustion.

4. Determination of degradation kinetics

II.

No significant degradation of parent spikexamine was observed under anaerobic conditions and therefore no degradation rate could be calculated (assumed stable under anaerobic conditions).

Results and Discussion

The distribution and characterisation of radioactivity for the test soils incubated at 20°C following application of [cyclohexyl-1-¹⁴C]-spiroxamine are summarized in Table CA 7.1.1.2-2.



	unde	under anaerobic conditions [% AR]									
				Ir	cubation	time (DA	Г)		. 4		
Compound	Repli-		DAT			, , , , , , , , , , , , , , , , , , ,	DBF		_6)	<i>`</i> O'	
-	cate	0	10	30	7	14	31	75 🦼	1180		
	А	100.1	74.3	64.4	61.5	65.2	63.1	65.0	61.9		
Spiroxamine	В	99.7	76.5	67.0	62.9	65.7	4 60.9	55	\$3.3	Ô	
	Mean	99.9	75.4	65.7	62.2	65.5	62.0	60.2	≈ 62.6	ľ	
	А	0.5	4.2	7.1	√ 7.1	6.70	8.2	07.3	¥ 7, 70 ¥	, o ^r	
M01 (desethyl)	В	0.2	4.4	6.9	7.1	75¥	7.1 🧹	6.60	61	Ô,	
	Mean	0.3	4.3	7.0	7.1	\$6.9	7.60	6.%	6.9	×	
MO2 (deama	А	0.4	3.1	5, 1 -) B) 4	5.4	[™] 4.9 ⊘	6.4	A.6	4.8		
M02 (despro-	В	0.5	2.8	\$ \$74	5.1	5.8	5.2	⁰ 4.3	A.S		
pyl)	Mean	0.4	3.0	& 5.3 m	° 5.3	\$\$.4 ·	5.8 C	4.A	×4.7		
	А	n.d.	3.5	O 3.3 O	3.3	3.0	r 1.0	n.d.	≰ n.d. 。		
M03 (N-oxide)	В	0.2	3.1	32	@3.2 &	2 1.0 ^O	2,6	On.d.	n.d		
	Mean	0.1	3,3	3.3 ~	≫ 3.2	2:0	ÕĨ.8 🤬	, n.d. 🛇	pÇa.		
	Α	n.d.	61	گې 5.8 ٍ℃	5.6	. Å.8 🔬	A.3 S	62	A.7.7		
M06 (acid)	В	n.d.	A6.0 &	5.2	~5.4	💭 4.6 Õ	6	Ø3.6	7.8		
	Mean	n.d. 📈	[♥] 6.1 [®]	535	[∞] 5.5 ∕∕	47	\$ <u>.</u> 4	\$9.9 _{&} }	7.7		
M11 (degethed	Α	n.d. 🖓	063	En.d.	r 1.3	_rΩĭ.	0 1.0 Č	n.d.y	n.d.		
M11 (desethyl acid)	В	nØ.	, [∞] ₩.d.	0.4	,ØŽ	0.9	0.8	Q,1	n.d.		
aciu)	Mean	r.d.	⁹ 0.2	0.2	1.3 J	V 0,5Q	1.0	01.1	n.d.		
Minor un-	A 🚕	n.d.	1.2	p.d.	O 0.9 🤊	n.d.	°~0.6 (6 n.d.	0.9		
knowns (total)	B 🗞	n.d.	Ŵ,	🔊n.d. 🏑	n d 🕚	≪₽.d. <i>j</i>	∽n.d.~	1.3	1.1		
kilowiis (total)	Mean	pi,d.	© 1.4 (n.d	0 .5	k, n.d, 🕺	0.6	0.6	1.0		
Overlying Wa-	Mean		- °		8.2	6.©	~ 5.9	5.5	6.1		
ter	la la	- 8	~C	N A	r a		0				
Soil extracts	ĵ∲MeanO [®]	1007	99.6	≫ 86.9	7.68	78.6		77.6	76.7		
(sub-total)	Mean	100.7	≪93.6	86:9	85.0	S 84.9 S	83.8	83.1	82.9		
PU bung*	Mean	O _{n.a.} (n.d.	ød.	©n.d.	02	0.1	0.4	0.4		
Volatile traps**	Mean	n.aQ	<u>2</u> 9	8.7***0	15.5	14.3	15.5	14.6	15.6		
Non extracted soil residue	Mean	29 .5	£4.1	6.5	\$.8	6.8	9.3	10.0	10.5		
Total AR	Mean a	101.2	10006	ÅØ2.2 &	, 106 Å	106.2	108.7	108.1	109.4	1	

 Table CA 7.1.1.2-2:
 Degradation of [cyclohexyl-1-14C]-spiroxamine at 20°C in Refesol-02-A soil under anaerobic conditions [% AR]

n.a.: not analysed, n.d. Piot detected, DAY: days after treament, DF: days post flooding

* shown to complete parent spirotomine. Almost entirely carbon choxide. *** Content range 7.1-15.8% AR for other traps sampled at the content traps and the content traps and the content traps and the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps as a spirotomic of the content traps are traps are traps as a spirotomic of the content traps are tr

B. Material Balance

Mass balances ranged from 100.6 to 109.4% AR.

C. Extractable and Non-Extractable Residues

Extractable radioactivity from the soil declined from 100.7 at DAT 0 to 86.9% AR by DAT 30. Extractable radioactivity from the soil furtheodeclined to 76.7% AR by DPF 118. Radioactivity in the overlying water increased to 8.2% AR at DPF 7 and subsequently declined to 6.1% AR after DPF 118. Non-extractable residues ONER) increased from 0.5% AR at DAT 0 to 6.5% AR by DAT 30 and further increased to 10.57 AR by DPF 118. Further investigation of NER at the end of the stud (i.e. DPF 118) showed the majority of the applied radioactivity associated with the humin fraction.

D. Volatile Radioactivity

Significant levels of volatile degradates were evolved during the aerobic phase, reaching levels of 7.1 to 15.8% AR by 30 DAT. During the anaerobic phase, the amount of volatility evolved from the 30 DAT sampling interval was at most 1.1% AR.



E. Degradation of Parent Compound

Following application of [cyclohexyl-1-¹⁴C]-spiroxamine, the amount of parent in the soil extracts decreased from 99.9% AR at DAT 0 to 65.7% AR by DAT 30 (time of flooding). During the flooded phase, the amount of parent in the combined overlying water and soil extracts changed from a botal of 62.2% AR at DPF 7 to 62.6% AR at DPF 118.

Under flooded conditions degradation of [cyclohexyl-1-¹⁴C]-spiroxamine was minimal and there was no appreciable increase in the level observed of any metabolites.

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F. Degradation Kinetics

There was no appreciable decline during the flooded phase in the level of spiroxamile. No Orther Anetic evaluation was conducted, spiroxamine is reasonable stable under maerobic conditions.

G. Isomers of Parent Compound

The isomeric composition of parent spiroxamine throughout the study is posented in Table CA 7.1.1.2-3 (content as actual % AR) and Table CA 7.1.1.2-4 (content as normalised ratio).

Table CA 7.1.1.2-3: Isomeric content of [cyclohexy]-1-14C -spiroxamine at 20°C in Refesored2-A soil under anaecobie conditions [%AR]

			<u>o</u> ř i	ncubation	time (DAT	r cr	<u></u>	ĵ
Compound		DÀŤ			Å Å	γ Ω PF		
	0 A		30 ^{AO}	Ô7 Α L	14	<u></u> 31 ^в О	759	118 ^C
Spiroxamine B1	15.9	≪"11.6	A A	7.0	~ 8 .7 °,	8.0	. 7.9	8.9
Spiroxamine B2	17.5 🔊	113	_∭0.7_©	11.3	11.3		Q 11.0	10.4
Spiroxamine A1	34.7%	24.9	22. 3	2 2.5 Å	» 22.4 ×	√1 6.5 ~	20.9	21.9
Spiroxamine A2	32.0	\$26.0 Q	21 🕵	20.7 V	228	25.2	20.4	21.5
Spiroxamine	190 .1	74.2	_ @ 4.4 _	\$ 61\$	65.2 () 60 <i>:</i> \$	60.2	62.6
(total)		, 6 [°] ,		<u>~~~~</u>		Q.		

Table CA 7.1.1.2-4: Isomeric composition of [cyclonexy]-1-14C] spiroxamine at 20°C in Refesol.02-A sul under an acrobic conditions [percentage content]

<u>k</u> y		V W	<u> </u>	ncubation	time (DAT)		
Compound	<u>\$</u>	DAT	N R	~	2	DPF		
Ű				7 A	^{>} 14 ^A	31 ^b	75 ^C	118 ^C
Spiroxamine Ba	6.9	^م 15,60	b .0	0 [°] 11.40 [°]	13.3	13.1	13.2	14.3
Spiroxamine 12	97.4 C	15.9	A6.5	18,3	17.3	18.3	18.4	16.7
Spiroxamine A1	34.6 ^{©®}	\$9 .5	₽ [™] 34.6Q	\$6.6	34.4	27.1	34.7	34.7
Spiroxanune A2	3,2°D	35.0 [©]	5,25	° 33.7	35.0	41.4	33.8	34.4
Spiroxamine	A190.1	74.3	¢4.4 °	61.5	65.2	60.9	60.2	62.6
(total)% AR				,				

DAT: days after treatment, DPO: days of flooding

A Replicate A (By; B - Replicate B only; C – Mean of replicates A and B

There was no significant change in the isomeric composition of the overall spiroxamine present in the samples over the chratic of the study i.e. 16/17/35/32 at DAT 0 to 14/17/35/34 at DPF 118.

III. Conclusions

Spirosaming did not degraded significantly in soil under anaerobic conditions (20°C).



Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) OECD 307 (required guideline). The study is consid soil. ered valid to assess the anaerobic degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in soil.

Ò

Existing studies, previously evaluated

Data Point:	KCA 7.1.1.2/01
Report Author:	1998 Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Report Year:	
Report Title:	Anaerobic aquatic metabolism of the active ingredient KWG 9168 s
Report No:	PF4288 O' , , , , , , , , , , , , , , , , , ,
Document No:	M-006010-02-1 A & C Q & C & C & C & C & C & C & C & C &
Guideline(s) followed in	US EPA Pesticide Assessment Guidelines, SubdivisionN, Chemistry:
study:	Environment Fate \$ 162-3 Anaerovic Aquatic Metabolisto Studies
Deviations from current	Yes (refer below)
test guideline:	Some minor deviation(s) not relevant for the repability of the study (described in
Previous evaluation:	study seemary, yes, evaluated and accepted of the second s
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes A V V V V V

The details of this study are fully submarised uncer point KCA 9.2.2.306.

Son photolysis CA 7.1.1.3

In view of the proposed use partern for spirotomine, as a post-emergence spray applied fungicide for application to cereals crops and vines exposure to similation sold surfaces is envisaged. However, the active substance spire amine has a low UV absorbance (molar decadic absorption > 10 L per mol per cm) therefore studies investigating soil photolysis are not required.

Nevertheless, an existing stude investigating the degradation of spiroxamine under sunlight which was evaluated during the previous EU review is available (KCA 7.1.1.3/01) and has therefore been included.

Substance	Report reference	Document no.	Comment
Spiroxatome	KCA 4.1.1.3401	<u>MS906150-01-1</u>	Submitted for first approval of spirox- amine, 1999. Reviewed under UP. Consid-
- A		<u> </u>	ered valid and acceptable.

The soil photol sis of spirox mine has been investigated in one study at 25°C. In addition, a further study has been conducted to determine the quantum yield.



Existing studies, previously evaluated

Data Point:	KCA 7.1.1.3/01
Report Author:	
Report Year:	1995
Report Title:	Photolysis of KWG 4168 on soil surfaces (according to EPA guidelines)
Report No:	PF4076
Document No:	<u>M-006150-01-1</u> © 4 × × ×
Guideline(s) followed in	EPA, Pesticide Assessment Guidelines, Subdivision N, Chemistry: Erroron-men-
study:	tal Fate § 163-1, Photodegradation studies on Soll
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted
	DAR (1997), RAR (2010), RAR (2013) 🐥 🖉 👋 🐝
GLP/Officially recog-	Yes, conducted under GLP/9111Clary recognised resting tagrittes
nised testing facilities:	A P C Q O P P
Acceptability/Reliability:	Yes where a start and a start a st

Executive Summary

The photolytic degradation of spirokamine@n soil surfaces was investigated in air-dired logn soil, prepared as a thin-layer within glass meubation vessels with a thickness of yout 20mm. The test item, [cyclohexyl-1-¹⁴C]-spiroxaming/dissolved in acetopprile/water (1999 v/v), was applied evenly to the soil surface at an application rate of 12.43 mg/kg (the target application rate of 13.3 was reported as equivalent to an annual application rate of 2 kgas./ha based on a soil mixing depth of 1 cm and soil density of 1.5 g/cm³). Treated soil samples were exposed to artificial irradiation from a Xenon lamp (with < 280 nm cut-off filter) with continuous irradiation for a period of 17 days at $25 \pm 1^{\circ}$ C. Two dark control samples wrapped in altiminium foil were treated stuthe same application rate and incubated under the same conditions

Material balances were 000.5 to 1064 % AR for irrediated samples and 101.0% AR for dark controls.

Levels of spiroxamine reduced over the study period in irradiated samples from 100.6 to 60.8% AR. The only significant degradation products observed were M01 (spinoxamine-desethyl, max 9.1% AR) and M020spiroxamine@despropyl, mox 6.1% AR) Se. metabolites already observed in studies investigating degradation under aerobic conditions. Other degradation products observed in minor amounts were M03 (spiroxamme-N-oxide maximum 6.2% AR) M15 (spiroxamine-ketone, maximum 2.7% AR, M05 (spiroxamine-hydroxy, maximum 0.4% AR and other mknown metabolites detected at maximum individual occurrence 2.0% AR, C

In the dark controls, M01 spirox mine desether is formed at 2.4% AR, M02 (spiroxamine-despropyl) is formed at 1.6% AR, M03 (spiroxamine-N-oxide) is formed at 2.1% AR, M05 (spiroxamine-hydroxy) is formed at 0.1% AR. All other unknowns are present at <0.3% AR.

The reported (non FOCUS) degradation ate of piroxamine under sunlight was equivalent to 119 solar days (Phoenix location). Photolysis of the active substance on soil is not a significant degradation pathway.

I. Materials and Methods

A. Materials ¹⁴C]-spifoxamine



	* Denotes position of $[^{14}C]$ -radiolabel ∂
Specific Activity:	3.63 MBq/mg
Radiochemical Purity:	* Denotes position of [¹⁴ C]-radiolabel
2. Test System (soil)	
The study was performed using one to	est soil as characterized in Table CA 7.1 14 1
The study was performed using one a	est soil as characterized in Table CA 7.1.15-1.
Table CA 7.1.1.3-1: Physico-chem	ical properties of test soll way of the way of the soll way and the soll way and the soll way and the solution
Parameter	Well Ranger Well Ranger Well Ranger Comparison County Comparison Comparison County Compariso
Soil Designation	Walt Dances
Geographic Location	California, USA
City	
Country	California, USA 5
Textural Classification (USDA)	$\begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & & $
Sand [50 - 2000 µm]	(***) (*
Sint $[20 - 2000 \mu\text{m}]$ Silt $[2 - 50 \mu\text{m}]$	$(\%) \qquad (\%) $
pH in H ₂ O (1:1) in CaCl ₂ (1:1)	
in H ₂ O (1:1)	0 5 × 0 08.7 4
in CaCl ₂ (1:1)	
Organic Carbon (%)	
Cation Exchange Capacity (meq/100 g)	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $
Water Holding Capacity (g H2O per 100	
dry soil)	
75% of ¥/3 bar	15.2
Microbial biomass ong microbial Skg	
soil) At 0 DAT	$\frac{\partial g}{\partial r}$ $\frac{\partial r}{\partial r}$
B. Study Design	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $

1. Experimental Conditions

Soil was air dried to a soil moisture of opproximately 10% and sieved to 2mm. Prior to use, soil was acclimatised at 20-22°C for 48 hours. Portion of fresh soil (3 g dry weight) were added to borosilicate glass incubation wessels, fitted with martz plass covers, to give a soil depth of *ca*. 2mm (surface area 10.2 cm²). The soil samples were uncubated inside static glass units with a trap for volatile products containing a polyute than plug and sodolime (to trap $^{14}CO_2$) connected to each unit.

The test dem [c β lohexyl-1- $\frac{14}{20}$]-spiroxamine (37.29 µg), dissolved in acetonitrile/water (240 µL, 1+99 v/v), was applied evenly to the soil surface (equivalent to an actual application rate of 12.43 µg/g soil dry weight, Units were irradiated continuously with light from an Heraeus Suntest xenon lamp, with two dark control samples tightly wrapped in aluminium foil to block light. The target application rate was described as 13.3 mg/kg based on an application rate of 2 kg/ha, 1cm depth and density of 1.5 g/cm³ (this is equivalent to 2.67 mg/kg using default assumptions of 5 cm depth and density of 1.5 g/cm^3). The temperature of both irradiated and non-irradiated samples was maintained at a temperature of 25 ± 1 °C



throughout the incubation period. The photolytic degradation was studied with continuous illumination under artificial sunlight for a period of up to 17 days. The artificial sunlight was provided by a xenon arc lamp with filters to cut off any radiation below 280nm.

2. Sampling

Duplicate vessels were taken from both irradiated and non-irradiated systems after 0, 3, 4, 11 and 17 days (equivalent to 80 days sunlight Phoenix location). The duplicate dark controls were also taken for analysis at 17 days.

3. Analytical Procedures

Prior to opening, headspace in the vessels were purged into volatile raps under vacuum The polyure than plugs were extracted with ethanol and analysed by LSC. ¹⁴ CO_2 was liberated from soda lime by addition of 18% HCl and captured in scintillation occktail for LSC analysis.

Soil samples were extracted at ambient temperature four times with acetonitrile (5mL) under agitation for 30 mins. SoxTec extraction was subsequently performed using methanol (30mL) at 170°C, Radioactivity extracted from soil was quantified by liquid scintillation counting (LSC). Unextracted radioactivity was determined by combustion and LSC.

Soil extracts were analysed without concentration using the primary TLC method.

- Normal phase (saturated system) with acetonitrile/water 25% ammorba ($80/18/2, x/\sqrt{v}$) mobile phase.

Confirmatory analysis (parent and metabolites) was conducted using the additional TIO methods:

- Normal phase (unsaturated system) with dichloromethane/ethyl_acetate (90/20, v/v) mobile phase.
- Reverse phase first ran (saturated system) with n hexane dichloromethane/2-propanol/ammonia (30/70/10/2 v/v/v) and second can (unsaturated system) with chloroform/ethanol (50/50, v/v) mobile phase.
- Normal phase (saturated system) with actionitrite/water 25% ammonia (95/5/0.6, v/v/v)

Degradation products were identified by comparison of the retention times of reference standards. The detection limit for a single peak in the extracts was \$0.3% of applied radioactivity.

4. Determination of degradation deinetics

The degradation rate of spiroxamine under irradiated conditions was estimated using Timme G. *et al* $(1986)^4$ and converted be equivalent days suffight order Protein location conditions.

The radiation intensity was measured via radiometer and actinometer (uranyl oxalate, 0.01M uranyl nitrate and 0.05M oxalic acid) at the beginning and end of the test. These intensity measurements were used to determine that 5.1 hours irradiation of the Sontest unit equalled 1 solar day at Phoenix, Arizona, USA

6

Results and Discussion

3

A. Data

The distribution and characterisation of radioactivity under irradiated conditions and in dark controls following application of [cyclopexyl-1-¹⁴C]-spiroxamine is summarized in Table CA 7.1.1.3-2.

⁴ Timme G., Frehse H. & Laska V. (1986). Zur statistischen Interpretation und graphischen Darstellung des Abbauverhaltens von Pflanzenschutzmittel-Ruckstanden, Part II. Pflanzenschutz-Nachrichten Bayer 39, 188-204, 1986.



Table CA 7.1.1.3-2	Degradation of [cyclohexyl-1- ¹⁴ C]-spiroxamine at 25°C in Wolf Ranch soil	
	irradiated under aerobic conditions [% AR]	

Compound	Der	Incubation time (DAT)					
Compound	Rep.	0	3	7	<u>s</u> 11	Ô7 (
	А	-	-	-	~ -	<u> </u>	
Spiroxamine	В	-	-	_ @) -	-~~	
-	Mean	100.6	88.8	71.9	62.6	608	
MO1 (minute 1	А	-	õ		- , 🏷	. ~ .	
M01 (spiroxamine-de-	В	-	- 7	<u></u>	-0	J - JU	
sethyl)	Mean	0.6	2.7	ð 7 .9	8.6	S 9.1	
	А		-	K -	<u>,0</u> -		
M02 (spiroxamine-	В	- 🕀	-	t bî	ð - S	- ~	
despropyl)	Mean	0.50	2.0	s.6	\$ 5.9	[©] 6.1	
	А	&-, ĉ	° N	× - «	× Š		
M03 (spiroxamine-N-ox-	В	0Ø		4.3	- L	A -	
ide)	Mean	A 0.5 ~	@1.5 Q	4.3	6.20	2 4.7	
	А		N - >>	A- 0		- A	
M15 (spiroxamine-ke-	B Ø	y in a	× . ~	0 ⁴ - , , , , , , , , , , , , , , , , , ,	<u> </u>		
tone)	Mean	4.1.8	~ 2. 7 ×	Ž.	× 1.4 °	1.4	
	A	[™] n.d. [™]	× - ~	~~ <u>^</u>	Š "Č	1 ² -	
M05 (spiroxamine-hy-	B	næd.	× - ~	00	Č [×]	× -	
droxy)	Mean 🔊	<u> <u> </u></u>	<u>I</u>	0.40	≫ 0.1 ‰	0.1	
	A	~(? n.d.	Ý 0	Ċ, Č,	- 0	-	
UK1	B	~ n.¢	Ø - 🦘) G	-	
~	, Mean		0.3	× 0.9.		0.7	
		n.d.	0- 4	-		-	
UK2	[™] B ≫	n.d.C	<u>, y</u> - 0	× (× -	-	
	r. Mean ~		Ĵ° 0.4₽	0.8	0.7	0.9	
UK3					-		
UK3	B &	n.d.	0	l d	_		
	Mean [©]		0.3	<i>@</i>]1.7	1.3	1.2	
	ÂQ 1	p.H. a	r -	× -	-	-	
Diffuse radioactivity &	B D	n.d. ~		~	_	-	
minor untrowns	🔍 Mean 🛇	~^ O ^v	W0.1 . O	0.9	1.5	2.0	
	A A	O 81,96	66.6 ⁴	65.60	58.81	60.74	
Ambient extract		\$ 8 .36	68,93	66.47	58.35	61.79	
	Mean O	×85.16~	-Q7.8	66.04	58.58	61.27	
		0 19.57	30.73	31.28	27.30	27.73	
Soxtec		2, 1894	31.62	30.08	32.45	23.05	
A .	Mean 🔊	× 18.86 ≪	31.18	30.68	29.88	25.39	
	[∞] A _≈	A101.53	97.40	96.88	86.11	88.47	
Total Extractables ^A	A Bo	106:50	100.55	96.55	90.80	84.84	
Total Extractables	Mean (98.98	96.71	88.46	86.65	
		3.51	2.99	5.23	12.45	12.11	
Non-extractables		0.74	3.04	4.89	8.04	13.93	
	Mean	2.12	3.04	5.06	10.24	13.02	
<u> </u>		0.0	0.50	1.53	1.85	1.88	
	B	0.0	0.93	1.33	1.83	1.88	
Z Z A	Mean	0.0	0.93	1.42 1.47	1.71	1.93	
A	NICAII	0.0	0./2	1.4/	1./0	1,74	



Compound	Don		Incubation time (DAT)				
Compound	Rep.	0	3	7	11	17 。	
	Α	0.0	0.08	0.06	0.06	0.04	
Other volatiles	В	0.0	0.06	0.07	0.07	0.04	
	Mean	0.0	0.07	0.07	0.07	0.04	
	Α	105.04	100.95	103.66	\$ 100.46	×102.50	
Total radioactivity	В	107.24	104.57	102.91	100.61	> 100.75	
	Mean	106.14	102.76	103.29	100.54	100.63	

n.d.: not detected, DAT: days after treatment,

* Complete resolution was not achieved between metabolites Movand M05 during LC analysis. A estimation of the separate amounts was made during the study but this must be viewed as approximate

A Sum of ambient and SoxTec extractions

B. Material Balance

Material balances ranged from 100.5 to 106.1% AR for ifradiated samples and 101 03% AR for samples incubated in the dark.

C. Extractable and Non-Extractable Residues

The majority of the applied radioactivity was extractable throughon the study. For irradiated samples treated with [cyclohexyl-1-¹⁴C]-spirosemine, total extractable radioactivity ranged from 104.02% AR at DAT 0 to 86.65% AR at DAT 17. The total of non-extractable residues (NFR) increased throughout the study, from 2.12% AR at DAT 0 to $k_{2.02}^{\circ}$ AR by the end of the study (DAT $k_{2.02}^{\circ}$).

For samples incubated in the dark with [cyclohexyl] -¹⁴Cf spirozamine, total extractable radioactivity was 90.14% AR at DAT 17. The total of non-extractable residues (NER) was 3.88% AR at DAT 17.

D. Volatile Radioactivity

Radiolabelled carbon dioxide accounted for 0.72 to 1.92% of the applied radioactivity in the irradiated samples. In samples oncubated in the dark 04 CO accounted for 2.99% ÅR. Only trace amounts of radioactivity were receivered from the polyarethane plug (maximum of 40.07% of applied).

E. Degradation of Pacent Compound

Levels of spiroxamine reduced over the study period in irradiated samples from 100.6 to 60.8% AR. The only significant degradation products observed were M01 (spiroxamine-desethyl, max 9.1% AR) and M02 (spiroxamine desproyl, max 6.1% AR) i.e. metabolites already observed in studies investigating degradation under aerobic conditions. Other degradation products observed in minor amounts were M03 (spiroxamine-N-oxide maximum 6.2% AR) M15 (spiroxamine-ketone, maximum 2.7% AR, M05 (spiroxamine-hydroxy, maximum 0.4% AR and other anknown metabolites detected at maximum individual occurrence of 2.0% AR

In the dark controls, M01 (spirovamine desethal) is formed at 2.4% AR, M02 (spirovamine-despropyl) is formed at 2.1% AR, M03 (spirovamine-hydroxy) is formed at 0.1% AR, All other unknown are present at <0.3% AR.

F. Degradation Kinetics

An experimental DT_{50} of 25 days invaliated exposure was calculated. Correcting the half-life for solar days gives an estimation of the environmental half-life under solar conditions at Phoenix of 119 days. The experimental data has not been re-evaluated according to the FOCUS guidance document on degradation whetice (FOCUS, 2014) as the minimal degradation observed was sufficient to confirm that photolysis of the active substance on soil is not a significant degradation pathway.

E Conclusions

The degradation rate of [cyclohexyl-1-¹⁴C]-spiroxamine was only slightly enhanced in the presence of sunlight. The only significant degradation products observed were M01 (spiroxamine-desethyl, max 9.1% AR) and M02 (spiroxamine-despropyl, max 6.1% AR) i.e. metabolites already observed in studies investigating degradation under aerobic conditions. Other degradation products observed in minor



amounts were M03 (spiroxamine-N-oxide, maximum 6.2% AR), M15 (spiroxamine-ketone, maximum 2.7% AR, M05 (spiroxamine-hydroxy, maximum 0.4% AR and other unknown metabolites detected at maximum individual occurrence of 2.0% AR.

The reported (non FOCUS) degradation rate of spiroxamine under sunlight was equivalent to 100 solar days (Phoenix location). Photolysis of the active substance on soil is not a significant degradation paraway.

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2012

The study was conducted to study guideline(s) EPA 163-1 (similar to required guideline). The study is considered valid to assess the Photodegradation of [cyclohexy] 1-14Cl spiroxamine on soil.

CA 7.1.2 Rate of degradation in soil

 \bigcirc

Overview:

New and existing laboratory route and rate studies considered reliable were evaluated for degradation rates normalized to reference conditions following FOGUS kinetics (2014). DT_{50} and DT_{90} values were calculated both for an evaluation of possistence and for comparison with relevant study triggers. Modelling DT_{50} values and formation fractions (f.f.) were calculated for use in deriving endpoints for predicting environmental concentrations. The data were used to attempt calculation of kinetic endpoints for spiroxamine and its metabolites (101 (approxamine-desethyl)), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid).

Input data were generated according to the data handling recommendations of FOCUS (2014a). The kinetic modelling of the aboratory date was conducted using the CAKE v3.4 software package. The FOCUS (2014a) flowcharts for calculating persistence and modelling endpoints have been followed. The spiroxamine calculated DT₅₀ values rapiged from 7.2 to 142 days and DT₉₀ values ranged from 81.2 to 6% days. The geometric mean of the unetric analysis DT₅₀ value was 75.4 days. M01 (spiroxaminedesethyl) persistence DT₅₀ values ranged from 28.9 to 555 days and DT₉₀ value range from 95.8 to >1,000 days. The geometric mean DT_{50} value was 168.6 days. The arithmetic mean of the formation fraction from parent vas 0.483. The M02 α spiroxamine-despropyl) persistence DT₅₀ values ranged from 26.6 to the CUS defa a value of 1,000 days and DT₉₀ values ranged from 88.2 to 3,320 days (again the FOCLUS default). The geometric mean DT₅₀ value was 219.1 days. The arithmetic mean of the formation fractions from parent was 0.138. The M03 (spiroxamine-N-oxide) persistence DT₅₀ values ranged from 46.7 to 107 days and DT₉₀ values ranged from 55.4 to 358 days. The geometric mean DT₅₀ value was 46.4 days. The arithmetic mean of the formation fractions from parent was 0.149. Acceptable fitting could only be performed for persistence endpoints in one soil for M06 (spiroxamine-acid) resulting in a number of presented default values. The persistence DT₅₀ value was 49.6 days to 1,000 days whilst DT_{90} values was 165 days to 3,320 days. The geometric mean of modelling DT_{50} values was, therefore, calculated as 479.6 days but this is highly influenced by the default values and the real DT_{50}



is likely much shorter (based on the one reliable kinetic fit). The formation fraction from parent was 0.0947.

The dissipation behaviour of spiroxamine was investigated in Europe in eighteen field sites across five. studies. The study design for each study did not exclude surface loss processes such as photonysis or volatilisation; therefore, they are considered to follow the "legacy" study design according to EESA (2014) guidance. The data from these studies are considered appropriate to derive persistence/trigger and modelling endpoints and were analysed using the CAKE version 3.4 (2020) software package to derive suitable kinetics. Thiskinetic analysis to determine DT₅₀ and DT₅₀ values for comparison with relevant study triggers and persistence criteria was performed using non-hormalised data, in accordance with the flowcharts for persistence/trigger endpoints provided bo FOCUS (2014). Likewise, the O flowcharts for calculating modelling endpoints provided by EFSA (2014), and using data that have been normalised to reference conditions (20°C and pF 2 soil moisture contend) and subject to timestep pormalisation procedures, were followed to derive DegT_{50, matrix} values; these endpoints were used for the selection of appropriate modelling values for use with regulatory Predicted Environmental Concentration (PEC) models.

The spiroxamine persistence/trigger DT 5 values ranged from 0.5 to 59,6 days and DT 90 values ranged from 43.5 to 433 days. The spiroxamine modelling D 250 values (at 20°C and pF 20 rangel from \$6.1 to 133 days, with a geometric mean of 42.9 days. If not including propped trials model and DT 50 values (at 20°C and pF 2) ranged from 23 A to 78 days, with a geometric mean of 43.9 days

M01 (spiroxamine-desethyl) persistence trigger DT₅ values Danged from 7.8 to 223 days and DT90 values ranged from 59 to 742 days. Modelling DT₅₀ values ranged from 23.4 to the default 1,000 days, with a geometric mean of 66.2 days, Formation factions were not determined as formation may have been affected by photolytic factor according to EFSA (2014). If not including cropped trials, modelling DT₅₀ values (at 20°C and pF 2) tranged from 29.4 to 2000 days, with a geometric mean of 89.8 days.

M02 (spiroxamine-despropy) persistence/trigger DT₅₀ values ranged from 21 to 161 days and DT₉₀ values ranged from 69.6 to 533 days. Modelling DTF values ranged from 27.7 to 196 days, with a geometric mean of 69.1 days. Formation fractions were not determined as formation may have been affected by phoolytic actors according to FFSA (2014). If not including cropped trials, modelling DT₅₀ values (at 20°C and pF 2) ranged from 44.3 to 196 days with Decompetic mean of 93.8 days.

An assessment of the statistical difference of the kinetic evaluation of the lab and field studies was performed using the ECSA endpoint XL. This assessment determined that the field studies were statistically different to the lab dataset and as ouch modelling endpoints are taken from the field studies in

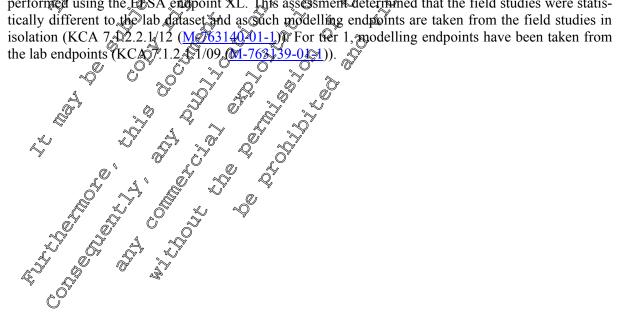
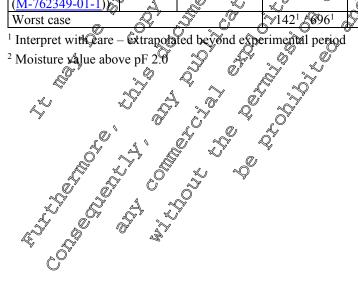




Table CA 7.1.2-1:	Overall summary of best-fit kinetic parameters (persistence endpoints) for	
	aerobic degradation of spiroxamine in soil (laboratory studies) $\mathscr{D}_{\mathfrak{g}}^{\circ}$	

			r or spiroaum		J	
Soil	pH (H2O)	Temp (°C) / % MWHC	DT ₅₀ / DT ₉₀ (days)	Normalised DT ₅₀ / DT ₉₀ (days)	χ^2 error	Kineticorodel
BBA 2.2/Speyer 2.2 (KCA 7.1.1.1/01 (<u>M-006135-01-1</u>))	6.3	20 / 40 ²	66.6 / 296 ¹	66.6/296 ¹	۵۶ 3.2	O ^T DFOP
Laacherhof (KCA 7.1.1.1/02 (<u>M-006141-01-1</u>))	8.1	20 / 40	22.5 / 128	14.2 / 80.9	3.3 2	DFOF
Monheim 3 (KCA 7.1.1.1/02 (<u>M-006141-01-1</u>))	6.5	20 / 40	33.29 [°] 176 ¹ .	30,77 160,27		
Howe (KCA 7.1.1.1/02 (<u>M-006141-01-1</u>))	7.1	20 / (75% 0.33 bar) X	29.90168 ¹	23.6 932.7		GFOP OF
Wolf Ranch (KCA 7.1.1.1/04 (<u>M-006148-01-1</u>))	7.8	20 / (75% of 0.33 par)	⁽⁴⁾ √75 / 29 9 ¹	\$3.0 / \$11.1 ¹		DFOP
Hoefchen am Ho- henseh (KCA 7.1.1.1/05 (<u>M-303803-01-1</u>))	7.0		9.2 / 98.6 F 2.7 0	4, 7.2 / 9 .6		∽ ∽ DFOP
Longwoods (KCA 7.1.1.1/06 (<u>M-762349-01-</u> <u>1</u>)0)	7.8 7.8 6 7	520 / pK2.0	013.1781.2 ·	013.1%81.2 %		DFOP
Refesol 02-A (KCA 7.1.1.1/06 (M-762349-0)		\$0 / pt 2.0	116 / 510 ¹	3116 / 40 ¹	S 1.9	DFOP
Refesol 03-G (KCA 7.1.1.1.9/06 (<u>M-762349-01-1</u>))	5.9 5.9	20 ⁹ pF 20		#421 / 696 ¹	1.5	DFOP
Speyer 65 (KCA 7.1.1.1/06 (<u>M-762349-01-1</u>))	97.3 Å	200 pF 2.0	1351/51	1371 / 514 ¹	1.7	DFOP
Worst case			≫142 ¹ €96 ¹	§ 142 ¹ / 696 ¹		





	aerobic d	egradation o	of spiroxamine in	n soil (fiel	d studies)		Ŵ	7
Study	Soil (USDA)	Location	pH (CaCl2)	DissT50 (days)	DissT90 (days)	χ2 er- ror (%)	Kinetics	<i>S</i>
KCA	Silt loam	Höfchen	6.5	13.8	145	11.8	J DFOPO	
7.1.2.2.1/01 (<u>M-</u>	Loam	Laacher Hof	6.8	32.6	196	6.3	DEOP	Ô
$\frac{006116-01-}{1}$	Sandy loam	Elm Farm/ Thurston	7.5 ക	0.8	Ç 197	ZĂ	DFOP) ,
<u>1</u>)	Loamy sand	Pakenham	7.3	0.5 Q	132	@ 8.2	DFØP	â
	Silt loam	Höfchen	64	5600	393 🌋	9 8.1Q	FÓMC	, V
KCA 7.1.2.2.1/02	Sandy loam	Laacher Hof	6.6	20.1	¢ 127	Srs .	DFOP	7
(<u>M-</u>	Sandy loam	Maasen	[▼] 5.9 °	0 [×] 8.4 [×]	2571	⊳ ^10.6 ≪	DFØP	
<u>006126-01-</u> <u>1</u>)	Silt loam	Swisttal- Hohn	5.9.0 5.9.0 0 0 0 0 0 0 0 0 0 0 0 0	59	Ø84.7 Ø	7,9 0.3	FOMC	
	Clay loam	Albig	× 7.8	6.0	74	6.3	DFQ P	
KCA	Sandy loam	Elm Fatrm/ Thurston &			×732	5.2 5.2 5.3	Brop	
кса 7.1.2.2.1/03	Sandy loam	Patenham	<u> </u>	<u>_</u> @9.5	192	<u>6.3</u>	🔊 DFOP	
(<u>M-</u>	Sandy loam	Fim Farm Thurston	Q 72 6	9.10	A33	6.7°	DFOP	
<u>006127-01-</u> <u>1</u>)	Sandy loam	Pakenham	TO DE	12,2	[©] 247 °	9.Q	DFOP	
<u>1</u>)	Silt loam	Touf- freville		~ 6.1 ×	58 [°] A	3.8	DFOP	
KCA	Loam 🖓 🐧	Lauchan		· 2.1		9.1	DFOP	
7.1.2.2.1/04 (<u>M-</u> 006128-01-	Silty@fay loam	Filetto	57 7.6 ²	59.6°	295	16.9	DFOP	
1)					_0			
<u>I)</u> KCA	U Longarda 🖓	Isaudun		2.1 ×	93.3	3.9	DFOP	
7.1.2.2.1/05		O &		Ő "Ø	• 75.5	5.7	DIGI	
(<u>M-</u> 006129-04	Sandy loam	©Nogarole Rosca	0 ⁻⁷ 7.9 ⁷ 0	3.5	43.8	1.9	DFOP	
<u>1) </u>				<u> </u>				
*			Worst Case	9.1 ⁹	433	-		
		Ĵ z .	H depondence		N	ю		
			<u></u> 8 8					

Table CA 7.1.2-2:	Overall summary of best-fit kinetic parameters (persistence endpoints) for
	aerobic degradation of spiroxamine in soil (field studies)

CA 7.1.2.1

Laboratory studies

CA 7.1.2.1.1 Acrobic degradation of the active substance

The rate of aerobic degradation in soil of the active substance has been investigated, as part of the studies listed under Point CA 7.1.1.1. in five studies (KCA 7.1.2.1.1/01 to KCA 7.1.2.1.1/05) which were evaluated during the previous EL review. In addition:

one new study (KCA 7.1.2.1.1/08 (<u>M-762349-01-1</u>)) has been conducted mainly to address the new requirements of EPSA, 2019¹

- two torther studies were included during the last evaluation and therefore they have been included for completeness (KCA 7.1.2.1.1/06 (M-036125-01-1) provides a comparison of laboratory and field degradation studies each individually summarised more fully elsewhere and CCA 7.1.2.1.1/07 (M-347082-01-1) provides a kinetic evaluation of degradation rates from laboratory soil studies which has since been superseded)

- one new study (KCA 7.1.2.1.1/09 (M-763139-01-1)) has been conducted to provide an up-to-



date kinetic assessment of degradation rates observed in all laboratory studies to modern requirements (FOCUS 2014²)

1	,		
Substance	Report reference	Document no.	Comment
Spiroxamine	KCA 7.1.1.1/01; KCA 7.1.2.1.1/01	<u>M-006135-01-1</u>	
Spiroxamine	KCA 7.1.1.1/02; KCA 7.1.2.1.1/02	<u>M-006141-01-1</u>	Submitted for Grist approval of spirox amine, 1999. Reviewed under UP. Consid- ered valid and acceptables
Spiroxamine	KCA 7.1.1.1/03; KCA 7.1.2.1.1/03	<u>M-006141-01-1</u>	
Spiroxamine	KCA 7.1.1.1/04; KCA 7.1.2.1.1/04	<u>M-006148-00-1</u>	
Spiroxamine	KCA 7.1.1.1/05; KCA 7.1.2.1.1/05	<u>M-303803-01-1</u>	Submitted for first revewal of spirox amine, 2010. Review of under UP. Consid-
Spiroxamine	KCA 7.1.2.1.1/06; KCA 7.1.2.2.1/06	M-036125401-1	eredvalid and acceptable 4
Spiroxamine	KCA 7.1.2.1.1/07	M-347082-01-1	
Spiroxamine	KCA 7.1.1.1/06; KCA 7.1.2.1.1/08	<u>M. 162349 01-1</u>	New data not yet reviewed under UP.
Spiroxamine	KCA 7.1.2.1.1/09	<u>M-763139-01-1</u>	

The rate of degradation of spirotamine in soil under aerobic conditions in laboratory studies has been investigated in ten soils. A new kinetic evaluation has been performed (see KCA 7.1.2.1.1/09 (M-763139-01-1) below) and the resulting best fit kinetic parameters (persistence endpoints) are summa-rised in Table CA 7.1.2-1.7

New studies, not previously valuated

	KCA,7.1.2,1.1/08
Data Point:	KCA(7.1.2, 1.1/08 X X X X
Report Author:	
Report Year:	2020
Report Title.	[14C] spiroxamine: Route and rate of degradation in four soils under aerobic con-
	ditoris at 20°C - Interim report $\sqrt[n]{0}$
Report No:	× C/19/055 0 × × 4
Document No:	<u>M1-76249-014</u> m O A
Guideline(s) followed in	(EUCNo. 283/2013(PC) No., 1107/2009
study:	QEED 300 (2002) 0 0 0
· · · · · · · · · · · · · · · · · · ·	Sone y y y
test guideline:	
Previous O valuation:	No not previously anomitted
GLP#Officially recog#	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/R@iability:	Yest

The details of this study are fully summarised under point KCA 7.1.1.1/06.



Existing studies, previously evaluated

Data Point:	KCA 7.1.2.1.1/01
Report Author:	
Report Year:	1994
Report Title:	Aerobic degradation of KWG 4168 in BBA soil 2.2 2
Report No:	PF4027
Document No:	M-006135-01-1
Guideline(s) followed in	BBA: Part IV, 4-1
study:	
Deviations from current	Yes (refer below)
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in
C	study summary)
Previous evaluation:	study summary) yes, evaluated and accepted DAR (1997) RAR (2010) BAR (2017)
	DAR (1997), RAR (2010), BAR (2017)
GLP/Officially recog-	Yes, conducted under GLEOfficially recognised Osting facilities
nised testing facilities:	
Acceptability/Reliability:	Yes A Y Y Y Y Y
Data Daint:	
Data Point:	KCA7.1.2.1.102
Report Author:	
Report Year:	
Report Title:	Aerobi degradation and metabolism of KWG 4168 in soil
Report No:	PF4034 \$ \$ \$ \$ \$ \$ \$ \$ \$
Document No:	M-036141-0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
Guideline(s) followed in	BBA: Part IV, 40 5 5 0 4
study:	
Deviations from entrent	Yes (refer below)
test guideline; O	Some minor deviation(s) not relevant for the reliability of the study (described in study summary)
Describer of the strength of t	
Previous evoluation:	yes, evaluated and accepted DAR (1997) RAR (2010) RAR (2017)
Ê ^Q ()	The degradation rates of spiroxamme (1997) and (2008)) were
· × · · ~	Ancluded in the following survey ($\underline{M-0.00125-01-1}$).
GLP/Officially recog-	Yes, Conducted under GLP/Officially, recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	
Acceptantity (Ketiantikev)	Y_{0}

The details of this study are fully summarised under point KCA 7.1.1.1/02.



Data Point:	KCA 7.1.2.1.1/03
Report Author:	0
Report Year:	1994
Report Title:	[Cyclohexyl-1-14C] KWG 4168 residues in following crops
Report No:	PF4043
Document No:	<u>M-006096-01-1</u>
Guideline(s) followed in	US EPA §165-1 Confined accumulation studies on rotational crops, 1983
study:	
Deviations from current	Yes.
test guideline:	OECD 502 guideline (January 2007) requires the plant-back intervals for suc
	ceeding crops. The longest interval of 270 to 265 days to represent crops sown
	the following year was not conducted in this study.
Previous evaluation:	yes, evaluated and accepted by the second seco
	DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes A R Q O O O A
1 2 2	
The details of this study a	tre fully summatized under point KCA 7.1. K 1703 2 2 5
	are fully summarised under point KCA 7.1.1(1/03:0)
Data Point:	KCA 7.1.2.1.1/04
Report Author:	
Report Year:	
Report Title:	Depredation and metabolism of KWG 41 @ in soil aerobic soil metabolism
Report No:	PF4274 Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
Document No:	$\frac{1}{9}$
0	
Guideline(s) followed in	US ERA Pesticide Assessment Guidelines, Subdivision N \$162-1: Aerobic soil metabolism studies (1982)
study:	
	Yes (refer below) Some nimor deviation(s) not belevant for the reliability of the study (described in
test guideline:	
Previous evaluation:	yes, evaluated and accepted at the second at the second at the second accepted at the second at
Trevious evaluation.	\mathcal{R} AR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GLP/Officiall@recograded testing facilities
nised testing facilities:	
Acceptability/Reliability:	
The details of this study a	re full@summarised under point KCA 7.1.1.1/04.
Q.	
Data Dainti ©	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Data Point: ©	
Report Author:	
Report Sear:	2068
Report Title:	1.3-Diaxolane 14C spiroxamine: Metabolic screening for degradation path-
	ways nøder accobic conditions in soil
Report No:	MEF-08/214
Document No:	MØ03805901-1 Q
Guideline(s) followed in	U 95/36/EC amending 91/414/EEC; OECD 307; US EPA, Subdivision N, Sec-
	Dion 162-1 9
Deviations fromourrent	Note
test guideline	
Previous evaluation	ves, evaluated and accepted
	RAR (2010), RAR (2017)
GLP/Qfocially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	, ,
Acceptability/Reliability:	Yes

The details of this study are fully summarised under point KCA 7.1.1.1/05.



Data Point:	KCA 7.1.2.1.1/06
Report Author:	
Report Year:	2000
Report Title:	Dissipation of spiroxamine in soils - survey of results from studies conducted un- der field and laboratory conditions
Report No:	MR-251/00
Document No:	<u>M-036125-01-1</u>
Guideline(s) followed in	BBA: Part IV, 4-1
study:	
Deviations from current	None \mathcal{L} \mathcal{O}^{φ} \mathcal{L} \mathcal{O}^{φ} \mathcal{O}^{φ}
test guideline:	
Previous evaluation:	yes, evaluated and accepted where the second s
	RAR (2010), RAR (2019)
GLP/Officially recog-	No, not conducted under GLPOfficially recognised testing facilities v
nised testing facilities:	
Acceptability/Reliability:	Yes A m Q Q A O Y Y

Executive Summary

This study was previous considered during the evaluation of spiroxamide (RAR (2010), RAR (2017) and is therefore included again for completeness. The study compares laboratory vesus field degradation rates derived in other studies namely the aboratory degradation rates observed in studies KCA 7.1.1.1/01 (M-006135-01-1); KCA 7 1.1.1/02 (M-006141 01-1); KCA 7.1.1.1/04 (M-006148-01-1); KCA 7.1.1.1/05 (M-303803-07-1) and KCA 7.1.1.1/06 (M-762249-01-2) versus the rates observed in field studies KCA 7.1.2.2.1/01 (M-006127-07-1); KCA 7.1.2.2.1/04 (M-006128-01-1); KCA 7.1.2.2.1/03 (M-006127-07-1); KCA 7.1.2.2.1/04 (M-006128-01-1); KCA 7.1.2.2.1/05 (M-006129-01-1); KCA 7.1.2.2.1/03 (M-006127-07-1); KCA 7.1.2.2.1/04 (M-006128-01-1); and KCA 7.1.2.2.1/05 (M-006129-01-1)). Evaluation of the degradation cates observed in laboratory and field studies is superseded by the new kinetic evaluations performed in studies KCA 7.1.2.4.1/09 (M-762-39-01-1) and KCA 7.1.2.2.1/12 (M-763140-01-1), espectively

Assessment and conclusion by applicant:	
The study and its data are considered as supplementary data with the use in risk as	sessment.
Data Point: Q KC\$7.1.2.0.1/07 & S	
Report Author	
Report Year: 020090 AS 0	
Report Tote: S Kingtic evaluation of laboratory soil degradation studies with	KWG4168-N-oxide
to determine input parameters for model calculations	
Reposer No: 2 AFEF-090309	
Document No: $\sqrt[4]{M-347082-01-Y}$	
Guideline(s) followed in nor applicable	
study:	
Deviations from current None	
test guideline: \mathcal{A} \mathcal{A}	
Previous evaluation: xes evaluated and accepted	
\mathcal{A}^{*} Or \mathcal{A}^{*} & KAR (2010), RAR (2017)	
GLOOfficially recognised testing fa	acilities
nised testing facilities:	
Acceptability/Reliability: Yes	

Executive Summary

This study was previous considered during the evaluation of spiroxamine (RAR (2010), RAR (2017)



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and is therefore included again for completeness. The study performs a kinetic evaluation according to FOCUS 2006⁵ of the degradation of spiroxamine metabolite M03, where observed, reported in studies KCA 7.1.1.1/01 ($\underline{M-006135-01-1}$); KCA 7.1.1.1/02 ($\underline{M-006141-01-1}$); and KCA 7.1.1.1/04 ($\underline{M-006448}$, <u>01-1</u>). The kinetic evaluation reported in this study is superseded by the new kinetic evaluation performed in study KCA 7.1.2.1.1/09 ($\underline{M-763139-01-1}$) on all the same laboratory soil degradation studies.

Assessment and conclusion by applicant:

The study and its data are considered as supplementary that a with no use in risk assessment

Data Point:	KCA 7.1.2.1.1/09
Report Author:	
Report Year:	
Report Title:	Spiroxamine: Kinetie assessment of Taboratory aerobic soil studies
Report No:	0471836-KIN2 A & Q & Q & Q & Q & Q & Q & Q & Q & Q &
Document No:	$\underline{M}_{-763139-01-1} \xrightarrow{\sim} \xrightarrow{\sim} \xrightarrow{\sim} \xrightarrow{\sim} \xrightarrow{\sim} \xrightarrow{\sim} \xrightarrow{\sim} \sim$
Guideline(s) followed in	FOCUS 2000 FOCUS 2014
study:	
Deviations from current	None No, not previously submitted No, not previously submitted Not previously submitted Not previously submitted Not previously submitted Not previously submitted Not previously Not previo
test guideline:	
Previous evaluation:	No, not previously submitted a construction of the second se
GLP/Officially recog-	not applicable Yes
nised testing facilities:	
Acceptability/Reliability:	Yes A A A A A A A A A A A A A A A A A A A
Executive Summary	$\frac{ ' \operatorname{Yes} \mathcal{A}_{\mathcal{A}}_{\mathcal{A}_{\mathcal{A}_{\mathcal{A}_{\mathcal{A}_{\mathcal{A}_{\mathcal{A}}_{\mathcal{A}_{\mathcal{A}_{\mathcal{A}}_{\mathcal{A}_{\mathcal{A}}}}}}}}}}$

Executive Summary

The degradation of spirocomine and the formation of its metabolites has been investigated in the laboratory in five [cyclohexy] 1^{-14} C] or [k3-dioxolane-¹⁴C]-spiroxamine applied studies with eight EU soils and two US soils included under aerobic conditions (see studies under CA 7.1.1.1/01 (<u>M-006135-01-1</u>), CA 7.1.1.1/02 (<u>M-006141-014</u>), CA 7.1.1.1/04 (<u>M-006148-01-1</u>), CA 7.1.1.1/05 (<u>M-303803-01-1</u>) and CA 7.1.1.1/06 (<u>M-702349.01-1</u>))

The kinetic endpoints from these studies according to the guidance of FOCUS (2014^2) were re-calculated. DT₅₀ and DTF values were calculated for evaluation of persistence and for comparison with relevant study triggers. Modelling DT₅₀ values and formation fractions (f.f.) were calculated for use in deriving endpoints for podicting environmental concentrations. The data were used to attempt calculation of kinetic endpoints for spurchanger and its metabolites M01, M02, M03 and M06. Input data were generated according to the data bandling recommendations of FOCUS (2014). The kinetic modelling of the laboratory data was conducted using the CAKE v3.4 software package. The FOCUS flowcharts for calculating persistence and modelling endpoints have been followed.

The derived persistence and modelling endpoints for spiroxamine, M01, M02, M03 and M06 are summarised in Table CA 7.1.2.1.1.4 and Cable CA 7.1.2.1.1-2, respectively.

Materials and Methods

The soil degradation data presented in studies under CA 7.1.1.1/01 (<u>M-006135-01-1</u>), CA 7.1.1.1/02 (<u>M-006141-01-2</u>), CA 7.1.1.404 (<u>M-006148-01-1</u>), CA 7.1.1.1/05 (<u>M-303803-01-1</u>) and CA 7.1.1.1/06

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⁵ FOCUS (2006) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp.



(M-762349-01-1) has been re-evaluated according FOCUS guidelines (2006, 2014).

Input data were generated according to the data handling recommendations of FOCUS (2014a). Where true replicates were available for each sampling time, all values for each soil were used individually in *A* the optimisation. The amounts of parent at time zero were set to the initial mass balance value $\hat{\mathbf{D}} \hat{\mathbf{e}}$, the total radioactivity recovered in the 0 day soil as a percentage of the radioactivity applied) corrected for radiochemical purity. The initial amounts of metabolites in parent dosed studies were set to 0° . If feeessary, the handling of values below the LOD and LOQ was performed according to the procedure recommended by FOCUS (2014a) as follows:

- All values between LOD and LOQ were set to the actual measured value. If the actual measure • concentration was not reported, $0.5 \times (LOQ + LOD)$ was used.
- All samples < LOD just after detectable appoints were set to 0.5% LOQ •
- All samples after the first non-detect (< LOD) were mitted unless positive detections above LOQ were made later in the experiment. In that case, samples were included up to the first nondetect (< LOD) which is not followed by later postave satisfies above LOQ. For metabolites the same procedure was applied to samples before the first detectable and unt.

All values reported as not detected (n. 6, 0% or not reported (n.r.) were or side as SOD. For time zero, the mass balance is used as the parent residue value corrected for ratiochemical parity. Full details of the reported residues (% AR) and the values considered in the fittings are detailed in the study report (pages 20-26). m

The kinetic modelling of the aboratory data was conducted using the CAKE (version 3.4) software package. The data were evaluated with the single first order (SFO) and first order multi-compartment (FOMC) models, and if necessary, with the double first order in parallel (DFOP) and hockey-stick (HS) models. Data were directly fitted, unsweighted, with the complete usable data set and unconstrained initial concentration (M_0) . To give the best chance of finding the global minimum (i.e., the true best-fit values) the model default initial parameters were examined and amended if necessary to provide appro-

Kinetic assessments were performed using the degradation schemes presented in Figure 7.1.2.1.1-1. As CAKE v3.4 can only simulate 3 primary metabolites, 1006 was modeled in a separate run. In the initial fitting, all possible flows to sink compartments were included. Based on the results of the initial estimation, flows were kept for removed for simplification of the degradation scheme, as recommended by

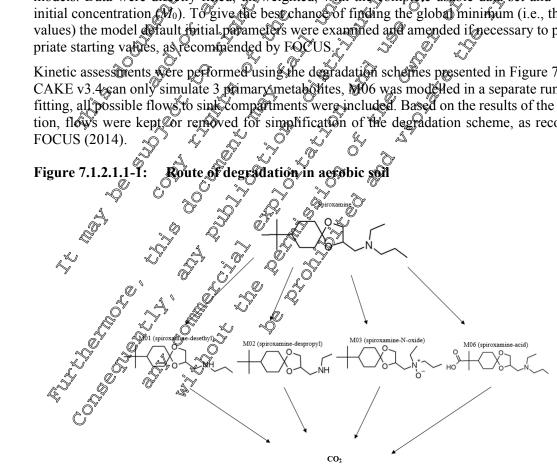
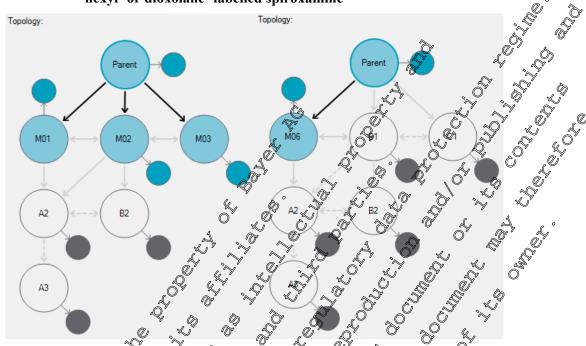




Figure 7.1.2.1.1-2: Degradation scheme used in kinetic analysis of all soils treated with cyclohexyl- or dioxolane- labelled spiroxamine



The acceptability of kinetic fits was judget both visually and according to the χ^2 error and the t-test functions as recommended by FOCUS. The visual assessment is recommended as the main tool for assessing goodness of fit. However, it is also recommended that a χ^2 error of less than 15% and a t-test probability of greater than 95% (p < 0.05) for estimated degradation rate constants indicate an acceptable fit. The χ^2 error was not considered as an absolute cut-off criterion as FOCUS guidance indicates that there will be cases where the error is higher than 15% but the fit still represents a reasonable description of the degradation behaviour. It such situations, examination of plots of residuals for systematic error is considered important.

The t-test assesses whether degradation rate constants differs significantly from zero (i.e., no degradation). Alternatively, confidence intervals can be examined on this assessment, the t-test was chosen for assessing confidence in rate constants. When fitting the FOMC model, FOCUS guidance indicates that the t-test is not appropriate as a measure of confidence for the gamma-distribution parameters α and β . Therefore, if a FOMC fit indicated slow degradation, confidence intervals for β were examined to determine if they were high compared to the parameter estimate, which would indicate that the parameter estimate was not reliable.

When calculating modelling endpoints for a metabolite, it was considered important to derive a formation fraction wherever possible. In the FOCUS flowsheets, if the SFO fit for a metabolite is not considered acceptable, a case-by-case decision is required. The first option given is to assess the decline of the metabolite after its maximum (top-down' pethod). However, this method does not allow formation fraction assessment. The second option given as to fix the formation fraction to a worst-case value (usually 1) and use this in combination with a worst-case DT_{50} (usually 1000 days). However, this method almost always results in a clear overestination of observed metabolite residues. The final option given is to use alternative – but conservative – estimates that describe the observed patterns. In this assessment, alternative – but conservative estimates were chosen, implemented by fixing the formation fraction to the fitted value and using this in combination with a conservative DT_{50} , or vice versa. The parameter to amond and use this in combination with a conservative DT_{50} , or vice versa. The parameter to anonal and use the observed metabolite residue and nong the in combination with a conservative DT_{50} , or vice versa. The parameter to anonal and use value were chosen based on expert judgement and iterative amendments to give a conservative description of the observed metabolite residue pattern.

The FOCUS (2014a) flowcharts for calculating persistence and modelling endpoints were followed.

If necessary, the kinetic endpoints derived for each soil were normalised to FOCUS reference conditions



(soil temperature of 20°C and soil moisture content equal to pF 2) following the procedures recommended by FOCUS.

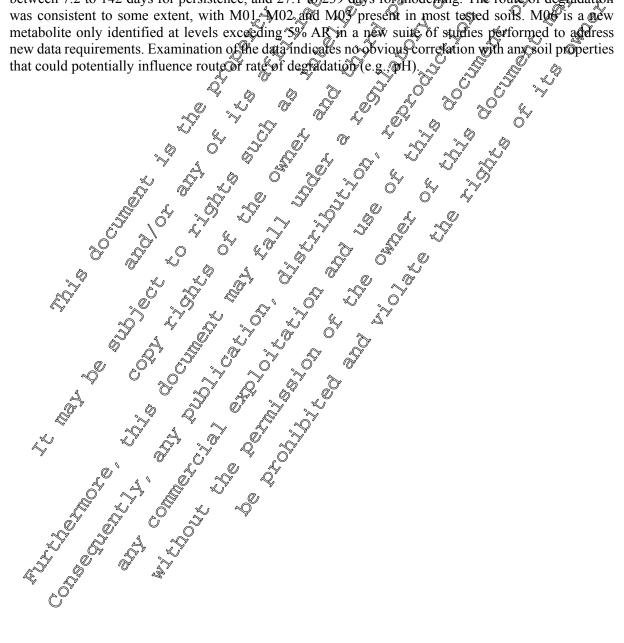
II. **Results and Discussion**

Each soil has been considered following the steps in the flowcharts and the considerations are discussed in detail in Appendix 3: (of this document). Parent endpoints were derived from kinetic fits of parent only data (i.e., not including metabolite data) in order to avoid changes in metabolite evaluations influ-encing parent endpoints. Metabolite endpoints, including formations fractions, were derived from final kinetic fits (i.e., including all data). The full outputs from all kinetic fits used, including the initial parameters and flows, are presented in full in the study report (Appendix of the study report)

The resulting persistence or best-fit endpoints are provented in Table CA 7, 1.2.1, P1.

The resulting modelling endpoints are presented in Table CA 7:1, 10

It is noted that the rate of degradation of spiro samine saries between soils with a range of DT50 Values between 7.2 to 142 days for persistence, and 27.1 to 239 days for modelling. The route of degradation was consistent to some extent, with M01, M02, and M09 present in most tested soils. M06 is a new metabolite only identified at levels exceeding 5% AR in a new suite of studies performed to address





Soil properties				Spiroxa	mine			A M	01	La OPer		NO.		
Soil name	рН (H2O)	Temp (°C) / % MWHC	DT50 / DT90 (days)	Normal- ised DT50 / DT90 (days)	χ ² er- ror (%)	Kinetic model	DT 50 / DT 90 (days)	Normal- ised DJ 59 (DJ 90 (days)		Kinetic	DT50 DT50 Q(days)		χ ² efs <i>C</i> For (%) <i>C</i>	Kinetic
CA 7.1.1.1/01 (N	1-006135-0					. 62		/ 40			<u> </u>	C	f.Or	
BBA 2.2/ Speyer 2.2	6.3	20 / 402	66.6 / 296 ¹	66.6/ 296 ¹	3.2	19FOP	\$5.3 ⁺ / 1,840 ¹ ,	\$5 ¹ / 1,840 ⁴	A	OFOP/ SFQ	3,320 ³	× 9,000 / 5 3,320	NA	DFOP/ SFO
CA 7.1.1.1/02 (N	<u>1-006141-0</u>	<u>)1-1</u>) 1995			4 De	100			× ⁰ ^y	1024	0 ³	aí		
Laacherhof	8.1	20 / 40	22.5 / 128 ¹	14.2 / 80.9 5		DFOP	1067 ¹ / ▷ 554 ¹ ⊘	350.80°		SEC	3,3203 *	0~1,000/ 3,320 ³	NA	DFOP/ SFO
Monheim 3	6.5	20 / 40	33.2 / 176 ¹	30 2 60.2	J.S.O	DFOP	$366^{1}/$	543.3 ¹ / @1801.8 ¹	6 41	DPOP/ SFQ_	3 ,320 ³	0,3,320 ³	NA	DFOP/ SFO
Howe	7.1	20/ 75% 1/3 bar	29.9 168	23.66 132.71	-133M	DEOP	202 LV 0 21	159.6 ¹ / \$30.9 ¹	j.7	DFOP/ SFO	1:0007 3,320 ³	1,000 / 3,320 ³	NA	DFOP/ SFO
CA 7.1.1.1/04 (N	1-006148-0	<u>1-1) 1997</u>	1,¢	Ope		\mathcal{V}^{r} \mathfrak{h}	Jen je				<i>y</i>	,		L
Wolf Ranch	7.8	20/ 75% 1/3 bar	75 / 299 ¹	53.0%	3.9	BFOP	78 D	55027 ©183.61	18.1	DFOP/ SFO	95.4 / 317 ¹	67.4 / 223.8 ¹	19.0	DFOP/ SFO
CA 7.1.1.1/05 (N	1-303803-0	<u>1-1</u>) 2008		C m	, al	í, g ^t	, ⁷ (1)		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<i>"</i>				
Hoefchen am Hohenseh	7.0	20 / 55 ²	7,230 93.6	7.2093.6	¥.4	DFOP	707/ 2611	D∛ 261' ∿	10.9	DFOP/ SFO	78.8 / 262 ¹	78.8 / 2621	14.8	DFOP/ SFO
CA 7.1.1.1/06 (N	<u>1-762349-0</u>			A CLA	1,012		Ø.	×C		1				
Longwoods	7.8	20%pF 2.0	13.¥/ 81.2	JC1 / 81.2	0 ¹ 3.2	D. DFOP	\$28.9 / 95.8 %	28.9 / 95.8	5.9	DFOP/ SFO	26.6 / 88.2	26.6 / 88.2	3.3	DFOP/ SFO
Refesol 02-A	7.1	20 / pF 2.0	1,165 1,165	11605101	J.9	J OP OP	219 ¹ / 727 ¹	219 ¹ / 727 ¹	9.3	DFOP/ SFO	204 ¹ / 678 ¹	204 ¹ / 678 ¹	5.6	DFOP/ SFO
Refesol 03-G	5.9	20 / pF 20 1	6960 6960	E1421/@2		DFOP	350 ¹ / 1,160 ¹	350 ¹ / 1,160 ¹	5.8	DFOP/ SFO	128 / 426 ¹	128 / 426 ¹	7.6	DFOP/ SFO
Speyer 6S	7.3	2.0 PF	514 O.S	C. 1371/ C	1.70	DFOP	70.7 / 235 ¹	70.7 / 235 ¹	7.4	DFOP/ SFO	65.2 / 217 ¹	65.2 / 217 ¹	11.4	DFOP/ SFO
	7.3 15 W	orse case :	1000 06961 - TJOVE		LOIM		555 ¹ /1,840 ¹	555 ¹ /1,840 ¹		•	1,000/ 3,320	1,000/ 3,320		



1	Soil properties			MO	3	a C ^{II}	a.	M0	d)	Ő.
Soil name	pH (H2O)	Temp (°C) / % MWHC	DT ₅₀ / DT ₉₀ (days)	Normalised DT ₅₀ / DT ₉₀ (days)	χ ² error (%)	Binetic model	DT ₅₀ (DT ₅₀ (Cays)	Normalised DT ₅₀ / DT ₅₀ (days)	χ ² exior (%)	Kinetic S model
CA 7.1.1.1/01 (N	<u>I-006135-01-1</u>)	1994		• • • •	N.L			(U3()5)	Jule 4 Cla	
BBA 2.2/ Speyer 2.2	6.3	20 / 40 ²	29.8 / 98.8	29.8 / 98.8	e 18.0	DFOR / SFO		2 Det obs	erred) ^{LE}
CA 7.1.1.1/02 (N	<u>-006141-01-1</u>)	1995			E T	xe ^y à	A 9.0°	The it's		
Laacherhof	8.1	20 / 40	58.1 / 193 ¹	36.7 1221	10.7 × 1	DFOP STO		Not obs		
Monheim 3	6.5	20 / 40		K I Not obs	erved 6	K K K K		O ^V Not obs	erved	
Howe	7.1	20 / (75% 1/3 bar)	2 F		erved 35	DFOP ASFO	oduction oduction	Not obs	erved °	
CA 7.1.1.1/04 (N	<u>-006148-01-1</u>)	1997	a la		e S	16 - 1	Our Clarker	TREILE OW	HE .	
Wolf Ranch	7.8	20 / (75% 1/3 bar), 00	V152 / 5071	100 3581	15.1 C	DFOP STO		March Swot obs	erved	
CA 7.1.1.1/05 (N	-303803-01-1)		- 1.6 e.	<u>Poly</u>	a di contra di c	o <u>r ' tr</u>		£,		
Hoefchen am Hohenseh	7.0	120/ 55 ²	STR FO	F Not obs	erved		+10-1-5-1 	Not obs	erved	
CA 7.1.1.1/06 (N	[-762349-01-1]	2020		- EO.	N 8.1 V	40 9	, Opp			
Longwoods	7.8	20 / pF 2 0		167/55.4 ¢	V 8.1 V	DFOR / SFO	~49.6 / 165 ¹	49.6 / 165 ¹	18.5	DFOP / SI
Refesol 02-A	7.1	20 / pE 200	53.1 176 ¹	©\$3.1 / 175 ¹	40	DEOP / SEQC	≥ 1,000 / 3,320 ³	1,000/3,320 ^{1,3}	16.1	DFOP / SI
Refesol 03-G	5.9	20/pF 2.0	1 49.9 / 166	49.9 / 166 ¹	Ø9.3 C	DFOP / SFO	1,000 / 3,320 ³	1,000/3,320 ^{1,3}	32.1	DFOP / SI
Speyer 6S	7.3	\$07 pF 2.65	¹ 79 621	\$ 09 / 262 ¹	™ 14.3©	DFO / SFO	191 ¹ / 635 ¹	191 ¹ / 635 ¹	23.5	DFOP / SI
component not obs - Interpret with car - Moisture value al - FOCUS default	erved in correspo e – extrapolated b pove pF 2.0	20/ pF 2.0 20/ pF 2.0 Worst-case : nding soil beyond experimenta the formation of the second se	$\frac{227307}{2}$		ard vio		1,000 / 3,3201	1,000/ 3,3201		



Soil pr	operties			Spirox	amine	. O	S.	a.y	M01	<u> </u>	and
Soil name	рН (H2O)	Temp (°C) / % MWHC	DT _{50 mod} (days)	DT 50 mod 20°C / pF 2 (days)	χ ² error (%)	Kinetic model	DT _{50 mod} (days)	20°C / pF 20°C / pF 2 (days) ~(M01 f.f. f.	(%)	
CA 7.1.1.1/01 (M-00613	<u>5-01-1</u>) 1994			/	all a	\$ OF (ST ST	e de la companya de l	- C F	all a	,e
BBA 2.2/ Speyer 2.2	6.3	20 / 40 ²	98.9	98.9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	DFQP	1,000	₹ .000 ³	0.162	¢ NAKO	SFO
CA 7.1.1.1/02 (M-00614	<u>1-01-1</u>) 1995			~0 ¹		H.C.Y	A F		, tô	A C	
Laacherhof	8.1	20 / 40	45.4	287 ×	3.3	DFOP S		105.5	0.137	6.2	SFO
Monheim 3	6.5	20 / 40	61.7	* 56.1	5.0 G	DFOP	$3,000^{3}$	$\Omega^{3}_{,000^{3}}$	0.15Q	♥ NA	SFO
Howe	7.1	20 / (75% 1/3 bar)	59.5 🎾	436	CD3.8	TP DFOP V	2021 CT 2021 CT 78.20	15906	6.090	° NA	SFO
CA 7.1.1.1/04 (M-00614	<u>8-01-1</u>) 1997		e ^{rt}	pi ș		L.		JULLE OF	L OW	>	
Wolf Ranch	7.8	20 / (75% 3 1/3 bas	96. 3	08.0	0 ⁴¹ 3.6	DFOP	78.20	JOUSSE	₹\$0.182	18.1	SFO
CA 7.1.1.1/05 (M-30380	<u>3-01-1</u>) 2008	0,0	<u></u>		VID .		D. L.	· Or			
Hoefchen am Hohen- seh	7.0	20 / 55 ²	65.P	\$65.4	7.0 3	FOME	.7810 ⁻¹	₹\$ ^{78.0}	0.134	7.54	SFO
CA 7.1.1.1/06 (M-76234	<u>9-01-1</u>) 2020	_ (av G	£.0s	A LA	e ^e (
Longwoods	7.8	20 / pF 2.0	270	1 7.1 .	چ ³ .7 ش	FOM	3€	34	0.246	7.55	SFO
Refesol 02-A	7.1	20 2.0	a + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +	170 ¹	1.00	DANOP .	©219 ²	219 ²	0.225	9.3	SFO
Refesol 03-G	5.9	207 pF 2.0	239 5	2391	P.5	O DFOP K	304 ²	304 ²	0.258	5.8	SFO
Speyer 6S	7.3 🏷	20/p520 ¹	ad Balls	\$ O163 ¹ \$ (0 ⁵² 1.7 C	DEOP	70.7	70.7	0.242	7.4	SFO
	TOON .	Geom	etric mean	75,4%		Geon Geon	netric mean :	168.6	-		
. 5	I Pre-	<u>Al</u>	lependence :	No		Arith	metic mean :	-	0.183		
Interpret with care – ext Moisture value above p Conservative value (def	F 2.0 ault) E 1 TTTO TE 1 TTTO TE 1 2010 C 1 200	ndexperimental any conducer c			and a	pH o	lependence :	No			



Soil pr	operties				M02		. C ^{\$}		al l	M03	- cojime	
Soil name	рН (H2O)	Temp (°C) / % MWHC	DT _{50 mod} (days)	DT _{50 mod} 20°C / pF 2 (days)	f.f. from parent	χ ² error (%)	Kinetic model	DT 50 mod (days)	DT50 mod 20°C / pF 2 (days)	E Hirom	error (%)	Kinetic model
CA 7.1.1.1/01 (M-0061	<u>35-01-1</u>) 199	94			a.					A F		Dj
BBA 2.2/ Speyer 2.2	6.3	20 / 40 ²	1,000 ³	$1,000^3$	0.100	E 9 39	SFO		29.8	0.125 C	1800	SFO
CA 7.1.1.1/02 (M-0061	<u>41-01-1</u>) 199	95			-2 ⁵		A. 15	<u>z 9:0</u> .	Those.	1. KP	al ^o	
Laacherhof	8.1	20 / 40	$1,000^3$	1,0003	0.08	3.36	SEO	√5 8.1	36.7	[%] 0.06		SFO
Monheim 3	6.5	20 / 40	$1,000^3$	1,000	<u></u> 051	<u></u> NĂ	SFO K	0,00	^{be} 0 ¹	Not observed		
Howe	7.1	20 / (75% 1/3 bar)	1,000 ³	\$,000 ³	\$ 0.07 ₀₀	NAD	SEO	320th	ent .	Not observed	0	
CA 7.1.1.1/04 (<u>M-0061</u>	<u>48-01-1</u>) 199		all v		G ^{VL-}	al i			-1. M	WILL		
Wolf Ranch	7.8	20 / (75% 1/3 bar)	C ^{U95.4}	67.4	3 0.1 Ber ^D	19.0	ST.C.	ĝ	CUID7 C	0 .171	15.1	SFO
CA 7.1.1.1/05 (<u>M-3038</u>	803-01-1) 200)8 ^{Oue}	~9.I	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	a C	10° - 10			- E			
Hoefchen am Hohen- seh	v	20/ 55 ²	75.9 × C	75.9	0.147	NOT OF	SFO 3	Chile to	0*	Not observed		
CA 7.1.1.1/06 (<u>M-7623</u>	<mark>49-01-1</mark>) 202	20	<u> </u>				d'h	, Olth				
Longwoods	7.8	20 / pF 2.0	31.205	3122	ON SE	4.85	SFO C	19.8	19.8	0.199	14.9	SFO
Refesol 02-A	7.1	20/pF			0.166	5.6°	SFO	53.1	53.1	0.160	11.2	SFO
Refesol 03-G	580°I	20 / pp 2.0		c 2 120 t	0.224	7.6	SFO	48.0	48.0	0.192	9.3	SFO
Speyer 6S	۶.3	20/pE	-0 5 12		0.183) 11.4	SFO	79.0	79.0	0.137	14.3	SFO
		Geom	tric mean :@	219.60	a		Geom	etric mean :	46.4	-		
	TROTE	1 Agithm	etic mean :	- This	<u>x</u> @.138		Arithn	netic mean :	-	0.149		
	mlo*	pH de	pendence :	V No vo	/		pH d	ependence :	No	-		
Interpret with care – o Moisture value above Conservative value (o	efaulty and	COTUNE COTUNE	ental period \$	61 Oluie								



5011	properties				<u>M06</u>	a Č ^V		/	
Soil name	рН (H2O)	Temp (°C) / % MWHC	DT _{50 mod} (days)	DT 50 mod 20°C / pF 2 (days)	f.f. _{from} parent	d metabolites M01, x ² error (%) Kinetic model (%) Kinetic model (%) Kinetic model (%) Kinetic Model (%) Kinetic Model (%) Kinetic Model (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) Kinetic (%) (%) (%) (%) (%) (%) (%) (%)	· prope	CO ^{TECT}	on regime and on regime and on tents contents contents there ore
CA 7.1.1.1/06 (<u>M-7</u>	<u>62349-01-1)</u> 202	20			Ő.			Pr X	OP TO
Longwoods	7.8	20 / pF 2.0	52.9	52.9	0:039 0:039	SFO	Pair dation	and its	Co for
Refesol 02-A	7.1	20 / pF 2.0	1,000 ³	1,000	0.0903	NÀ ÎL LÌPÔ	TOTA JOD		ED.
	5.9	20 / pF 2.0	1,0003	\$,000 ³	0.060 ³	NACO SEO	a guct mer		et °
Speyer 6S	7.3	20 / pF 2.0	1 people	3.000 ³	Ø.170	NA SFO	2 30 CDr 40	UCIE OWL	
Interpret with care Moisture value ab Conservative valu	- Langended and and and and and and and and and an	De guid be con this data		ermissi probably	Eal distri	x ² error (%) Ref. NA NA NA NA NA NA NA NA NA NA NA NA NA	t ights		



III. Conclusions

Persistence and modelling endpoints representing the degradation rates of spiroxamine and its metabolites M01, M02, M03 and M06 in a laboratory aerobic soil studies have been calculated in accordance with the guidance of FOCUS (2014). For M01, M02 and M06 alternative – but conservative – stimates were chosen in cases where acceptable fits were not possible. This was implemented by fixing the formation fraction to the fitted value and using this in combination with a conservative DT₅₀, or vice versa. The parameter to amend and its value were chosen based on expert judgement and iterative amendments to give a conservative description of the observed metabolite residue pattern.

The spiroxamine persistence DT_{50} values ranged from 7.2 to 142 days and DT_{90} values ranged from 80.9 to 696 days. The geometric mean of the modelling DV_{50} values was 75.4 days.

M01 persistence DT_{50} values ranged from 28.9 to 555 days and DT_{90} value range from 95.8 to >1,000 days. The geometric mean of the modelling DT_{50} values was 68.6 days. The arithmetic mean of the formation fractions from parent was 0.183.

The M02 persistence DT_{50} values ranged from 266 to 1,000 days (FOCUS default) and DT_{90} varies ranged from 88.2 to 3,320 days (FOCUS default). The geometric mean of the modelling DT_{50} values was 219.1 days. The arithmetic mean of the tormation fractions from parent was 0.138.

The M03 persistence DT_{50} values ranged from 167 to 107 days and DT_{90} values ranged from 55.4 to 358 days. The geometric mean of the modelling DT_{50} calues values values the arithmetic mean of the formation fractions from parent@vas 0.449.

Acceptable fitting could only be performed for persistence endpoints in one soil for M06 resulting in a number of presented default value. The persistence DT_{50} value was 49.6 days to 1.000 days whilst DT_{90} values was 165 days to 3,320 days. The geometric mean of modelling DT_{50} values was 479.6 days. The formation fraction from parent was 0.095.

Assessment and conclusion by applicant.

Study meets the current guidance and the requirements in 283 013, @

The study was conducted to gridelings) FOCUS 2006, 2004 (required guideline). The study is considered valid to assess best for and modelling DT_{30} values for spooxamine and associated metabolites in laboratory soil studies.

CA 7.1.2.1.2 Aerobio degradation of metabolites, breakdown and reaction products

The rate of aerobic degradation in soil of metabolites of spiroxamine has been investigated, as part of the studies listed under Point CA 7.1.1.1 in five studies conducted with the active substance (KCA 7.1.2.1.1/01 to KCA 7.1.2.4.1/05) which were evaluated during the previous EU review. These studies have been sufficient to address the requirements for metabolites, however, for metabolite M06 (spirox-amine-acid) which is now included in the definition of the residue for risk assessment in soil (see CA 7.4.1) and where it was not always possible to derive acceptable degradation parameters for use in modelling, thew study is being conducted and will be provided as soon as possible.

- ... surdy is being



	1
Data Point:	KCA 7.1.2.1.2/01
Report Author:	TBA
Report Year:	TBA
Report Title:	TBA
Report No:	TBA
Document No:	TBA
Guideline(s) followed in	OECD Guideline for Testing of Chemicals, No. 307
study:	Commission Regulation (EU) No 283/2013 in accordance with Regulation (EC)
	No 1107/2009
Deviations from current	None & O & O
test guideline:	
Previous evaluation:	No, not previously submitted
Remarks previous evalua-	Not applicable (New study, not previously submitted)
tion:	
GLP/Officially recognised	Yes, conducted under GLPOfficially recognised asting acilities
testing facilities:	
Acceptability/Reliability:	Yes why a A O A

A study investigating the aerobic degradation in soil of metabolite applied M06 is currently on-going and will be supplied as part of a top up submission (esomate September 2021).

CA 7.1.2.1.3 Anaerobic degradation of the active substance

New studies, not previously evaluated

The rate of anaerobic degradation in soil was investigated as part of the studies listed under Point CA 7.1.1.2, in two studies (KCA 7.1.2/0), and KCA 7.4.1.2/02 which were evaluated during the previous EU review. These studies sufficiently address the data requirement.

Data Point 2 , KCA/ $1.2.1.302$ 2 10 2
Report Anthor:
Report Year: $2021 \ll 5^{\circ}$ (2)
Report Title: [14C] piroxannine: Route an@rate of degradation in soil under anaerobic condi- tion at 20°
Report No: \mathcal{O} \mathcal{O} \mathcal{V} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O}
Document No 2 $\overline{0}$ $\overline{0}$ $\overline{762348-01}$ $\overline{2}$ $\overline{2}$
Guideline(s) followed in Composition Regulation (EU)No. 283/2013 in accordance with Regulation (EC)
study: " No 107/2009 "
\sim QECD 369 \sim \sim
Dextations from curtant Some of a
test guideline: $\mathcal{O}^{\vee} \mathcal{O}^{\vee} = \mathcal{O}^{\vee}$
Previous evaluation: No not previously submitted
GLP/Officiely recog- Stes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:
Acceptability/Refiability: Xes
The facile of this and the summerican and an acient KCA 71112/02

The details of this solidy are fully summarised under point KCA 7.1.1.2/02.

**2



Existing studies, previously evaluated

	(Č
Data Point:	KCA 7.1.2.1.3/01
Report Author:	
Report Year:	
Report Title:	Anaerobic aquatic metabolism of the active ingredient KWG 4168
Report No:	PF4288
Document No:	<u>M-006010-02-1</u> ©
Guideline(s) followed in	US EPA Pesticide Assessment Ordelines, Subarision N, Chepistry: 0 4
study:	Environmental Fate, § 162-3: Anaerobic Aquade Metabolism Studies
Deviations from current	Yes (refer below)
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in study and the study study of the study (described in study study and the study
	study summary)
Previous evaluation:	yes, evaluated and accepted of the second se
GLP/Officially recog-	Yes, conducted under GLP Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes 0 1 0 1 0 1 5 2

The details of this study are fully summarised under point KCA 102.2.3.466

CA 7.1.2.1.4 Anaerobic degradation of metabolites, breakdown and reaction products

The degradation rate of any metabolites of spirovamine under an aerobic conditions is adequately investigated in the studies conducted with the active substance under Point CA 7.1.2.1.2. Therefore, no further studies are provided.

CA 7.1.2.2

CA 7.1.2.2.1 Soft dissipation studies

ield studies

Based on the information presented under Points CA 71.1.1 and CA 7.1.2.1 and the summary of DT₅₀ values presented in Table CA 71.2.1 either the laboratory foil DT₅₀ of the active substance and metabolites M01 and M02 effecteds 60 days or the DT₅₀ exceeds 200 days. Consequently, soil dissipation studies have been conducted with analysis to these components. Additionally, either the laboratory soil DT₅₀ of metabolite M03 exceeds 60 days or the DT₆₀ exceeds 200 days, however, this had only occured in one soil from an older study. However, the observation of 203 DT₅₀ >60 days is confirmed in the Speyer 6S soil from KCA 7.1.1/06 (M-762349-02-1) confirmining the requirement for a field study. For M06, only a single reliable kinetic fit could be established which indicated a DT₅₀ < 60 days, but potential requirements for a field dissipation study can only be confirmed after the completion of the M06 rate study which is currently being conducted but is unavailable at the time of submission. This is considered a data gap, rather than an issue that prevents finalization of the risk assessment, as worst-case PEC values based on laboratory data can still be adequately derived.

The field dissipation of spiro camine has been investigated at a total of eighteen (n=18) locations in five 'legacy' European trials (KCA 7.1.2.2.1/01 to KCA 7.1.2.2.1/05) which were evaluated during the previous EU review on addition:

- Three further studies were included during the last evaluation to address stability of stored samples from the field dissipation trials
- ² one further study was included during the last evaluation and therefore has been included for completeness (KCA 7.1.2.2.1/06 (<u>M-036125-01-1</u>) provides a comparison of laboratory and field degradation studies summarised more fully elsewhere)
- two further studies were included during the last evaluation to address the kinetic evaluation of



the degradation observed in the field dissipation trails and have therefore been included for completeness. These evaluations have been superseded by a new study conducted to modern requirements (KCA 7.1.2.2.1/12 (<u>M-763140-01-1</u>))

one new study (KCA 7.1.2.2.1/12 (<u>M-763140-01-1</u>)) has been conducted to provide abup-to-date kinetic assessment of degradation rates observed in field dissipation trials to modern equirements (FOCUS 2014² and EFSA 2014⁶)

Substance	Report reference	Document no.	Comment S
Spiroxamine	KCA 7.1.2.2.1/01; KCA 7.1.4.3/01	<u>M-006116-01-1</u>	
Spiroxamine	KCA 7.1.2.2.1/02; CA 7.1.4.3/02	<u>M-006126-01-1</u>	Submitted for first approvad of spirox- amite, 1999. Reviewed under UP. Consid- ored valid and acceptable
Spiroxamine	KCA 7.1.2.2.1/03; CA 7.1.4.3/03		
Spiroxamine	KCA 7.1.2.2.1/04	<u>M-006128-01-1</u>	
Spiroxamine	KCA 7.1.2.2.1/05	1006129-01-1	Submitted for urst renewal of spirox
Spiroxamine	KCA 7.1.2.1.1/06; KCA 7.1.2.2.1/06	<u>M-038125-09-1</u>	Submitted for first renewal of Spirox
Storage stabili	ty 🏒		
Spiroxamine	KCA 7.1.2.2.1/07	<u>M-006082-57-1</u>	Submitted for first approval of spirox- amine, 1999. Reviewed under UP. Consid- ered valid and acceptable.
Spiroxamine	KCA 7.1.2 2.1/08	<u></u>	Suburited for first renewal of spirox-
Spiroxamine	KCA 7.1.2.2.149	<u>M-896074-01-1</u>	amine, 2010, Reviewed under UP. Consid- gered valid and acceptable.
Kinetic evalua	tion S		
Spiroxamine	KEA 7.152.2.1/409	<u>M-292744-021</u>	Submitted for first renewal of spirox- amule, 2010 Reviewed under UP. Consid-
Spiroxamine ~	KCA 7.1.2.201/11 C	<u> </u>	ered valid and acceptable.
Spiroxamine	KCA 7.1.2.2.1/12	<u>M-763740-016</u>	New data not yet reviewed under UP
		<u>ST-006079-01-10</u> <u>M-95074-01-10</u> <u>M-2597744-601</u> <u>M-2597744-601</u> <u>M-763940-0157</u> <u>M-763940-0157</u>	
e e e e e e e e e e e e e e e e e e e			

⁶ EFSA (2014) EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp., doi:10.2903/j.efsa.2014.3662.



Existing studies, previously evaluated

Data Point:	KCA 7.1.2.2.1/01
Report Author:	
Report Year:	1995
Report Title:	Dissipation of KWG 4168 in soils under field conditions (Germany and Great)
Report No:	RA-2078/93
Document No:	<u>M-006116-01-1</u>
Guideline(s) followed in study:	BBA Guideline IV-4.1 (1986)
Deviations from current test guideline:	Yes (refer below) Some minor deviation(sphot relevant for the reliability of the study (described in study summary)
Previous evaluation:	yes, evaluated and a cepted is the second seco
GLP/Officially recog-	DAR (1997), RAR (2010), RAR (2017) Yes, conducted under CIP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	$\underline{Yes} \qquad \underbrace{Q} $

Executive Summary

Soil dissipation of spiroxamine avas studied after application as an EC formulation containing 494 g/L to soil under field conditions (some with and some without vegetation) for up to 258 days at four sites located in Germany and Great Britain (Hofchen silt loam; Laacherhof, loam; Elm Farm, sandy loam and Pakenham, loamy sand).

Spiroxamine was applied at a single application or 0.5 L/ha (0.75 kg a.s./ha) in spring 1993.

Duplicate samples were collected immediately after the treatment and at intervals up to 258 days after the treatment (DAT). Samples were taken at the Höfenen site, at 0,7, 14,27, 60, 90, 120, 151, 180 and 239 DAT, at Laacherhof at 0, 7, 14, 28, 56, 90, 122, 152, 180 and 231 DAT, at Elm Farm at 0, 7, 14, 29, 56, 90, 120, 151, 180 and 258 DAT and at Pakenham at 0,0, 14, 28, 55, 91, 120, 148, 177 and 239 DAT.

Twenty soil core samples were taken from the treated as well as the soil core samples from the control plot directly post application. Core samples were taken to a depth of 30 cm and segmented into 10 cm soil layers prior to homogenisation and analysis. Soil samples were analysed for spiroxamine and the metabolites M01 (spiroxamine desetbyl) and M02 (spiroxamine-despropyl). Soil samples were extracted by Soxtec extraction with a solution of methanol water/ammonia (25%) (8:2:0.1. v/v/v). Parent and metabolites were quantitatively determined by liquid chromatography with MS-MS detection. A limit of quantification (LOQ) of 5 μ g/kg and a limit of detection (LOD) of 2 μ g/kg was reported for spiroxamine and the metabolites.

Starting from an application rate of 0.75 kg at ha and a soil density of 1.5 kg/L the theoretical total concentration in a 10 cm layer is 500 µg/kg soil. The concentration of spiroxamine in the 0-10 cm layer found immediately after application were 207, 262, 223 and 238 µg/kg for Höfchen, Laacherhof, Elm Farm and Patenham trial stres, respectively. This equates that at day zero 65.4%, 52.3%, 44.6% and 47.6% of the applied amount was/recovered.

During the whole test duration, nearly all residues remained in the 0-10 cm layers of the soil. The maximum concernation of spiroxamine was observed for the Höfchen (30122/1) trial site at 327 μ g/kg at 0 DAT Only in the Pakenham site was spiroxamine found in the 10-20 cm layer, the maximum value was 25.3 μ g/kg at Day 0. No mobility into soil layers below 20 cm was observed. The metabolites M01 and M02 were detected at all sites. The metabolite M01 reached a maximum of 38.1 μ g/kg at DAT 28 in the Pakenham trial site. The metabolite M02 reached a maximum of 43.7 μ g/kg at DAT 28 in the Pakenham trial site in the 0-10 cm layer. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and



by Dr GroB, Bayer

M02, no residues were found at levels greater than LOQ (5 μ g/kg) at any time point.

The DT₅₀ and DT₉₀ of spiroxamine determined in the study was reported for each site. However, greevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT_{50} values from laboratory and field dissipation^O studies (EFSA 2014), was performed in the report presented under point KCA 7 1.2.2.1/12 (M-7631 4) 01-1).

I. **Materials and Methods** Ś

A. Materials

1. Test Items

'spiroxamine' Spiroxamine (product code 30-0122915, Suspension concentrate formulation 0494

> nalwsed and certified at March G PF-EAT, D-57368 Leverkusen

Certificate of analysis:

Batch no.:

Purity:

2. Trial locations & Soils

¢, The study was performed at two different transitions of Germany (Höfchen and Laacherhof) and Great Britain (Elm Farm and Pakenham). Site soil is characterised in Table CA 7.1.2.2.1-1. The field soil dissipation trial consisted of one peated and one untreated plot on each site. No pesticide history was , Ç given for previous years before the triat for either site. Ş

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Stated

Table CA 7.1 2.2.1-1 Location, site description and climate data of test sites

Trial designation	301221/1	° 30124/8 @	30262/7	30263/5
Soil Designation	€ B offchen	Laacherhof	© [♥] Elm Farm	Pakenham
Vegetation	Bare son O	With vegetation A	With vegetation ^A	With vegetation A
			Elm Farm	Elm Farm
	Q Dentsche	Dentsche S	Development Sta-	Development Sta-
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Versuchsguter 2	Versuchsgüter 3	tion	tion
Geographic Location	D-SI 399 Burscheid	D-40789 Monheim	GB Bury St. Ed-	GB Bury St. Ed-
	Hönchen	Laacherhof	munds	munds
	FQr4011	S Fbar715	Thurston, Suffolk	Thurston, Suffolk
			Field 6, Block 4	Field 6, Block 4
Comptry	Gerimany Q	Germany	Great Britain	Great Britain
Textural Classifica- tion (USDA)	Saft loans	Ç Loam	Sandy loam	Loamy sand
Sand [50 - 2000 µm]) (%)		51.3	65.2	83.3
Silt [2 30 µmb(%)	<u>∧</u> (~)69.9	34.0	19.1	10.9
Clay < 2 μm (%)	12.8	14.7	15.7	5.8
platin Cach	6.5	6.8	7.5	7.3
Organie matter (%)	1.57	1.86	1.96	1.51
Organic carbon (%)	0.97	1.08	1.14	0.88



Trial designation	301221/1	30124/8	30262/7	30263/5
Cation Exchange Ca- pacity (meq/100 g)	15.0	10.0	13.0	8.0 °
Soil Moisture capac- ity (g/100g soil)	44.6	33.4	34.1	348
Size of plot (m ² )	225	75	325 0	325
Spray equipment	Agrotop Spaying- Boom	Agrotop Spaying- Boom روزی	Knapsack <del>Sp</del> rayer Fredo 2	Knapšáck Spráyer, Frodov2
Nozzle type	Teejet XR 11004 VS	Lumarck 03-¥10 F	Teejet 8003 VS	Teejet 9003 XS

The report does not provide details on crop type and extent & coverage for the overage sites in the study However for 4 Α study KCA 7.1.2.2.1/04 (M-006128-01-1), which uses son of the same site, the cover crop as spring barles

#### **B. Study Design**

#### 1. Experimental Conditions

A single application of a nominal 0.75 kg a4s./ha as an emphisifiable concentrate (EC) was performed to bare soil on 22nd April 1993 (Höfchen) and to vegetation on 30th April 1993 (Baacherhof), 9 July 1993 (Elm Farm) and 9th July 1993 (Pakenham). Ô Ø

During the trials, soil cultivation and maintenance was performed according to the used local agricultural practice. No irrigation was caffied out on any of the sites, Weather data was collected at a location near to the site during the study period; this data includes the recan ait temperature ainfall and sunshine hours.

Soil dissipation of spiroxamine was studied for 258 days

#### 2. Sampling

Trials were sampled on mediately after treatment and at intervals up to 258 days after the treatment. Samples were taken at the Höfchen site, acto, 7, 14, 27, 60, 90, 120, 151, 180 and 239 days after treatment (DAT), at Laacheinof at 0, 7, 14, 28, 56, 90, 122, 152, 180 and 231 DAT, at Elm Farm at 0, 7, 14, 29, 56, 90, 120, 151, 180 and 258 DAT and at Pakenhan at 0, 7, 14, 28, 55, 94, 120, 148, 177 and 239 DAT. Control samples (10 cores) were taken on the first and on the last sampling day from the control plots.

At each sampling point 20 cores were collected using a pushing sampling system (Wacker Hammer) down to a depth of 30 cm (dimeter 50 mm) per sampling interval. Locations of sampling were statistically distributed over the plot to get representative samples. Samples were transported in a cooler box containing dry ice Defore being fored at -18° Guntil malysis at the laboratory.

The frozen soil cores were cutinto by cm segments. Ten control sample) to twenty (treated samples) of such segment of one later were milled and carefully homogenised.

#### 3. Analytical Procedures

Soil samples were analysed for spiroxamine and the metabolites M01 (spiroxamine-desethyl) and M02 (spiroxamine-despropyl). Replicate sub-samples were analysed by Method 00374 (RA-607/94) (M-019207-02-1), involving aquid chromatograp by.

Ő,

In summary, the method in vive Soxtec extraction with refluxing with a solution of methanol/water/ammonia 25%, 8:2:0, v/y/v). After solvent evaporation to the aqueous remainder the internal standard were added. Admit of quantification (LOQ) of 5 µg/kg was reported, and a limit of detection  $(LOD) \ll 2 \mu g/kg$  for spiroxappine and the metabolites.

Procedural recovery samples were analysed. Untreated soil samples were fortified with known amounts of spiroxappine, M01 and M02 and carrying these samples through the procedure alongside the treated samples.



#### 4. Determination of degradation kinetics

The  $DT_{50}$  and  $DT_{90}$  of spiroxamine determined in the study were reported for each site. However, aneevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (20142) and the EFSA guidance on deriving DegT₅₀ values from laboratory and field desipation studies (EFSA 20145), was performed in the report presented under point SCA 7.1.2.2.1/12 (MO) 763140-01-1).

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#### II. **Results and Discussion**

#### A. Analytical Methodology

Full details and acceptable validation data to support this method (Method 003)4 (RA607/9) are presented in Document M-CA 4, Section 4.1.2 (M4019207-02-1). The method complies with the E regulatory requirements outlined within SANCO/5929/99 rev. 4 and is witable for the determination of spiroxamine and its metabolites in soil samples by HPLC/MS/MS.

Analytical performance was determined by analysing known amounts of sphoxartune and internal standards. The mean recovery of spiroxamine, M01 and M02 was 87.  $\mathbb{N} \pm 13\%$ , 89.  $\mathbb{R} \pm 5.8\%$  and  $\mathbb{R} \cdot 1 \pm 67\%$ of the nominal treatment rate respectively, over a fortification range of 5 to 500 µg/kg

#### **B.** Data

10-20

20-30

B≪Q

Mean

В

Total residues detected in each treated plot are presented in the report The results for spirovamine and its metabolites are presented below as soft residue concentrations (on a µg/kg dry weight basis) for each of the treated plots in Table CA 7.1.2.2.1-2 to Table CA 7.4.2.2.1.13

		Sas µg	g/kg		J.		O (		.'Y 1	enen en	/1 0550 U
Depth	Repli-	Î, Î		S.	$\sim$ $^{\circ}$	Ŷ.	y Ta				
[cm]	cate	<b>38</b> ,	Ŷ	مي الالا	27 🖉	^س 60 ^م		×120	151	180	239
	A Õ	\$37 ≰	ن ⁰ 200 (	180	143	Z 2	6.2	V 38.3	38.6	41.0	33.4
	₽¢?	307	218	169	ð <del>5</del> 4	71.6	40.7	35.6	45.6	46.9	31.7
0-10 🐊	¢	349	ð <b>9</b> 4	~~	<u> </u>		. O ^y	-	-	-	-
* 2	D	<b>3</b> 25 "	[~] 228 🛫	· Ô		&-	S ⁷ -	-	-	-	-
	Mean 🔊	327	210	175	<b>248</b>	⁰ 72.4 ≫	38.4	36.9	42.1	44.0	32.5

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M.d.

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**WLOQ** 

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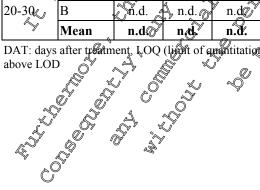
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Rd.

n.d. 🔊

	× 4	-	SY .	N N		4 i ^v	
Table CA 7.1.2.2.1-2;	Residers	of spiroy	xamine in	10-30 Om	horizons o	f soil <b>s</b>	BHöfchen expressed
			0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
<u></u>	is µg/kg		, \$	s s s s s s s s s s s s s s s s s s s	0	L,	

DAT: days after treatment, LOQ (light of quantitation) = 5 µg/kg, LOD (limit of detection) = 2 µg/kg, n.d. = not detected



<ĽØŐ

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n.d

n.d.



Table CA 7.1.2.2.1-3: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soi	l at
Höfchen expressed as µg/kg	<i>°</i>

epli-												
cpn-					DA	<b>\T</b>						
te	0	7	14	27	60	90	120	Q51	180	239	J	
	14.4	30.9	21.7	19.8	8.5	6.2	5.9	° 7.4	7,9,	<u>5</u> 1	~	
	18.2	33.5	22.2	21.4	10.7	6.6	<lqq< td=""><td>7.5</td><td><b>O</b></td><td>6.0</td><td>ÌQ ,</td></lqq<>	7.5	<b>O</b>	6.0	ÌQ ,	
	10.5	27.2	-	-	ġ,	-	ő, -	- 🎽	( _ ~ )	-65	Ŵ	
	10.5	33.0	-	-	-	- 6	Ş -	- 0		×.	, de la companya de l	
ean	13.4	31.1	21.9			6.4	<loq< td=""><td><b>J</b></td><td>7.9</td><td>O5.5 🎢</td><td>1</td></loq<>	<b>J</b>	7.9	O5.5 🎢	1	
	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	A.d.	Qn.d.	n.d.,	n.d		
	n.d.	n.d.	n.d.	n.d.	n₀d.	"@ń.d. "**	🛿 n.d. 🕜	n.¢	n:đ	A.		
ean	n.d.	n.d.	<loq< td=""><td>Ji.d.</td><td>တိုn.d. ္လ</td><td>n.d.</td><td>næ.</td><td>વ્ર.સ.</td><td>n.d.</td><td>n.d.</td><td></td></loq<>	Ji.d.	တိုn.d. ္လ	n.d.	næ.	વ્ર.સ.	n.d.	n.d.		
	n.d.	n.d.	n.d. 🔬	n.d 🔊	n.¢	IQI.	n.d.	👡 n.d. 🛛	n.d.	n.d.		
	n.d.	n.d.	n.d.	n.d.	∼n,d.	Dn.d. L	▶ n.d. C	n.d	n.d.	a,d.		
ean	n.d.	n.d.	<løq< td=""><td>يَّn.d. 🚽</td><td>n.d.</td><td>≻ n.d.^O</td><td></td><td>n.d.</td><td><b>And.</b></td><td>)n.d.</td><td></td></løq<>	يَّn.d. 🚽	n.d.	≻ n.d. ^O		n.d.	<b>And.</b>	)n.d.		
	ean ean	14.4         18.2         10.5         10.5         ean         13.4         n.d.         n.d.         n.d.         n.d.         n.d.         n.d.         n.d.         n.d.	14.4         30.9           18.2         33.5           10.5         27.2           10.5         33.0           ean         13.4         31.1           n.d.         n.d.           n.d.         n.d.	14.4         30.9         21.7           18.2         33.5         22.2           10.5         27.2         -           10.5         33.0         -           ean         13.4         31.1         21.9           n.d.         n.d.         n.d.         n.d.           n.d.         n.d.         n.d.         n.d.	14.4         30.9         21.7         19.8           18.2         33.5         22.2         21.4           10.5         27.2         -         -           10.5         33.0         -         -           10.5         33.0         -         -           10.5         33.0         -         -           10.4         n.d.         n.d.         n.d.           n.d.         n.d.         n.d.         n.d.	14.4 $30.9$ $21.7$ $19.8$ $8.5$ 18.2 $33.5$ $22.2$ $21.4$ $10.7$ 10.5 $27.2$ -       - $-$ 10.5 $33.0$ -       - $-$ 10.5 $33.0$ -       - $-$ ean       13.4 $31.1$ $21.9$ $20.6$ $29.6$ n.d.       n.d.       n.d.       n.d.       n.d.         n.d.       n.d.       n.d.       n.d. $n.d.$ n.d.       n.d.       n.d. $n.d.$ $n.d.$ n.d.       n.d. $n.d.$ $n.d.$ $n.d.$ n.d. $n.d.$ $n.d.$ $n.d.$ $n.d.$	14.4 $30.9$ $21.7$ $19.8$ $8.5$ $6.2$ 18.2 $33.5$ $22.2$ $21.4$ $10.7$ $6.6$ 10.5 $27.2$ -       -       -         10.5 $33.0$ -       -       -         10.5 $33.0$ -       -       -         10.5 $33.0$ -       -       -         ean $13.4$ $31.1$ $21.9$ $20.6$ $29.6$ $6.4$ n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.         n.d.       n.d.       n.d.       n.d.       n.d.       n.d. $n.d.$ ean       n.d.       n.d.       n.d. $n.d.$ $n.d.$ $n.d.$ n.d.       n.d. $n.d.$ $n.d.$ $n.d.$ $n.d.$ n.d. $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$	14.4       30.9       21.7       19.8       8.5       6.2       5.9         18.2       33.5       22.2       21.4       10.7       6.6       <1.00	14.4       30.9       21.7       19.8       8.5       6.2       5.9       7.4         18.2       33.5       22.2       21.4       10.7       6.6       <1.00	LOQ       7.5         n.d.         n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.         n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.         ean       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.         n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.         n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.       n.d.	14.4       30.9       21.7       19.8       8.5       6.2       5.9       7.4       7.9         18.2       33.5       22.2       21.4       10.7       6.6       <1.00	14.4       30.9       21.7       19.8       8.5       6.2       5.9       7.4       7.9       5.1         18.2       33.5       22.2       21.4       10.7       6.6       <1.00

DAT: days after treatment, LOQ (limit of quantitation) = 5  $\mu g k g$ , LQD (limit @ detection) = 2 k g/kg, no. = not detected above LOD

Table CA 7.1.2.2.1-4:	Resideres of	M02 (spiro	kanoine-desi	oropy) in	0-30 cm	horizons of soil	at
1	Höfchen exp	ressed as µg	kg (mean)			Ô	

		<u> </u>	O^"	```````	<u> </u>	0	~	y 🔗	Q		1
Depth	Repli-	°~y"	.1	- Q	Stande	🖉 <b>R</b>	st 🗸	, S	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
[cm]	cate	<b>~9</b>		¢14 (	ົ 27 🏷	60	90	<u>د</u> ا20 «	<b>151</b>	180	239
	A	¢14.1	31.70	24.	2258	29.7 .7	a	0 6.8 🖒	6.8	7.2	5.2
	В	170	3,4,9	24.4	~23.6 🗳	910.5 ¢	7.4	5 <b>D</b>	6.6	7.2	5.7
0-10	60	×927	28.5		× - ×	~~~	6 0	Š.	-	-	-
	٦ م س	\$9.7 K	⁰ 36.0	_~	, Q	Ś.	Ő(	V -	-	-	-
\$A	Mean	12.6	32,8	24.6	23.2	©10.1	7.40	6.4	6.7	7.2	5.4
	A	đđ.		©n.d.	n.d	nd	IQI.	n.d.	n.d.	n.d.	n.d.
10-20	В	n.d. 🕻	×LOQ	n.	n.d.	&n.d.	<u>s</u> n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	n. <b>d</b> .	n@ł.	"ŋ.d.	Çn.d.	^O n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	A	Rd.	, În.d.	∫ [©] n.d. ^	11.4~8	n	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	A NB	©n.d. 🦳	n.d 🏸	n d≯	<b>n</b> .d.	≫ŋ.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	🗳 Mean	n.d.	n.a.	And.	۵n.d. ۲	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

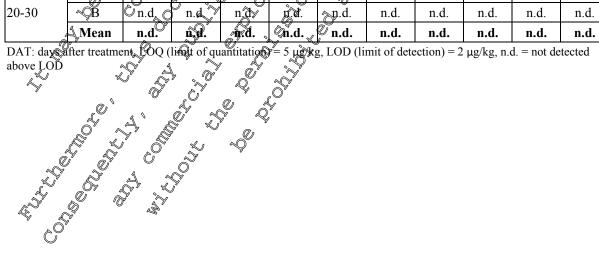




Table CA 7.1.2.2.1-5: Residues of spiroxamine in 0-30 cm horizons of soil at Laacherhof e	ex-
pressed as µg/kg	6

		<b>I</b>	•									$\sim$
Depth	Repli-					D	АT					
[cm]	cate	0	7	14	28	56	90	122	₹52	180	231	9
	А	241	210	181	156	100	48.6	42.5	\$39.9	39.0%	24Q	
	В	284	200	161	169	114	51.0	43.6	37.4	355	~Q6.3	ð
0-10	С	254	207	-	-	- &	-	Ľ,	-	°∕∕ °≉		3
	D	268	247	-	-	Ę,	-	<u></u>	- (	, -¢	, O	o de la composición de la composicinde la composición de la composición de la compos
	Mean	262	216	171	162	<b>40</b> 7	49.8	<b>43.0</b>	38%6	35.3	N X	0″
	А	n.d.	n.d.	<loq< td=""><td><loq< td=""><td></td><td><loq< td=""><td><loq< td=""><td>stad.</td><td>"n.d. (</td><td>n.d.</td><td>/</td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td></td><td><loq< td=""><td><loq< td=""><td>stad.</td><td>"n.d. (</td><td>n.d.</td><td>/</td></loq<></td></loq<></td></loq<>		<loq< td=""><td><loq< td=""><td>stad.</td><td>"n.d. (</td><td>n.d.</td><td>/</td></loq<></td></loq<>	<loq< td=""><td>stad.</td><td>"n.d. (</td><td>n.d.</td><td>/</td></loq<>	stad.	"n.d. (	n.d.	/
10-20	В	n.d.	n.d.	n.d.	<loq< td=""><td>n.d.</td><td>&lt;<b>⊉</b>ØQ</td><td>. ¶uÕQ</td><td>[™]n.d. \[©]</td><td>11.q</td><td>n 🖉</td><td></td></loq<>	n.d.	< <b>⊉</b> ØQ	. ¶uÕQ	[™] n.d. \ [©]	11.q	n 🖉	
	Mean	n.d.	n.d.	<loq< td=""><td><koq< td=""><td>⊲<b>b</b>ÔQ</td><td>.⊗LOQ≭</td><td>~LOQ</td><td>n.d</td><td>ñ,d.</td><td>×u.d.</td><td></td></koq<></td></loq<>	<koq< td=""><td>⊲<b>b</b>ÔQ</td><td>.⊗LOQ≭</td><td>~LOQ</td><td>n.d</td><td>ñ,d.</td><td>×u.d.</td><td></td></koq<>	⊲ <b>b</b> ÔQ	.⊗LOQ≭	~LOQ	n.d	ñ,d.	×u.d.	
	А	n.d.	n.d.	n.d.	₽ [°] OQ ×	n.d. Č		112-Q.	æd.	Ln.d. 🚄	n.d °	
20-30	В	n.d.	n.d.	n.d. 💉	🔊 n.d 🔊	n.d.	n.ď.		©n.d. [°]	n.d	n.@.	
	Mean	n.d.	n.d.	n.d.	n.d.	n.d.	<b>"</b> n.d. <i>"</i>	🖌 n.d. 🥎		<b>#.</b> .d.	Ja.d.	

DAT: days after treatment, LOQ (limit of quaditation)  $\neq 5 \ \mu g$  by, LOD (limit of detection) = 2  $\mu g$  kg, n.  $\phi^{\pm}$  not detected above LOD

Table CA 7.1.2.2.1-6: Residues of MOI (spinoxamure-desethyl) in 0-30cm hopizons of soil at ,Ô Laacherhof expressed as µg/kg Ô

		N	<b>%</b>	Ĉi 1	Ÿ ₹	<u> </u>		Ô	^		
Depth	Repli-	\$ (		y c	-	$\mathbf{D}_{A}$	AT ू\$′		S.		
[cm]	cate	Ū,	7	LA [®]	28	<b>Š</b> 6	90	لاً ¥ً¥ً¥ً	152	180	231
	A	<i>ą</i> .5	A9.2	27.6	33.0 🖌	¢~29.3 (	15.8	16.8	14.3	14.6	9.1
	B C VO	c 6.3 Ĉ	18.8	27.1~	33.00	32, <b>®</b> /	17.5	15.7	13.2	14.1	10.3
0 10		9.Q	20.2	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Ň	Ø- ^	Ş -	-	-	-
- AND	P	6.1	<b>@0.3</b>		ý- (	× - 2		-	-	-	-
		[©] 7.2 ©	19.6	27,3		31.0	16.7	16.2	13.7	14.4	9.7
	A 🖉	nd	n Ø	n.d.		~n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	∘ <b>, f?.ð</b> .	n.d.	_€ ©n.d. ∘ _¢	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	√n.d. ∢	n.d		n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
(	Ĩ A Å	n.đ.	n d.	n.d.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30		<u>m</u> .d. ·	M.d.	On.d. 👡	Ôn.d.	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	n.d.	∕″n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

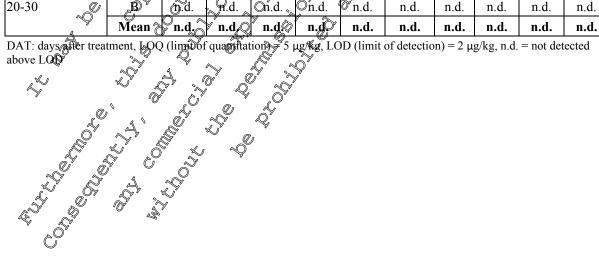




Table CA 7.1.2.2.1-7: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of	soil at
Laacherhof expressed as µg/kg	<i>a</i> .°

			-								<u> </u>	ð
Depth	Repli-					D	АТ				<u>`</u>	
[cm]	cate	0	7	14	28	56	90	122	<del>)</del> -152	180	231	0
	Α	7.0	18.1	26.2	29.7	25.8	13.9	14,7	12.9	13.0/	231 80	
	В	6.4	17.2	25.0	29.6	28.6	14.6	<u>1</u> 4.1	11.7	£ <b>2</b> .2	<b>~9</b> .4	Ô
0-10	С	8.5	18.6	-	-	õa -		<u> </u>	- ,	8 - 8	2 - L	į
	D	6.2	18.8	-	- «	<b>F</b> -	@	-	- () \$2.3		<u> </u>	
	Mean	7.0	18.2	25.6	29 A	27.2	1402	14.4	\$2.3	£2.6	\$ <b>8.</b> 7 ¢	,0″
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🔎		n.d ©	n an
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.@	n.d.	n.d.	n.Ô	n.Q.	
	Mean	n.d.	n.d.	n.¢	n.¢	n.d		"n.d.	æd.	°⁄79γ.d.	≪n.d.	
	А	n.d.	n.d.	n.a.	n,d.	ŋ.d.		n.d.	Øn.d. A	n.d. 🛋		
20-30	В	n.d.	n.d. 💡	An.d. 🦻	Øn.d.∼	n.d.	♥ n.d₄	n.dÇ	n.d.	næ	n@. 	
	Mean	n.d.	n.d 🖴	n.d.	n.d.	n,d	વ્રસ.	`n∳d.	n.d.	<b>≪ŋ.d.</b>	An.d.	

DAT: days after treatment, LOQ (limit of quadritation)  $\neq$  5 µg/g, LOP (limit of detection) = 2 µg/g, n  $\phi^2$  not detected above LOD

Table CA 7.1.2.2.1-8: Residues of spiroxamine in 9-30 cm horizons of soil at Elm Farm expressed as µg/kg Ŵ Ô  $\sim$ 

	L		<u>«</u> .	er e	Ş <del>∕</del>	,		Ô	- -		
Depth	Repli-			ř "Q	, "C	, DA	\T_\$\$´	2	Z.		
[cm]	Cale	Ū, Ū	7	JA.	<u>s</u>	56	». <b>90</b>	×120	<b>\$151</b>	180	258
	A	<b>Å</b> 47	<b>%</b> 6.0	90.1	85.8	₹54.5 🤇	43.8	39.8	27.5	27.2	16.4
	B C	( 24 <u>1</u> Ĉ	[≫] 93.2€	122~	84.6	56Ø	47.4	41.8	27.0	25.0	15.3
		180,	81.9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		S.	<i>©</i> - '	4	-	-	-
- C	<u></u>	₫23	0109		ý- 2	- 4	· -	-	-	-	-
		[©] 223 ©	92.5	106	84,9	55.5	45.6	40.8	27.2	26.1	15.8
	A 🖑	26	<loq< td=""><td><loq< td=""><td>5,3</td><td>∧ts.d.</td><td>≪<b>E</b>OQ</td><td><loq< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></loq<></td></loq<>	<loq< td=""><td>5,3</td><td>∧ts.d.</td><td>≪<b>E</b>OQ</td><td><loq< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	5,3	∧ts.d.	≪ <b>E</b> OQ	<loq< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.	n.d.
10-20	, P	, <i>\$</i> ∕Å	5.5	©¢ÊOQ _≈		n.d.	CLOQ	n.d.	n.d.	n.d.	n.d.
	Mean	✓ 6.5	×LOQ	· <loq< th=""><th><lqq< th=""><th>n.đ.</th><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></lqq<></th></loq<>	<lqq< th=""><th>n.đ.</th><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></lqq<>	n.đ.	<loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<></th></loq<>	<loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<>	n.d.	n.d.	n.d.
		n	n d.	, n.d.	5.1	J.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	B	<u>)</u> .d. ·	"H.d.		O'n.d. 4	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Â.	Mean 🎓	₽ n.d.^	n.d.Q	n.d.	<l00< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></l00<>	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

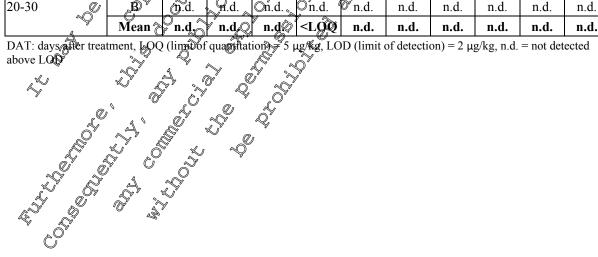




Table CA 7.1.2.2.1-9: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soil	at
Elm Farm expressed as µg/kg	

			-	•	8 8							ð
Depth	Repli-					D	AT					, G
[cm]	cate	0	7	14	29	56	90	120	<b>~</b> 151	180 _@	258	J
	Α	5.5	35.3	34.1	35.9	30.6	18.4	16.8	10.1	9.3	<u>,59</u>	
	В	<loq< td=""><td>34.8</td><td>40.5</td><td>39.7</td><td>28.8</td><td>19.3</td><td><u>k</u>6.0</td><td>10.1</td><td>\$.8</td><td>×\$.9</td><td>ð</td></loq<>	34.8	40.5	39.7	28.8	19.3	<u>k</u> 6.0	10.1	\$.8	×\$.9	ð
0-10	С	<loq< td=""><td>37.5</td><td>-</td><td>-</td><td>õa -</td><td></td><td><u>~</u>_</td><td>- , '</td><td>× - ×</td><td></td><td>4</td></loq<>	37.5	-	-	õa -		<u>~</u> _	- , '	× - ×		4
	D	<loq< td=""><td>35.8</td><td>-</td><td>- «</td><td><b>F</b> -</td><td>@</td><td>-</td><td>- Č ¥0.1</td><td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td><td>Ŵ</td><td>o^r</td></loq<>	35.8	-	- «	<b>F</b> -	@	-	- Č ¥0.1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ŵ	o ^r
	Mean	<loq< td=""><td>35.8</td><td>37.3</td><td>37.8</td><td>29.7</td><td>189</td><td>16.5</td><td>\$0.1</td><td>0.0</td><td>0 *</td><td>$\bigcirc^{\prime}$</td></loq<>	35.8	37.3	37.8	29.7	189	16.5	\$0.1	0.0	0 *	$\bigcirc^{\prime}$
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🔬		n.d	V
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.O	n.d.	n.d.O	n.¢	n.Q.	
	Mean	n.d.	n.d.	n.¢	n.¢	n.đ.	pKd.	"n.d.	Jand.	°~19.d.	≪n.d.	
	Α	n.d.	n.d.	n.a.	m.d.	d.	@n.d. 👌		On.d. 1	n.d. 🛋		
20-30	В	n.d.	n.d. 👷	취.d. 🗞	©n.d.∼	n.d.	n.ds	n.dC	n.d.	n.đ	n@.	
	Mean	n.d.	n.d 🖇		n.d.	n.d.	પ્રસ.	ĵn,∕d.	"n.d.	<b>≪ŋ.d</b> .	Sn.d.	

DAT: days after treatment, LOQ (limit of quantitation) = 5  $\mu_0$  kg, LOB (limit of detection) = 2  $\mu_0$  kg, n.d. = not detected above LOD

Table CA 7.1.2.2.1-10: Residues	of M(02 (sp	irooxamine-o	despropyly	in 0-30	cm horizons of soil at
Table CA 7.1.2.2.1-10: Residues Elm Farm	(20151/7)	xpressed as	f≱g/kg ∅ [°]	Č)	, or intervention

		•	<u> </u>	Ci ^V	¥ €		1 ~	()			
Depth	Repli-	\$ (		y k			AT S		L.S.		
[cm]	cate "	04	7	JA [®]	29	56	e, 90	×120	<b>S</b> 151	180	258
	A	<i>\$</i> .9	\$6.6	36.8	A38.0 🖉	32.8 🔇	21.5	19.Ø>	11.8	13.5	8.7
	₿ ,	C 5.5 Ĉ	₹37.3€C	₹ 42.4 [~]	40 A	32	21.7	19.1	11.7	12.5	8.3
0-10	B C C	5.6	38.8	~->		S.	<u> </u>	Ş-	-	-	-
	<u> </u>	≪∰OQ	37.2		ý- (	- 2	× _ · ·	-	-	-	-
	- Can'	≺LOQ	37.5	39,67	39,2	32.4	24.6	19.0	11.8	13.0	8.5
	A 🖑	nd	n 🕡 🎽 n.d.	n.d.	n.d.	≈n.d.	∕n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, <b>P</b>	s, fP.ð.		"An.d. 🦕	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	🖗 n.d. 🏹		n.d.	n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
		n 🎝	n d.	⊾n.d.	n.d.	ø.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30		and .		On.d. 👡		Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	on.d.^		n.d.Q	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

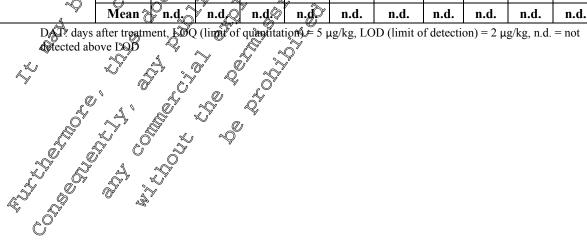




Table CA 7.1.2.2.1-11: Residues of spiroxamine in 0-30 cm horizons of soil at Paken	ıam ex-
pressed as µg/kg	

	I.	•										
Depth	Repli-		DAT									
[cm]	cate	0	7	14	28	55	91	120	<b>&gt;</b> 148	177	239	0
	Α	236	76.2	89.1	50.7	65.2	47.3	28.4	16.7	177 16.∜	1209	
	В	234	87.5	89.3	80.2	67.9	54.4	<u>2</u> .5	14.2	A.2	Qr1.9	Ô
0-10	С	248	81.4	-	-	ĉa -	- /	<u>~</u> -		لې _ کړ	- 2	
	D	233	68.2	-	- 4	- ⁻	@	-	- Č \$15.5	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	K.	, o ^g
	Mean	238	78.3	89.2	65.4	66.5	500	28.0		ð <u>5</u> .4	J X	,0″
	А	25.4	7.5	10.3	STOD	n.d.	QOQ	,≪LOQ,	Ç n.d. 🗶	, n.d. 🗘	n.d 🖉	ν '
10-20	В	25.2	8.1	10.5 🗸	8.2	n.d.	nd	n.d.	n.d. ^{O°}	n.¢	n Ø	
	Mean	25.3	7.8	104	5.&°	n.đ.	n%d.	<b>.</b>	and.	`~ <b>p</b> .d.	Kn.d.	
	А	<loq< td=""><td>n.d.</td><td>n.a.</td><td><b>≨LOQ</b></td><td>m.d.</td><td>m.d.</td><td>h.d.</td><td>Ön.d. A</td><td>n.d.A</td><td>n.d ∘</td><td></td></loq<>	n.d.	n.a.	<b>≨LOQ</b>	m.d.	m.d.	h.d.	Ön.d. A	n.d.A	n.d ∘	
20-30	В	<loq< td=""><td>n.d. 👷</td><td>🖓n.d. 🗞</td><td>©n.d.∼</td><td>, n.d. *</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.đ</td><td>nØ. M.d.</td><td></td></loq<>	n.d. 👷	🖓n.d. 🗞	©n.d.∼	, n.d. *	n.d.	n.d.	n.d.	n.đ	nØ. M.d.	
	Mean	<loq< td=""><td>n.d 🖓</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n d.</td><td>'n,d.</td><td>n.d.</td><td><b>≪ŋ.d.</b> ₄</td><td>M.d.</td><td></td></loq<>	n.d 🖓	n.d.	n.d.	n.d.	n d.	'n,d.	n.d.	<b>≪ŋ.d.</b> ₄	M.d.	

DAT: days after treatment, LOQ (limit of quadration)  $\neq$  5 µg/g, LOP (limit of detection) = 2 µg/kg, n  $d \neq$  not detected above LOD

Table CA 7.1.2.2.1-12: Residues of Mol (spinoxamine-deserbyl) in 0-30cm hopizons of soil at Pakenham expressed as µg/kg Ì Ô

		vQ /	¥ .		G a	<u> </u>		Ô	<u>^</u>		
Depth	Repli-	\$ (		y C	e	۳ D	AT ू\$″		S.		
[cm]	cate "	0 <u> </u>	7	_} <b>}</b> ≉	28	<b>Š</b> 5	<b>91</b>	×120 į	148	177	239
	A	8.9	\$5.1	32.1		/	32.0	15.5	8.4	8.9	7.1
	B A	( 13. <u>2</u> Ĉ	38.9	y 38.1 [∞]	34 7	35@	31.4	13.9	8.5	8.9	6.9
0-10	B C C	10.4	38.9 38.4	~->		54	Ø- ^	Ç -	-	-	-
l ô	, De	<u>0.0</u>	<b>A</b> 7.5		ý- (	- Z	× -	-	-	-	-
		[©] 10.6 ©	40.0	35,1		37.7	31.7	14.7	8.4	8.9	7.0
10-20	A	nd	<løq< td=""><td><loq< td=""><td>p.d.</td><td>∧n.d.</td><td>∼n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></løq<>	<loq< td=""><td>p.d.</td><td>∧n.d.</td><td>∼n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	p.d.	∧n.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	Ŗ	san A.	< LOQ	¢ĽOQ,	On.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∛n.d. ∢	~LOQ	<l00< th=""><th>n.d</th><th>n.đ.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></l00<>	n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
	A A	n 🎝	n d.	⊾n.el.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30		<u>m</u> .d. ·	. fr.d.	On.d. 👡	Ôn.d.	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	n.d.	n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

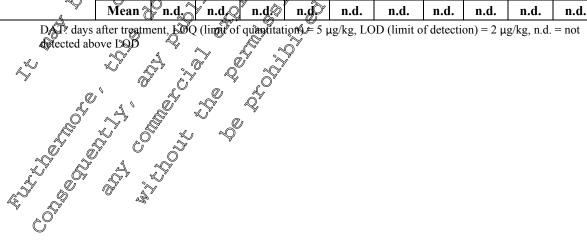




Table CA 7.1.2.2.1-13: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of so	il at	
Pakenham expressed as µg/kg	Ŵ	

Depth	Repli-					D	АТ					S.
[cm]	cate	0	7	14	28	55	91	120 (	<b>⊳148</b>	177	239	U
	Α	9.0	40.0	36.6	45.5	46.1	39.1	20.8	10.4	177 11.5⊮	<u>9</u> 9	
	В	13.5	43.0	43.1	41.9	41.7	39.8	20.3	11.2		×8.9	Ô
0-10	С	10.9	43.1	-	-	õa -	- "	$\sum_{i=1}^{n}$	-	🎽 - 🗞	2 - 2	ŕ
	D	10.1	51.1	-	- «	7 -	@	-	- () ¥0.8	- A	59.2 ( n.d.C	Ľ
	Mean	10.9	44.3	39.8	43 A	43.9	3924	20.5	\$0.8	<b>J</b> 1.4	<b>A9</b> .2 ç	0″
	Α	n.d.	<loq< td=""><td><loq< td=""><td>nd.</td><td>n.d.</td><td>Qn.d.</td><td>∘n.d. ∥</td><td>Ç n.d. 🔬</td><td>n.d. Ĉ</td><td>n.d @</td><td>ř</td></loq<></td></loq<>	<loq< td=""><td>nd.</td><td>n.d.</td><td>Qn.d.</td><td>∘n.d. ∥</td><td>Ç n.d. 🔬</td><td>n.d. Ĉ</td><td>n.d @</td><td>ř</td></loq<>	nd.	n.d.	Qn.d.	∘n.d. ∥	Ç n.d. 🔬	n.d. Ĉ	n.d @	ř
10-20	В	n.d.	<loq< td=""><td><loq(< td=""><td>n.d.</td><td>n.d.</td><td>n.d.@</td><td>n.d.</td><td>n.d.^O</td><td>n.Ø</td><td>n.Ø.</td><td></td></loq(<></td></loq<>	<loq(< td=""><td>n.d.</td><td>n.d.</td><td>n.d.@</td><td>n.d.</td><td>n.d.^O</td><td>n.Ø</td><td>n.Ø.</td><td></td></loq(<>	n.d.	n.d.	n.d.@	n.d.	n.d. ^O	n.Ø	n.Ø.	
	Mean	n.d.	<loq< th=""><th>n.<b>¢</b>k</th><th>n.¢</th><th>n.d.</th><th>pKd.</th><th>"n.d.</th><th>jed.</th><th>°~nyv.d.</th><th>Kn.d.</th><th></th></loq<>	n. <b>¢</b> k	n.¢	n.d.	pKd.	"n.d.	jed.	°~nyv.d.	Kn.d.	
	Α	n.d.	n.d.	n.a.	n,d.	ŋ.d.		n.d.	Øn.d. A	, n.d. 🛋	, n.d, ∘	
20-30	В	n.d.	n.d. 😵	A.d. 🧞	Øn.d.∼	n.d.	n.d	n.dC	n.d.	n	n@. d.	
	Mean	n.d.	n.d.	n.d.	n.d.	n,d.	પ્ર. શ.	ĵn≱d.	n.d.	<b>≪ŋ.d.</b>	An.d.	

DAT: days after treatment, LOQ (limit of quadration)  $\neq 5$   $\mu$  gAp, LOD (limit of detection) = 2  $\mu$  skg, n.  $\phi$  = not detected above LOD

#### C. Residues

No residue of spiroxamine, MOI and MO2 above the LOC of the analysical method could be found in the control samples.

Starting from an application rate of 0.79 kg as /ha and a soil density of 4.5 kg/b the theoretical total concentration in a 10 cm layers 500 ag/kg soil. The concentration of spiroxample in the 0-10 cm layer found immediately after application were 227, 262, 223 and 238  $\mu$ g/kg for Hørchen, Laacherhof, Elm Farm and Pakenham trial sites, respectively. This equates that at day zero 65.4%, 52.3%, 44.6% and 47.6% of the applied amount was recovered

For Höfchen (30122/4) trial site the mean residue concentration in the 0-10 cm soil segment decreased from 327 µg/kg at 0 DAT to 32 3µg/kg at 239 DAT. In the 10-20 cm and 20-30 cm layer spiroxamine was not tound at levels great than LQQ at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentration, reached a maximum of 319 µg/kg at 7 DAT and decreased to 5.5 µg/kg at 239 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 32.8 µg/kg at 7 DAT and decreased to 5.4 µg/kg at 239 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02 no residues were found at levels greater than LOQ (5 µg/kg) at any time point.

For Laacherhof (30124/8) trial size the mean residue concentration in the 0-10 cm soil segment decreased from 262 µg/kg at 0 D/FT to 23.2 µg/kg at 231 D/FF. In the 10-20 cm and 20-30 cm layer spiroxamine was not found at levels great than DOQ at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 33.0 µg/kg at 28 DAT and decreased to 9.7 µg/kg at 231 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 23.1 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 29.7 µg/kg at 28 DAT and decreased to 8.7 µg/kg at 231 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02, no residues were found at levels greater than LOQ (5 µg/kg) at any time point.

For Elm Farm (2015117) triat site the mean residue concentration in the 0-10 cm soil segment decreased from 223 µg/kg at (DAT to 15.8 µg/kg at 258 DAT. In the 10-20 cm layer spiroxamine was found on on soccasion, with the maximum value of 6.5 µg/kg found at DAT 0. In the 20-30 cm layer spiroxamine was not bund at levels great than LOQ at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 37.8 µg/kg at 29 DAT and decreased to 5.9 µg/kg at 258 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 37.8 µg/kg at 29 DAT and decreased to 5.9 µg/kg at 258 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 39.6 µg/kg at 14 DAT and decreased to 8.5 µg/kg at 231 DAT. In both the 10-20 cm and 20-30 cm layer for



the metabolites M01 and M02, no residues were found at levels greater than LOQ (5  $\mu$ g/kg) at any time point.

For Pakenham (30263/5) trial site the mean residue concentration in the 0-10 cm soil segment decreased set from 238 µg/kg at 0 DAT to 12.4 µg/kg at 239 DAT. In the 10-20 cm layer spixoxamine was found in⁶ small amounts, with the maximum value of 25.3  $\mu$ g/kg found at DAT 0 and degreasing to 5.8  $\mu$ g/kg at DAT 28. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 38.1 μg/kg at 28 DAT and decreased to 7.0 μg/kg at 239 DAT. For the metabolite, M02 m the OFO cm soil segment concentrations reached a maximum of 43.7  $\mu g/kg$  at 28 DAT and decreased to  $92 \mu g/kg$ at 239 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02, or residues were found at levels greater than LOQ (5  $\mu$ g/kg) at any time point.

#### F. Degradation kinetics

Degradation rates determined in the report are superseded by the report presented under point  $\sqrt{2}$ 

#### Gonclusion III.«

Following a single application of spirox mine at a nominal application, rate of 0.55 kg a.i/ha tounder field conditions without vegetation (Hopcherg) and with vegetation Laacherhof, Dim Farm and Pakenham) in spring 1993. The decline of proxamine and the formation and decline of its metabolites M01 and M02 was followed for up to 258 days after application at four sites in Germany and the UK.

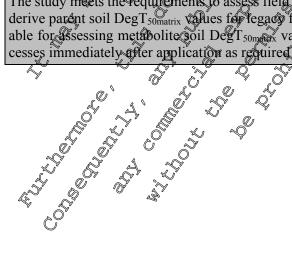
During the whole test duration, gearly all residues remained on the 6/10 cm layers of the soil. The maximum concentration of spiroxamine was observed for the Höfcher (30122/1) trial site at 327 µg/kg at 0 DAT. Only in the Pakenham site was spire xamine found in the 10-20 cm layer, the maximum value was 25.3 µg/kg at Day 0. No mobility into see layers below 20 cm was observed. The metabolites M01 and M02 were detected at all sites The metabolic M01 reache a maximum of 38,1 0p/kg at DAT 28 in the Pakenham trial site. The metabolite M02 reached maximum of 43.7 µg/kg at OAT 28 in the Pakenham trial site in the 0-10 cm layer. In both the 10-20 cm and 20, 90 cm layer for the metabolites M01 and M02, no residues were found at levels greater than LOQ (5 rg/kg at any time point.

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed on KCA 7.1.2 2.1/12 (M-763140-0).

## Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study is considered valid to assess the dissignation of spiroxamine under field conditions in soil. The study meets the requirements to assess field persistence of spiroxamine and its metabolites, and to derive parent soil DegT 50 matrix values for legacy field studies as defined by EFSA (2014). It is not suitable for assessing metabolite foil DegT 50mmer values as the design did not minimise soil surface processes immediately after application as required by EFSA (2014).





Data Point:	KCA 7.1.2.2.1/02	
Report Author:		~
Report Year:	1995	¢
Report Title:	Dissipation of KWG 4168 in soils under field conditions	p
Report No:	RA-2002/94	
Document No:	<u>M-006126-01-1</u>	
Guideline(s) followed in	BBA Guideline IV-4.1 (1986)	2
study:		·
Deviations from current	Yes (refer below)	Ø
test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the refubility of the roudy (described in study summary)	Ś
	study summary)	) ,
Previous evaluation:	yes, evaluated and accepted $Q^{*}$ $Q^{*}$ $Q^{*}$	
	DAR (1997), RAR (2010) RAR (2017)	
GLP/Officially recog-	Yes, conducted under GEP/Officially recognised testing facilities	
nised testing facilities:		
Acceptability/Reliability:	Yes v v v v v A	

#### **Executive Summary**

Soil dissipation of spiroxamine was studied after application as an FC formalation containing 401.4 g/L to bare soil plots under field conditions for up to 270 days at five trial sites in Germany (Hötchen, silt loam; Laacherhof, sandy loam; Maasen, sandy loam; Swisttal-Hohn, silt loam and Albig, clay loam/silty clay loam).

In spring 1994 a single application of a nonunal 0,75 kg a.s./ha as an entalsifiable concentrate formulation was performed to bare soil.

Twenty soil core samples were taken from the treaten as well as ten soil core samples from the control plot directly post application. Core samples were taken to a depth of 30 cm and segmented into 10 cm soil layers prior to homogenisation and analysed Samples were taken at the Höfchen site, at 0, 7, 14, 29, 56, 89, 118, 155, 190 and 270 days after treatment DATt at Laacherhof at 0, 7, 14, 28, 59, 87, 120, 152, 181 and 240 DAT, at Maasen at 0, 7, 14, 30, 60, 90, 120, 150, 180 and 240 DAT, at Swisttal-Hohn at 0, 7, 14, 30, 58, 91, 120, 050, 180 and 252 DAT and at Alber at 0, 7, 14, 30, 60, 90, 120, 150, 180 and 240 DAT.

Soil samples were analysed for spirovamine and the metabolites 101 (spiroxamine-desethyl) and M02 (spiroxamine-desproyl). Soll samples were extracted by Soxtec extraction with a basic solution of methanol/water/anthonia (25%) ( $\$2:0:1 \sqrt{v/v}$ ) Parent and metabolites were quantitatively determined by liquid chromatography with MS-MS detection. A limit of quantification (LOQ) of 5 µg/kg and a limit of detection (LOD) of 2 µg/kg was reported for spiroxamine and the metabolites.

Starting from an application rate of 0.75 kg a s/ha ard a soil density of 1.5 kg/L the theoretical total concentration in a 10 cm layer is 500  $\mu$ g/kg soil. The concentration of spiroxamine in the 0-10 cm layer found infinediately after application were 365, 395 284, 325 and 387  $\mu$ g/kg for Höfchen, Laacherhof, Maasen, Swisttal-Hohn and Albig rial sites, respectively. This equates that at day zero 73.0%, 79.0%, 56.8%, 65.0% and 77.4% of the applied amount was recovered from each site, respectively.

During the whole test duration, nearly all residues remained in the 0-10 cm layers of the soil. The maximum concentration of spiroxamine was observed for the Albig trial site at 386  $\mu$ g/kg at 0 DAT. Only in the Hötchen was spiroxamine found in the 10-20 cm layer, the maximum value of 9.4  $\mu$ g/kg was reported at 89 DAT. No mobility into soil layers below 20 cm was observed. The metabolites M01 and M02 were detected at all sites. The metabolite M01 reached a maximum of 45.8  $\mu$ g/kg at 14 DAT in Swistral-Holm in the 0-10 cm layer. The metabolite M02 reached a maximum of 43.6  $\mu$ g/kg at 7 DAT in Swistral-Holm in the 0-10 cm layer.

The  $D\mathbf{E}_{0}$  and  $DT_{90}$  of spiroxamine determined in the study was reported for each site. However, a reevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT50 values from laboratory and field dissipation

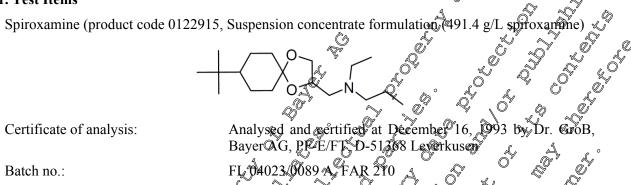


studies (EFSA 2014), was performed in the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

#### I. **Materials and Methods**

#### A. Materials

#### 1. Test Items



Certificate of analysis:

Batch no.:

Purity:

#### 2. Trial locations & Soils

te

7.1.2.2.1-14. The field soil dissipation trial consisted of one treated and one untreated plot on each site. No pesticide history was given for previous years before the triat for either site M Ò,

Ò

Table CA 7.1.2.2.	1-14: <b>Ľ</b> à	ocation.	site	descriptio	n and	climat	ic data	of test	sites	
		A	Ro		⊾Ø'	O ^V	6	$\sim$	8	
Trial designa-	<i>N</i>	S.	1	0	Ň,	×		<b>%</b> ,	°~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	

Trial designa- tion	\$ 4000 <b>6</b> /8	40007/65	×40008/4	40609/2	40010/06
Soil Designation	HOfchen	Haachershof	Maasen y	Synsttal-Hohn	Albig
Vegetation	Bare soil	Bange soil	Bare soil	[®] Bare soil	Bare soil
Geographic Lo- cation	Deutsche Verstehsgüter 2 De 1399 Sur- scheid Höfchen Efter 4018	Deutsche Versuchere D-40789 Mon Cheim Laacherhof Flur 15	Deutschand Nordost DS27249 Maasen An der Scheune Far 79/7	<ul> <li>Deutsche</li> <li>Versuchsgüter</li> <li>1</li> <li>D-53913</li> <li>Swisttal-Hohn</li> <li>Flur 790, J.</li> <li>Brünker</li> </ul>	Deutschland Südweat, D- 55234 Albig, Flur 37 Nr. 25 Im Odernhei- mer Weg
Country 🔊	¿Germany	Germany	Germany	Germany	Germany
Textural Classifi- cation (USDA)	Silt loam	Bandy Bam	Sandy loam	Silt loam	Clay loam/ silty clay loam
Sand [50 - 2000 μm] (%)	J 64 .	70.8	66.4	27.6	20.0
Silt $[2 - 50 \mu\text{m}]$ (%)	76.64 76.64		30.4	60.4	51.1
Clay [< 2 μm) (%)		<b>∞</b> 9.1	3.2	12.0	28.9
pH (in 0 M M CaCl solution)		6.6	5.9	6.7	7.8
(%)	۵.50 ۲.50	2.08	2.18	1.72	2.41
Organ©carbon (%)	0.87	1.21	1.27	1.00	1.40



Trial designa- tion	40006/8	40007/6	40008/4	40009/2	40010/06
Cation Exchange Capacity (meq/100 g)	1.50	8.0	8.0	9.0	
Soil Moisture ca- pacity (g/100g soil)	39.2	40.6	32.1	36.7 ***	
Size of plot (m ² )	227	255	^C 200	255	200

#### **B. Study Design**

#### **1. Experimental Conditions**

A single application of a nominal 0.75 kg a.s./ha as an emulsifiable concentrate (EC) was performed to bare soil on 21st April 1994 (Höfchen), 26^h April 1994 (Laacherhof), 10th May 1994 (Massen), 10th May 1994 (Swisttal-Hohn) and 21st May 1994 (Albig).

During the studies on bare soil mechanical weed control was performed. Noplant protection products or irrigation was carried out and any of the trail sites Weather date was collected at a location near to the site during the study period; this data includes the mean air temperature, rainfall and sunshine hours.

Soil dissipation of spiroxamine was studied for a maximum of 270 days.

#### 2. Sampling

Duplicate samples were collected framediately after the reatment and at intervals up to 270 days after the treatment. Core samples were taken to a depth of 30 cm (diameter 50 mm) and segmented into 10 cm soil layers prior to homogenisation and analysed. Samples were taken at the Höfchen site, at 0, 7, 14, 29, 56, 89, 118, 155, 190 and 270 days after treatment (DAT), at Laacherhof at 0, 7, 14, 28, 59, 87, 120, 152, 181 and 240 DAT, at Marsen at 0, 7, 14, 30, 60, 90, 120, 150, 180 and 240 DAT, at Swisttal-Hohn at 0, 7, 14, 39, 58, 91, 120, 150, 181 and 252 DAT and at Albig at 9, 7, 14, 30, 60, 90, 120, 150, 180 and 240 DAT. The control plots were sampled at the beginning and end of the study.

At each sampling point 20 eores were taken using a pushing sampling system (Wacker Hammer) down to a depth of 30 cm (diameter 50 mm) per sampling interval. Locations of sampling were statistically distributed over the plot to get representative samples. Samples over transported in a cooler box containing dry ice, before being stored at -18 C until analysis at the aboratory.

The frozen soil cores were cut into 10 com segments. Pen (control sample) to twenty (treated samples) of such segment of one dater were milled and carefully homogenised.

## 3. Analytical Procedures

Soil samples were analysed for spiroxamine and the metabolites M01 (spiroxamine-desethyl) and M02 (spiroxamine-despropris). Replicate sub-samples overe analysed by Method 00374 (RA-607/94) (M-019207-02-1), using HPLCMS/MS.

In summary, the method involved Soxtec extraction with refluxing methanol/water/ammonia (25%) (8:2:0.1, v/v/v). After solver evaporation to the aqueous remainder the internal standard were added. The LOQ ( $5 \sqrt{g}/kg$ ) of the method was  $2 \sqrt{g}/kg$  for parent and metabolites.

Procedural recovery samples were analysed. Untreated soil samples were fortified with known amounts of spiro amine M01 and M02 and carrying these samples through the procedure alongside the treated samples.

#### 4. Determination of degradation kinetics

The  $DF_{50}$  and  $DT_{90}$  of spiroxamine determined in the study was reported for each site. However, a reevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT₅₀ values from laboratory and field dissipation



studies (EFSA 2014), was performed in the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

#### II. **Results and Discussion**

#### A. Analytical Methodology

Full details and acceptable validation data to support this method (Method 00374 (RA-607/94)) are presented in Document M-CA 4, Section 4.1.2 (M-019207-02-1). The method complies with the EU@ regulatory requirements outlined within SANCO/3029/99 rev. 4 and is suitable for the determination of spiroxamine and its metabolites in soil samples by HPLCMS/MS.

Analytical performance was determined by analysing known amounts of spiroxantine and internal standards. The mean recovery of spiroxamine, M01 and M02 was  $2.1 \pm 13\%$ 89.8 ± 5,8% and 9 6.7% respectively, over a fortification range of 5 μg/kg.

#### **B.** Data

Total residues detected in each treated plot are presented in the report. The results for piroxanine and its metabolites are presented below as soik residue concentrations (on a ug/kg dry weight basis) for each of the treated plots in Table CA 7.1.2.2 15 to Table CA 7. 12.2.1 8.

#### Table CA 7.1.2.2.1-15: Residues of spirovamine in 0-30 cm horizons of soil at Höchen expressed as ug/kg 🔍 \$ ~ Re

	asp	ig/ Kg	× (	?		, ₀ ,	L'	×	0 /	Ŋ	
Depth	Repli-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	°~	~~~~~	Ø			0	) N	1	
[cm]	cate	) O	<b>%</b> 7	ِي <b>ٽ</b> ا 4	<b>29</b>		* 89.**	1,18	155	190	270
	A 🇞	303 ⁽	277 Č	327	250	179,	125	<b>%4</b> .4	81.9	58.2	59.2
	B	364	345	302	299	s <b>19</b> 7	×128 (k)	90.5 Č	ð 75.5	66.0	60.8
0-10	<i>S</i>	452	294	Q-,	\$ ⁷ - `	Kj.	- 0 [°]	Ś	-	-	-
	SD C	¥ 343	314	* -~	-0	-9	ź.	Q-	-	-	-
	Mean	365	308	315	249	188		87.5	7 <b>8.</b> 7	62.1	60.0
<u> </u>	Å	_≪ n.d.	n.d.	<b>LOQ</b>	¢ 5.7 ړ	9 [°] 7.9 (	10.8	6.7	<loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td></loq<>	n.d.
10-20	В 🔬		n.d n.d.	, n.đ	6.40	7.0	80	7.2	<loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td></loq<>	n.d.
<u>E</u> G	Mean	<lqq< th=""><th>næ.</th><th><lqq< th=""><th><b>A</b></th><th><i>.</i></th><th><b>9.4</b></th><th>7.0</th><th><loq< th=""><th><loq< th=""><th>n.d.</th></loq<></th></loq<></th></lqq<></th></lqq<>	næ.	<lqq< th=""><th><b>A</b></th><th><i>.</i></th><th><b>9.4</b></th><th>7.0</th><th><loq< th=""><th><loq< th=""><th>n.d.</th></loq<></th></loq<></th></lqq<>	<b>A</b>	<i>.</i>	<b>9.4</b>	7.0	<loq< th=""><th><loq< th=""><th>n.d.</th></loq<></th></loq<>	<loq< th=""><th>n.d.</th></loq<>	n.d.
\$ ¥	À	M.d.	≪n.d.		×LOQ	<loq< td=""><td>₹LOQ/6.2</td><td><loq< td=""><td>6.2</td><td><loq< td=""><td>n.d.</td></loq<></td></loq<></td></loq<>	₹LOQ/6.2	<loq< td=""><td>6.2</td><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	6.2	<loq< td=""><td>n.d.</td></loq<>	n.d.
20-30	S [™] B ,1	n.d.@	n.d	n.d.O	n.d.O	n¢d,	7.1/5.1	n.d.	<loq< td=""><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.
0.	Mean	n.d.	p.a.	<ÈØQ		<b>≤t</b> ÕQ	<loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td></loq<>	n.d.

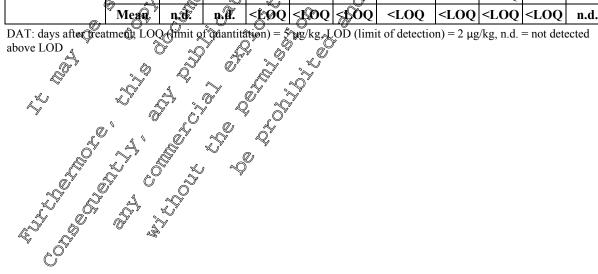




Table CA 7.1.2.2.1-16: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soil a	ıt
Höfchen expressed as µg/kg	

			1	• •	8							ð
Depth	Repli-					D	AT					
[cm]	cate	0	7	14	29	56	89	118	<del>)</del> -155	190 _@	270	U
	Α	12.4	14.7	19.2	22.5	19.6	19.2	16,	13.2	13.1	270 1608	
	В	13.3	15.9	18.9	23.5	20.4	19.9	<u>k</u> 6.9	13.5	£2.4	~Q*2.1	Ô
0-10	С	12.0	15.9	-	-	~~ -	- "	$\sum_{i=1}^{n}$	- 🧳	ا∛ - ا	- 2	ř
	D	9.6	18.6	-	_ 4	<b>F</b> -		-	- 0 \$ <b>13</b> .4	×,	Ŵ	
	Mean	11.8	16.3	19.0	23 A	20.0	196	16.5	\$3.4	ð <b>2</b> .7		K //
	Α	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. "		n.d	,×
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.©	n.d.	n.d. ^O	n.¢	n.V.	
	Mean	n.d.	n.d.	n.¢	n.¢	n.đ	pKd.	"n.d.	æð.	°~19.d.	Kn.d.	
	А	n.d.	n.d.	n.a.	n,d.	m.d.		n.d.	Ön.d. 🔊	n.d. 🕰	, n.d. ∘	
20-30	В	n.d.	n.d. 💡	An.d. 🦻	©n.d.∼	n.d.	n.ds	n.dÇ	n.d.	n	n@.	
	Mean	n.d.	n.d 🖴	n.d.	n.d.	n,d	વ્રસ.	ĵn≱d.	n.d.	<b>≪ŋ.d</b> .	An.d.	

DAT: days after treatment, LOQ (limit of quaditation) = 5 µg/g, LOP (limit of detection) = 2 µg/kg, n. 4 not detected above LOD

Table CA 7.1.2.2.1-17: Residues of M02 (spiroxamure-despropyly in 0-50 cm borizons of soil at Höfchen expressed as µg/kg Ì Ô

		$\sim$	<b>%</b> .	Ci ^V 4	<del>y a</del>				^		
Depth	Repli-				-		AT S		L.		
[cm]	Cale			14	~ <b>29</b>	/ <b>-</b> ¥	89	🖓 18 g	155	190	270
	A	10 ⁷ .0	A.S.5	17.4	Z2.4 🖌	°,≫19.7 (	18.6	15.5	10.2	12.0	10.3
	B C V	(, 12.5 Ĉ	5 14.5 Ç	× 18.6 [∼]	24 7	20 <i>Ø</i>	19.7	15.7	10.6	11.0	10.7
• - •		11.0	14.2	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		S.	Ũ- Ĵ	Ç -	-	-	-
so O	P	8.8	₫7.0	<u>,</u>	Ŋ- (	y - 2		-	-	-	-
		[©] 10.8 ©	14.8	18,0	23,5		19.2	15.6	10.4	11.5	10.5
10-20	A 🖉	nd	n 🕖 🎽	n.d.	n.d.		∕n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	s, fr.ð.	n.d.	©n.d. »	On.d.		O_ <loq< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.	n.d.	n.d.
	Mean	∛n.d. ∢	n.d		n.d	n.d.	<loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<>	n.d.	n.d.	n.d.	n.d.
	A A	n	n d.	<e⁄qq< td=""><td>n.d.</td><td>Q.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></e⁄qq<>	n.d.	Q.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	ß	<u>m</u> .d.	, fr.d.	05.4 👡	Ôn.d.	₿LOQ	8.9/n.d.	<loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td></loq<>	n.d.
4 N N N N N N N N N N N N N N N N N N N	Mean 🎓	<b>n.d.</b>	n.d _z Q			<loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.

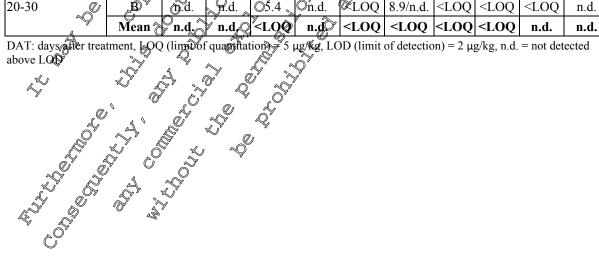




Table CA 7.1.2.2.1-18: Residues of spiroxamine in 0-30 cm horizons of soil at Laacherhof ex	Х-
pressed as µg/kg	

	L		0 0									ð
Depth	Repli-					DA	АT					
[cm]	cate	0	7	14	28	59	87	120	<b>&gt;</b> 153	181 🖉	240	U
	Α	385	223	233	180	87.3	70.7	38.7	31.7	30.6⁄	2803	
	В	408	260	247	179	98.0	68.5	39.1	33.4	<b>A</b> .6	<b>28</b> .2	Ô
0-10	С	422	240	-	-	ĉa -	- /	$\mathcal{L}^{*}$	- 🦿	ا≫ ا		í
-	D	366	263	-	- «	- ⁻	@	-	- () 32.5	×,	L.	
	Mean	395	247	240	180	92.6	69.6	38.9	32.5	30.1		
	А	n.d.	n.d.	<loq< td=""><td>≤ĽOQ</td><td><loq< td=""><td>Q.d.</td><td>n.d. 🧳</td><td>Ç n.d. 🗶</td><td>, n.d. 🕻</td><td>n.d</td><td>Ň</td></loq<></td></loq<>	≤ĽOQ	<loq< td=""><td>Q.d.</td><td>n.d. 🧳</td><td>Ç n.d. 🗶</td><td>, n.d. 🕻</td><td>n.d</td><td>Ň</td></loq<>	Q.d.	n.d. 🧳	Ç n.d. 🗶	, n.d. 🕻	n.d	Ň
10-20	В	n.d.	n.d.	n.d. 🗸	LOQ	<loq< td=""><td></td><td><loq< td=""><td></td><td>n.Ø</td><td>n.Q.</td><td></td></loq<></td></loq<>		<loq< td=""><td></td><td>n.Ø</td><td>n.Q.</td><td></td></loq<>		n.Ø	n.Q.	
	Mean	n.d.	n.d.	<lqq< th=""><th><løø< th=""><th><lqq< th=""><th>n%d.</th><th>&lt;ŁØQ</th><th>æd.</th><th>°~p.d.</th><th>Kn.d.</th><th></th></lqq<></th></løø<></th></lqq<>	<løø< th=""><th><lqq< th=""><th>n%d.</th><th>&lt;ŁØQ</th><th>æd.</th><th>°~p.d.</th><th>Kn.d.</th><th></th></lqq<></th></løø<>	<lqq< th=""><th>n%d.</th><th>&lt;ŁØQ</th><th>æd.</th><th>°~p.d.</th><th>Kn.d.</th><th></th></lqq<>	n%d.	<ŁØQ	æd.	°~p.d.	Kn.d.	
	А	n.d.	n.d.	n.d.	√ŋ, d.	m.d.	n.d.	h.d.	&LOQ(	/ <loq< td=""><td>n.d_∘</td><td></td></loq<>	n.d_∘	
20-30	В	n.d.	n.d. 😵	🖓n.d. 🗞	©n.d.∼	n.d.	∛n.d₄	n.d.	n.d.		n@.	
	Mean	n.d.	n.d 🖴	n.d.>	n.d.	n.d.	n dr. "	'n,d.	<b>≲ĽÓQ</b>	≪LOQ	An.d.	

DAT: days after treatment, LOQ (limit of quadration)  $\neq 5 \ \mu g$  (by, LOD (limit of detection) = 2  $\mu g$  kg, n. ( $\neq$  not detected above LOD

Table CA 7.1.2.2.1-19: Residues of MOI (spinoxamure-desethyl) in 0-30cm hopizons of soil at ,Ô Laacherhof expressed as µg/kg Ô

		N	<b>%</b> .	Ĉi 1	Ÿ ₹	~ ~		Ô	•		
Depth	Repli-	\$ (		y Č	-	,DA	AT ू\$′		S.		
[cm]	cale		.7	JAP -		Ő\$9	87	×120 (	<b>153</b>	181	240
		49.3	<b>46.</b> 7	23.8	് 30.7 🚽	≫20.6 🤇	25.3	17,7	16.2	16.2	17.3
	B C	(, 8.9 Ĉ	§ 19.2€			24@	25.8	18.6	17.5	15.6	16.7
	Ç VO	11.0	20.5	~->		Sr.	Ø- ^	Ş -	-	-	-
	Ŕ	Ø.3	20.3		ý- (	y - 4	× -	-	-	-	-
Ro	Mean	[©] 9.4 ©		25,1	28,7	22.6	25.6	18.1	16.9	15.9	17.0
10-20	A 🖉	nd	n 🖉 🎽	n.d.	n.d.	"M.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	Ŕ	∘ <b>_19.2</b> .	n.d.	©n.d. »	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
		🖌 n.d. 🏹	» n.d.	n.d.	n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
(		n de	n d.	n.d.	n.d.	p.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30		<u>m</u> .d.	, fl.d.	On.d. 👡		Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Mean 🎓	∽n.d.^	n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

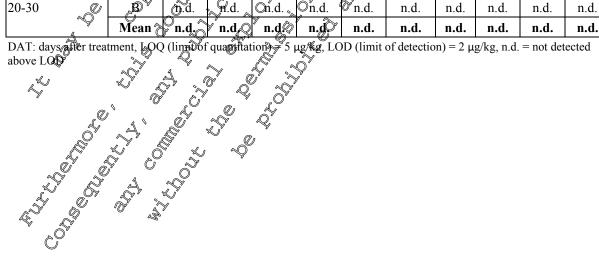




Table CA 7.1.2.2.1-20: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of	soil at
Laacherhof expressed as µg/kg	

												Õ.
Depth	Repli-					D	AT					Ç,
[cm]	cate	0	7	14	28	59	87	120	~153	181	240	
	Α	10.7	15.4	22.1	30.5	18.9	21.6	15,7	13.6	13.4	14Çi	
	В	8.8	17.0	24.9	26.9	20.6	22.5	<u>k</u> 5.1	15.6	\$ 3.5	Q4.1)
0-10	С	10.5	18.2	-	-	<u>~</u>		<u>~</u> _	- ,	الأ − ا		
	D	7.1	18.7	-	- «	F -	- 0	-	- Ô \$4.6	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		d d
	Mean	9.3	17.3	23.5	28A	19.8	220	15.4	\$4.6			\mathcal{O}^{\prime}
	Α	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🔎	, n.d. 🤇	44.1	
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	<loq< td=""><td>×∧</td><td>n.d.</td><td>n.d.O</td><td>n.đ</td><td>n.Q.</td><td></td></loq<>	×∧	n.d.	n.d.O	n.đ	n.Q.	
	Mean	n.d.	n.d.	n.¢	n.¢	<lqq< td=""><td>pKd.</td><td>"n.d.</td><td>æð.</td><td>`^ŋ≱.d.</td><td>≪n.d.</td><td></td></lqq<>	pKd.	"n.d.	æð.	`^ŋ≱.d.	≪n.d.	
	Α	n.d.	n.d.	n.a.	n,d.	ŋ.d.		n.d.	Øn.d. 🔊	n.d. 🛋		
20-30	В	n.d.	n.d. 💡	취.d. 🗞	©n.d.∼	, n.d. *	n.ds	n.dQ	<loq< td=""><td>n.đ</td><td>nđ. Sn.d.</td><td></td></loq<>	n.đ	nđ. Sn.d.	
	Mean	n.d.	n.d 🖇	n.d.	n.d.	n,d	પ્રસ.	ĵn≱d.	< £ ÓQ	≪ŋ.d.	An.d.	

DAT: days after treatment, LOQ (line) of quantitation $45 \mu g kg$, LOP (limit (detection) = 2 $\mu g kg$, n.d. = not detected above LOD

Table CA 7.1.2.2.1-21: Residues of spiroxamine in 0-30 cm horizons of soil at Maasen expressed as µg/kg Ô Ĉn

		₽₩₽	% .	er e	6 a	<u> </u>					
Depth	Repli-			y s	C	D A	ΔT 🌮	2,	L.		
[cm]	cate		7	14	3 0	60	90	×120	\$150	180	240
	A	286		136	¢155 ٍ (67.1	• 69.2×	48.2	66.5	74.1
	S C V	(27 <u>1</u> Ĉ	אָיַזין 17	142~	133	87Ø	75.9	63.6	44.0	62.7	54.5
		276	171 163	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		2	Ø- ;	¢.	-	-	-
^{SC}	<u></u>	<u>3</u> 05	J\$0 g		S - S	K	y	-	-	-	-
	Mean	[©] 284 ©	156	139	144	86.6	71.5	66.4	46.1	64.6	64.3
10-20	A 🖑	nd	n Ø	n.d.	∠L OQ		6.4	<loq< td=""><td><loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td></loq<>	n.d.
10-20	, P	s , fr2i .	n.d.	_© ∕n.a. _≥	^O n.d.	LOO	n.d.	n.d.	<loq< td=""><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	n.d.	<loq< td=""></loq<>
	Mean	🖌 n.d. 🔇		n.d.	<lqq< th=""><th>~ -</th><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<></th></loq<></th></lqq<>	~ -	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""></loq<></th></loq<>	<loq< th=""></loq<>
	A A	n đ	ng.	n.d.	n.d.	P OQ	n.d.	n.d.	6.9	n.d.	n.d.
20-30		<u>m</u> .d.	A.d.	On.d.		© ĽOQ	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	on.d.^	n.d.Q	n.d.	n.d	<loq< td=""><td>n.d.</td><td>n.d.</td><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	n.d.	n.d.	<loq< td=""><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.

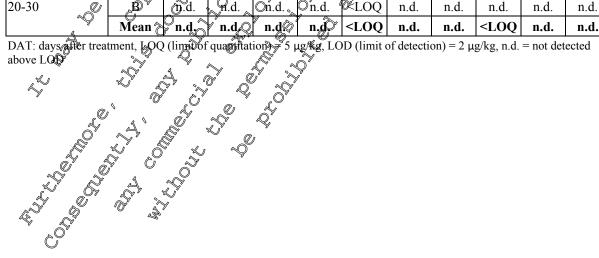




Table CA 7.1.2.2.1-22: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soil a	ıt
Maasen expressed as µg/kg	

			L	• 8	8							ð
Depth	Repli-					D	АТ					
[cm]	cate	0	7	14	30	60	90	120	~150	180 _@	240	U
	Α	5.4	13.4	16.4	19.8	15.0	18.6	19.5	14.1	20.2	2008	
	В	<loq< td=""><td>16.7</td><td>18.5</td><td>18.8</td><td>15.9</td><td>17.8</td><td>20.1</td><td>13.8</td><td>\$8.8</td><td>~\$6.3</td><td>Ô</td></loq<>	16.7	18.5	18.8	15.9	17.8	20.1	13.8	\$8.8	~ \$ 6.3	Ô
0-10	С	9.2	15.8	-	-	õa -	- "	<u>~</u>	- 🦨	ا∛ - ا	- 2	ř
	D	12.1	15.6	-	- «	- 12	@	-	- 0 ¥4.0	×,	L.	
	Mean	7.3	15.4	17.4	19 .S	15.5	182	19.7	\$4.0	J 9.5	A8.5 ç	0″
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🗶	n.d. 🤇	n.d	,×
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.Ø	n.d.	n.d. ^{©°}	n.Ô	n Ø.	
	Mean	n.d.	n.d.	n. ¢ k	n.¢	n.đ.	pKd.	"n.d.	æd.	°^ŋ.d.	Kn.d.	
	А	n.d.	n.d.	n.a.	n.d.	m.d.		n.d.	Øn.d. A	n.d. 🕰	n.d. ∘	
20-30	В	n.d.	n.d. 😵	An.d. 🧞	©n.d.∼	, n.d. *	♥ n.d₄	n.dC	n.d.	n 🖉	n@. 	
	Mean	n.d.	n.d 🖴	n.d.	n.d.	n.d.	વ્રસ.	ĵn,∕d.	n.d.	≪ŋ.d.	An.d.	

DAT: days after treatment, LOQ (limit of quaditation) = 5 µg/g, LOP (limit of detection) = 2 µg/kg, n. 4 not detected above LOD

Table CA 7.1.2.2.1-23: Residues of M02 (spiroxamure-despropyly in 0-30 cm borizons of soil at Maasen expressed as µg/kg Ì Ô

		\sim	% .	CV I	Ŷ_?	~ ~		Ô	•		
Depth	Repli-	\$ (y k	-		AT [™]		S.		
[cm]	Cale	U	7	L}4°	<u>_</u> 30	ŐÖ	90	×120	150	180	240
	A	<i>\$</i> .5	×12.1	15.6	9.9 ×	×12.6 (13.5	16.Ø>	11.0	14.4	19.3
	S ^B C	t, 5.3 Ĉ	₹15.0-C	r 16.7 [~]	18,20	130	12.9	14.5	10.1	15.1	13.2
(9 3	14.6	~->		Z,	Ũ- ^	Ç.	-	-	-
Š		<u></u> ⊕1.1	J3.8		ý- (- 2	× -	-	-	-	-
Ro.	Mean	[©] 7.8 ⊘	13.9	16,1	19,0	13.0	13.2	15.2	10.6	14.7	16.3
	A 🖉	nd	n 🖓	n.d.	n.d.	"M.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	∘ _19.2 .	n.d.	_O n.d. 🦕	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∛n.d. ∢	» n.d.	n.d.	n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
	A A	n	nd.	⊾n.d.	n.d.	Q.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	B	<u>m</u> .d.	"fl.d.	On.d.	Ôn.d.	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
N	Mean 🎓	on.d.^	n.d _/ Q	n.d.Q	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

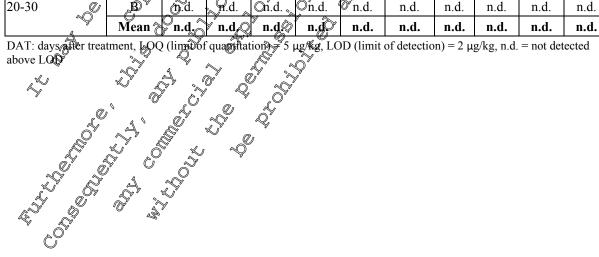




Table CA 7.1.2.2.1-24: Residues of spiroxamine in 0-30 cm horizons of soil at Swisttal-I	Hohn ex-
pressed as µg/kg	°

	I.											\geq
Depth	Repli-					DA	٩T			0		N.
[cm]	cate	0	7	14	30	58	91	120 (> 150	181	252	
	А	338	181	142	68.6	50.2	35.4	26.5	11.9	11.4	252. 89	
	В	328	184	142	72.0	50.3	28.6	28.6	11.8	Å.1	8.8	
0-10	С	289	169	-	-	ĉa -	-	$\mathcal{L}^{\frac{n}{2}}$	^	X - X	- ~	
	D	345	182	-	- 4	r -		-	- () 11.9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>8.9</u>	L
	Mean	325	179	142	70 .S	50.3	32.0	27.6	\$1 .9	J1.2)″
	А	n.d.	<loq< td=""><td><loq< td=""><td>STOD</td><td>n.d.</td><td>Q.d.</td><td><loq,< td=""><td>Ç n.d. _A</td><td>, n.d. 🗘</td><td>n.d @</td><td></td></loq,<></td></loq<></td></loq<>	<loq< td=""><td>STOD</td><td>n.d.</td><td>Q.d.</td><td><loq,< td=""><td>Ç n.d. _A</td><td>, n.d. 🗘</td><td>n.d @</td><td></td></loq,<></td></loq<>	STOD	n.d.	Q.d.	<loq,< td=""><td>Ç n.d. _A</td><td>, n.d. 🗘</td><td>n.d @</td><td></td></loq,<>	Ç n.d. _A	, n.d. 🗘	n.d @	
10-20	В	n.d.	n.d.	n.d. 🗸	LOQ	<loq< td=""><td>n.d. 🖉</td><td><loq< td=""><td>- / -</td><td><løq< td=""><td>n Ø.</td><td></td></løq<></td></loq<></td></loq<>	n.d. 🖉	<loq< td=""><td>- / -</td><td><løq< td=""><td>n Ø.</td><td></td></løq<></td></loq<>	- / -	<løq< td=""><td>n Ø.</td><td></td></løq<>	n Ø.	
	Mean	n.d.	<loq< th=""><th><l@q< th=""><th></th><th><lqq< th=""><th>n⊀d.</th><th><ŁØQ</th><th>≤QOQ</th><th>≫i QQ</th><th>Kn.d.</th><th></th></lqq<></th></l@q<></th></loq<>	<l@q< th=""><th></th><th><lqq< th=""><th>n⊀d.</th><th><ŁØQ</th><th>≤QOQ</th><th>≫i QQ</th><th>Kn.d.</th><th></th></lqq<></th></l@q<>		<lqq< th=""><th>n⊀d.</th><th><ŁØQ</th><th>≤QOQ</th><th>≫i QQ</th><th>Kn.d.</th><th></th></lqq<>	n⊀d.	<ŁØQ	≤ QOQ	≫i QQ	Kn.d.	
	Α	n.d.	n.d.	n.d.	n,d.	ALOQ			Øn.d. "		n.d. ∘	
20-30	В	n.d.	n.d. 🖌	~n.d. ∞	Øn.d.~	n.d. *	♥ n.d.	n.d.	n.d.	nd	n@. n.d.	
	Mean	n.d.	n.d 🖇	n.d.	n.d.	<1.0Q	n.d."	'n,d.	n.d.	≪ŋ.d. ₄	An.d.	

DAT: days after treatment, LOQ (limit of quadritation) = 5 µg/g, LOD (limit of detection) = 2 µg/kg, n. 6 = not detected above LOD

Table CA 7.1.2.2.1-25: Residues of MOI (spinoxamure-desethyl) in 0-30cm hopizons of soil at ,Ô Swisttal-Hohn expressed as µg/kg Ô

		N	%	Ĉi 1	Ÿ ₹			Ô	~		
Depth	Repli-	\$ (y Č	-		AT ू\$′		C.		
[cm]	cate	U-A.	7	_}ka°	<u>_</u> 30	Á 8	9 1	×120	\$150	181	252
	Â	8:0	×41.9	41.4	38.3 x	€23.5 €	22.0	19.5	7.9	8.4	5.3
	B B	c, 7.3 Ĉ	€47.7¢C	<i>U</i> .**	32 2	24Ø	19.3	19.Ž	8.0	8.1	6.2
0-10	B C C	71	44.9	~->		SF .	Ũ- ^	Ş -	-	-	-
- A C C C C C C C C C C C C C C C C C C	, P	6.9	3 5.8		ý- (- 2	× -	-	-	-	-
<i>P</i> ₂	Mean	[©] 7.3 ©		45,8	35,2	23.9	20.7	19.3	7.9	8.3	5.8
	A 🖉	nd	n 🖓	n.d.	n.d.	∧n.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	Ŗ	∘ _19.2 .	n.d.	©n.d. »		LOQ	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∛n.d. ∢	n.d	n.d.	n.ď	<loq< td=""><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.	n.d.	n.d.	n.d.
(0		n de	n d.	n.d.	n.d.	D.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	B ×	<u>m</u> .d.	, fr.d.	On.d. 👡	Ôn.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	∽n.d.^	n.d _/ Q	. ``	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

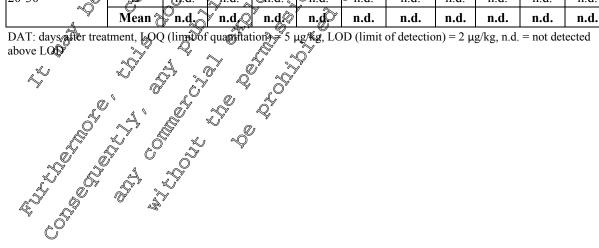




Table CA 7.1.2.2.1-26: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of s	oil at	
Swisttal-Hohn expressed as µg/kg		0

			-			-						ð
Depth	Repli-					D	АT				, Q	
[cm]	cate	0	7	14	30	58	91	120	⊳ 150	181	252	U
	Α	8.0	41.4	38.7	38.3	26.7	22.8	20.5	8.9	9.7	252 .69	
	В	7.6	45.8	47.5	31.2	26.9	20.7	19.7	9.4	9 .9	~ 7 .7	Ô
0-10	С	7.2	43.4	-	-	<u>~</u>		<u>, -</u>	^	× - ×		Ĭ
	D	7.5	43.7	-	_ «	F -		-	- () %9,1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
	Mean	7.6	43.6	43.1	34.8	26.8	2107	20.1	×9.1	9.8	A.1 🖉	, O`
	Α	n.d.	n.d.	n.d.	nd.	n.d.	Q OQ	<loq.< td=""><td>Ç n.d. 🗶</td><td>n.d. 🤇</td><td>n.d</td><td>Ň</td></loq.<>	Ç n.d. 🗶	n.d. 🤇	n.d	Ň
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	<loq< td=""><td>/ n.d.Ø</td><td><loq< td=""><td>n.d.^{©°}</td><td>n.Ø</td><td>n.d.</td><td></td></loq<></td></loq<>	/ n.d.Ø	<loq< td=""><td>n.d.^{©°}</td><td>n.Ø</td><td>n.d.</td><td></td></loq<>	n.d. ^{©°}	n.Ø	n.d.	
	Mean	n.d.	n.d.	n.dk	n.¢	<lqq< td=""><td></td><td><ŁØQ</td><td>æd.</td><td>°~ry.d.</td><td>Kn.d.</td><td></td></lqq<>		< ŁØ Q	æd.	°~ry.d.	Kn.d.	
	Α	n.d.	n.d.	n.a.	sn.d.	₫ ,OQ		n.d.	Øn.d. "	n.d. 🕰	n.d. ∘	
20-30	В	n.d.	n.d. 💡	A.d. 🦻	©n.d.∼	n.d.	n.d	n.dC	n.d.	n	n@.	
	Mean	n.d.	n.d 🖴	n.d.	n.d.	<loq< td=""><td>n dt.</td><td>n,d.</td><td>n.d.</td><td>≪ŋ.d.</td><td>An.d.</td><td></td></loq<>	n dt.	n,d.	n.d.	≪ŋ.d .	An.d.	

DAT: days after treatment, LOQ (limit of quaditation) = 5 µg/g, LOD (limit of detection) = 2 µg/kg, n. 4 + not detected above LOD

Table CA 7.1.2.2.1-27: Residues of spiroxamine in 0-30 cm horizons of soil at Albig expressed as µg/kg 🏷 Ô

	• 8		% .	er e	<u> </u>	, A		· Ø			
Depth	Repli-	¢ (y s	, - (, D A	ΔT Ž [©]		L.		
[cm]	cate	UL,	7	JAP	<u>s</u> ð	60	». 90	×120	\$150	180	240
	A	\$83	×209	135	چ ¹ 03 🔬	¢¥42.6 €	40.0	29.6	15.8	7.6	<loq< td=""></loq<>
	B C C	4 05 Ĉ	200	128~	102	41 <i>@</i>	41.6	23.5	14.8	8.7	7.7
		392	200 207	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		S-	Ø- 1	Ş.	-	-	-
\$ \$	<u></u>	<u>3</u> 66	087		S - C	 M	y -	-	-	-	-
Ro.	Mean	⁸⁰ 386 @		131	102	41.9	40.8	26.5	15.3	8.2	5.1
10-20	A	nd	<loq< td=""><td><loq< td=""><td>n.d.</td><td>∧ts.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td><td>∧ts.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	n.d.	∧ts.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	s fræl.	<loq< td=""><td>ÇÊ OQ</td><td>On.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	ÇÊ OQ	On.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∲n.d.∢	~LOQ	- LOØ		n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
	A A	n	<lqq< td=""><td>⊾n.el.</td><td>n.d.</td><td>J.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></lqq<>	⊾n.el.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
20-30	B	n.đ. n.d. n.d.	f.d.	On.d.	©n.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Â.	Mean 🎓	n.d.	<loq< td=""><td>\otimes</td><td>n.d</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	\otimes	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>

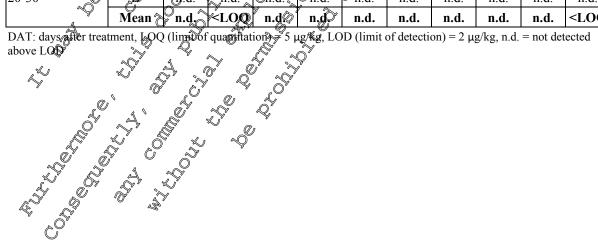




Table CA 7.1.2.2.1-28: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of	of soil at Al-
big expressed as µg/kg	°

	8	-	-	8 8							Ŵ	ð
Depth	Repli-					D	АТ				Z.	
[cm]	cate	0	7	14	30	60	90	120	~150	180	240	0
	Α	21.1	40.3	30.6	55.1	31.4	22.0	20.5	15.8	7.1×	<lqq< td=""><td></td></lqq<>	
	В	22.5	40.1	40.2	58.6	25.5	28.3	23.2	15.7	9 .0	~ 6 .4	Ô
0-10	С	19.6	26.0	-	-	õa -	- 4	<u>~</u>	- 🦿	الا لا		
	D	31.0	37.6	-	- «	F -	@	-	- Ô ¥5 .7			, 0 ⁹
	Mean	23.5	36.0	35.4	56 A	28.4	2502	21.9	\$5. 7	3.0	∕€ĽOQ	0.
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🔎	n.d. Ĉ		7
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.@	n.d.	n.d. ^O	n.¢	n.Q.	
	Mean	n.d.	n.d.	n. ¢ ,	n.¢.	n.d.		"n.d.	æð.	`^ŋ≱.d.	Kn.d.	
	А	n.d.	n.d.	n.a.	n,d.	ŋ.d.		n.d.	Øn.d. A	n.d. 🛋		
20-30	В	n.d.	n.d. 💡	🛱 .d. 🦕	Øn.d.~	, n.d. *	₿ n.d₄	n.dC	n.d.	n.¢	n@. 	
	Mean	n.d.	n.d 🖇	n.d.	n.d.	n,d	વ્ર.સ.	ĵn,∕d.	n.d.	∡ŋ.d .	Jn.d.	

DAT: days after treatment, LOQ (limit of quadration) \neq 5 µg/kg, LOD (limit of detection) = 2 µg/kg, n.6 \neq not detected above LOD

Table CA 7.1.2.2.1-29: Residues of M02 (spiroxamure-despropyly in 0-30 cm horizons of soil at Albig expressed as ug/kg

		- @-	% .	Ĉ,	y a	2		Ô	<u>^</u>		
Depth	Repli-	¢) (à Č	y k	e	ر م	AT S		S.		
[cm]	cate '	0	7	J¢Å [°]	3 9		90	×120	\$150	180	240
	A.	2 5.5	4 1.4	35.4	S0.8	30.2 🔇	€25.9	26.4	18.9	9.8	<loq< td=""></loq<>
	B C V	21.6	46.8	¥ 38.9 [∞]	53 0	29 B	30.0	19.8	17.6	9.1	8.3
		15.4	29.1	~~"			Ũ- Ĵ	Ç -	-	-	- <loq< td=""></loq<>
Š		<u>3</u> 1.8	38.9	<u>,</u>	2- 2	- L		-	-	-	-
		22.6	39.0	37,2	52,		28.0	23.1	18.3	9.5	5.4
	A 🖑	nd	n Ø	n.d.		And.	∕n.d.	<loq< td=""><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	n.d.	n.d.	<loq< td=""></loq<>
10-20	, P	s , f?.ð .	n.d.	©n.d. »,	On.d.	n.d.s	n.d.	<loq< td=""><td>n.d.</td><td><loq< td=""><td>n.d.</td></loq<></td></loq<>	n.d.	<loq< td=""><td>n.d.</td></loq<>	n.d.
	Mean	∛n.d. ∢	n.d		n.d	n.đ.	n.d.	<loq< th=""><th>n.d.</th><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<>	n.d.	<loq< th=""><th><loq< th=""></loq<></th></loq<>	<loq< th=""></loq<>
	A A	n.đ	n d.	n.d.	n.d.	d.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
20-30		<u>m</u> .d.	. €ŬOQ	On.d. 👡	Ôn.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
Â.	Mean ?	n.d.	∕×LO@	n.d.Ø	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>

DAT: days ther treatment, LOQ (limit of quartitation) 5 $\mu g/kg$, LOD (limit of detection) = 2 $\mu g/kg$, n.d. = not detected above LOD

C. Residues

No residue concentration of spiroxataine, M01 and M02 above the LOQ (5 μ g/kg) of the analytical method could be found in the control samples.

Starting from an application rate of 0.% kg a.s./ha and a soil density of 1.5 kg/L the theoretical total concentration in a 10 cm layer s 500 μ g/kg soil. The concentration of spiroxamine in the 0-10 cm layer found in mediately after application were 365, 395, 284, 325 and 387 μ g/kg for Höfchen, Laacherhof, Maasen, Swettal-Irohn and Albig trial sites, respectively. This equates that at day zero 73.0%, 79.0%, 56.%, 65.0% and 77.4% of the applied amount was recovered from each site, respectively.

For the Höfchen trial site the mean residue concentration in the 0-10 cm soil segment decreased from 365 μ g/kg at 0 DAT to 60.0 μ g/kg at 270 DAT. In the 10-20 cm layer spiroxamine was found on four occasion at values greater than the LOD, with the maximum value of 9.4 μ g/kg found at DAT 89. In the



20-30 cm layer spiroxamine was not found at levels great than the LOQ (5 μ g/kg) at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 23.0 μ g/kg at 29 DAT and decreased to 11.4 μ g/kg at 270 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 23.5 μ g/kg at 29 DAT and decreased to 10.5 μ g/kg at 270 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 23.5 μ g/kg at 29 DAT and decreased to 10.5 μ g/kg at 270 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 23.0 μ g/kg at 29 DAT and decreased to 10.5 μ g/kg at 270 DAT.

For Laacherhof trial site the mean residue concentration in the 0-10 cm soil segment decreased from 247 μ g/kg at 0 DAT to 28.3 μ g/kg at 240 DAT. In the 10-20 cm and 20-30 cm layer spiroxamine was not found at levels great than the LOQ (5 μ g/kg) at any time point. For the metabolite, M04 on the 0/10 cm soil segment concentrations reached a maximum of 28.7 μ g/kg at 28 DAT and decreased to 17.0 $^{\circ}$ $^{\circ$

For Maasen trial site the mean residue concentration in the 0-10 cm solf segment decreased from 284 μ g/kg at 0 DAT to 64.3 μ g/kg at 240 DAT. In the 10-20 cm and 20-30 cm byer spiroxamine was not found at levels great than the LOQ (5 μ g/kg) at any time point. For the metabolite M01 in the 0-10 cm soil segment concentrations reached a maximum of 19.7 μ g/kg at 20 DAT and decreased to 18.5 μ g/kg at 240 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 19.0 μ g/kg at 30 DAT and decreased to 16.3 μ g/kg at 240 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02 no residues were found at levels greater than the LOQ (5 μ g/kg) at any time point.

For Swisttal-Hohn trial site the mean restrice concentration in the 0-10 cm soil segment decreased from 325 μ g/kg at 0 DAT to 8.9 μ g/kg at 252 DAT. In the 10-20 cm and 20-30 cm layer spiroxamine was not found at levels great than the 100 (5 μ g/kg) at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 45.8 μ g/kg at 14 DAT and decreased to 5.8 μ g/kg at 252 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 43.6 μ g/kg at 7 DAT and decreased to 7 μ g/kg at 252 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M00 and M02, no residues were found at levels greater than the LOQ (5 μ g/kg) at any time point.

For Albig trial site the mean residue concentration in the 0-10 cm soil segment decreased from 386 μ g/kg at 0 DAT to 5. μ g/kg at 240 DAT. In the 10-20 cm and 20-30 cm layer spiroxamine was not found at levels great than the LOQ (5 μ g/kg) at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a praximum of 56.9 μ g/kg at 30 DAT and decreased to $<5 \mu$ g/kg at 240 DAT. For the metabolite M02 in the 0.10 cm soil segment concentrations reached a praximum of 56.9 μ g/kg at 30 DAT and decreased to $<5 \mu$ g/kg at 240 DAT. For the metabolite M02 in the 0.10 cm soil segment concentrations reached a maximum of 39.0 μ g/kg at 9 DAT and decreased to 5μ g/kg at 240 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02, no residue were found at levels greater than the LOQ (5 μ g/kg) at any time point.

F. Degradation kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.1.2.2.1/12 ($M^{2}/63140-01-0$)

Æ.

Conclusion

Following a single application of spiroxamine at a nominal application rate of 0.75 kg a.s./ha to bare soil in spring 594. The decime of spiroxamine and the formation and decline of its metabolites M01 and M02 was followed for up to 270 days after application at 5 sites in Germany.

During the whole test duration, nearly all residues remained in the 0-10 cm layers of the soil. The maximum concentration of spiroxamine was observed for the Albig trial site at 386 μ g/kg at 0 DAT. Only in the Höfchen was spiroxamine found in the 10-20 cm layer, the maximum value of 9.4 μ g/kg was reported at 89 DAT. No mobility into soil layers below 20 cm was observed. The metabolites M01 and



M02 were detected at all sites. The metabolite M01 reached a maximum of 45.8 μ g/kg at 14 DAT in Swisttal-Hohn in the 0-10 cm layer. The metabolite M02 reached a maximum of 43.6 μ g/kg at 7 DAT in Swisttal-Hohn in the 0-10 cm layer.

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degrada- \hat{C} tion kinetics (2014) is performed in KCA 7.1.2.2.1/12 (<u>M-763140-01-1</u>).

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study is considered valid to assess the dissipation of spiroxamine under field conditions in soil. The study meets the requirements to assess field persistence of spiroxamine and its metabolites, and to derive parent soil DegT_{50matrix} values for legacy field studies as defined by EFSA (2004). It is not suitable for assessing metabolite soil DegT_{50matrix} values as the design did not furning soil surface processes immediately after application as required by EFSA (2014).

Data Point:	KCA 7.1.2.2.103
Report Author:	KCA 7.1.2.2.3993 5 7 6 7 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
Report Year:	
Report Title:	Dissipation of KWG 4268 in soils under field Conditions (Great Britain and
	France to the former of the fo
Report No:	$R_{A,F}^{2}$
Document No:	<u>M-006127-01-1</u>
Guideline(s) followed in %	BBA Guideling IV-4 C 1986
study:	BBA Guideling IV-4 (1986)
Deviations from current	Yes (refer below) Some namor deviation(s) not refer and for the rehability of the study (described in
test guideline:	Some monor deviation(s) not relevant for the reliability of the study (described in
	study sammary
Previous evaluation:	yes, evaluated and accepted and accepted and accepted and accepted and accepted acce
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	DAR (1907), RAR (2010), RAR (2017)
GLP/Officially recognised testing facilities:	res, conducted under the POrthelany recognized testing facilities
nised testing facilities: 📈	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Acceptability/Reliability	$Y est = \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2}$
Executive Summa	

Soil dissipation of spiror amine was studied after application as an EC formulation containing 491.4 g/L to spring cereat crop onder field conditions for up to 244 days at five trial sites in Great Britain (Elm Farm; sandy beam and Old Hall Farm; sandy loam) and France (Touffreville, silt loam). Spiroxamine was applied as an emulsifiable concentrate formulation at a single application at two different applications rates of either 3.0 l/ha (45 kg a.s./ha; sites 40097/1 and 40099/8) or 1.5 L/ha (0.75 kg a.s./ha; sites 40100/5, 40101/3 and 40193/5) in spring 1994.

Twenty soil core samples were taken from the treated as well as ten soil core samples from the control plot directly pograpplication. For samples were taken to a depth of 30 cm (except trial 40193/5 which from 119-234 DAT, was sampled to 50 cm depth) and segmented into 10 cm soil layers prior to homogenisation and analysed. Samples were taken at the Elm Farm (trial 40097/1 and 40100/5) site, at 0, 7, 14, 28, 56, 90, 121, 149, 182 and 244 days after treatment (DAT), for the Old Hall Farm (trial 40097/1 and 40101/3) site, at 0, 7, 46, 28, 55, 90, 120, 150, 181 and 240 DAT and for the Touffreville (trial 40193/5) at 0, 7, 14, 28, 56, 88, 119, 146, 182 and 234 DAT.

Soil samples were analysed for spiroxamine and the metabolites M01 (spiroxamine-desethyl) and M02 (spiroxamine-despropyl). Soil samples were extracted by Soxtec extraction with a basic solution of methanol/water/ammonia (25%) (8:2:0.1 v/v/v). Parent and metabolites were quantitatively determined



by liquid chromatography with MS-MS detection. A limit of quantification (LOQ) of 5  $\mu$ g/kg was reported, and a limit of detection (LOD) of 2  $\mu$ g/kg for spiroxamine and the metabolites.

Starting from an application rate of 1.5 (0.75) kg spiroxamine/ha and a soil density of 1.5 kg/s the theoretical total concentration in a 10 cm layer is 1000 (500)  $\mu$ g/kg soil. The concentration of spirox-amine in the 0-10 cm layer found immediately after application were 479, 684, 46, 327 and 609  $\mu$ g/kg for Elm Farm (40097/1), Old Hall Farm (40099/8), Elm Farm (40100/5), Old Hall Farm (40101/3) and Touffreville (40193/5) trial sites, respectively. This equates that at day zero 47.9%, 684%, 49.2%, 65.4% and 61.8% of the applied amount was recovered from each site, respectively.

During the test duration, nearly all residues remained in the 0-10 cm (ayers of the soil. However, spiroxamine was also found in the 10-20 cm layer in four of the trial sites investigated, the maximum value of 32.2  $\mu$ g/kg found at DAT 0 at the Old Hall Farm that site (40099/8, 1,5 kg a.s. ha application). In the 20-30 cm layer spiroxamine was found on one occasion at values greater than the LOQ, with the maximum value of 8.6  $\mu$ g/kg found at 0 DAT at the Old Hall Farm trial site (40101/3, 0.75 kg a.s./ha application). No mobility into soil layers below 30 cm was observed. The metabolites M01 and M02 were detected at all sites. The metabolite M01 reached a maximum of 99.9  $\mu$ g/kg at 14 DAf in the Old Hall Farm trial site (40099/8, 1.5 kg a.s./ha application) in the 0-10 cm layer.

The DT₅₀ and DT₉₀ of spiroxamine determined in the study was reported for each site oil. However, a reevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT50 values from laboratory and field dissipation studies (EFSA 2014), was performed in the report presented under point KCA7.1.2.2.1/12 (M-763140-01-1).

Material

### A. Materials

#### 1. Test Items

Purity

Spiroxamine product code 122905, Suspension concentrate formulation (491.4 g/L spiroxamine)

Certificate of analysis Analysis Analysis Analysis Certified at December 16, 1993 by Dr. Groß,

Batch no A

04023/0089 A, FAR 210

Bayer AG, PF-E/FT, D-51368 Leverkusen

# 2. Trial locations & Soils

The study was performed in Great Britain and France at five different sites. Site soil is characterised in Table CA 7.1 2.1-30. The peld soil dissipation trial consisted of one treated and one untreated plot on each site. No pesticide his ory was given for previous years before the trial for either site.

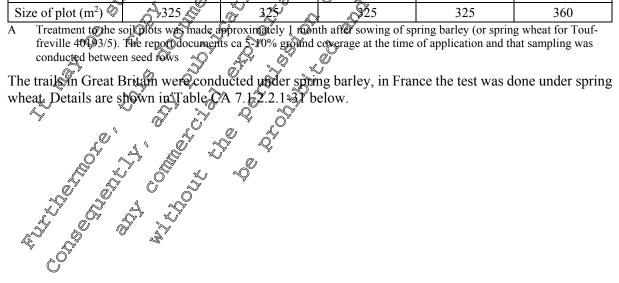
Not State

each site. No pesticide history was given for previous years before the trial for either site.



Trial designation	40097/1	40099/8	40100/5	40101/3	40193/5@°
Soil Designation	Elm Farm	Old Hall Farm	Elm Farm	Old Hall Farm	Touffrextile
	Elm Farm,	Old Hall Farm,	Elm Farm,	Old Hall Farm,	La Ferme du
	Development	Pakenham	Development	Pakenham	Plessis,
	Station	GB Bury St.	Station	GB Bury St.	F-27440, Touf-
Geographic Loca-	GB Bury St.	Edmunds, Suf-	GB Bury St.	Edmunds, Suf-	🔍 Oreville, La 🛒 🦓
tion	Edmunds	folk	Edmunds	of folk	Pointe Aux,
tion	Thurston, Suf-		Thurston, Suf-		Normands
	folk		folk (	× v	
	Field 7, Block	4	ØField 7, Block	, O ັ	
	4		≽ 4 [™] ≶		
Country	Great Britain	Great Britan	Great Britain	Great Britain	France
Vegetation	With vegeta-	With vegeta-	With vegeta-	With vegeta-	With vegeta-
vegetation	tion A	tion 🔍 🔬	tion A O	tion No	tion ^A
Textural Classifi-	Sandy loam	Sandy loam	Sindu Acom	San San	Silt load
cation (USDA)	Sandy Ioann	Samery Ioann	Sandy boam		Shi loan
Sand [50 - 2000	560				
μm] (%)	56.8	0° /4/9 . S	\$ 56.8		0 12.9
Silt [2 – 50 µm]				o o s	, w
(%)	24.9	j 15.6 Q		$\sim 0^{5.6}$	* 70.8
Clay [< 2 $\mu$ m] (%)	18.3	× 104	× ~18.3		16.3
pH (in 0.01 M	Ŭ Š		Ø Å		
$CaCl_2$ solution)	<b>\$</b> 4 O	~ ^{7.0}	7.4	× ~7.0 ~~	7.2
Organic matter			V 0 4.		
(%)	1.86	\$ 3.23 D	_`≫1.86 O	× 3.23	2.22
	<u> </u>			0 4	
Organic carbon	ð.08 2	«√° 1.88» «	9 1908 4	<b>1.88</b>	1.29
<u>(%)</u>					
Cation Exchange	5 14 ×		140 ×	<i>a</i> ,	
Capacity	0° 14 6	13	\$ ¹⁴⁰	13	12
(meq/100,g)		Ň,			
Soil Moisture ca-	37:4 4				
pacity (g/100g	°∑ 37.¥ w	A\$5.8 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	37.4	45.8	42.4
soil)	325	, Z	$0^{\nu}$		
Size of plot (m ² )			, <b>\$</b> 25		

#### Table CA 7.1.2.2.1-30: Location, site description and climatic data of test sites





Trial No.	Сгор	Variety	Date of Sowing	Applica- tion rate of spi- rox- amine [kg/ha]	Seed Rate [kg/ha]	Growth Stage at applica- tion [BBCH]	Crop Covering of the Soil [%]	Dare of Harvest	
40097/1 (Elm Farm)	Spring Barley	Alexis	30 th March 1994	1.5	گ 180	× 13		369 Oc-« tober 9 9 1994	
40099/8 (Old Hall Farm)	Spring Barley	Alexis	21 st March 1994	1,5	180	0 × 21-22		ber 1994	¥
40100/5 (Elm Farm)	Spring Barley	Alexis	30 th March 1994	≪ 0.75¢°	× 180 ×			30 th Oc- tober 1994 ₀	
40101/3 (Old Hall Farm)	Spring Barley	Alexis	21 st March 1094	×0.75				3 rd Octo- ber 3994	
40193/5 (Touf- freville)	Spring Wheat	Ysathis	28 th & March 1984	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		2 ³ 13 2 ⁵	<u> </u>	20 th Oc- cober 1994	
B. Study D	esign	Z Z		The second se	4 Q4		8 %		

# **1. Experimental Conditions**

A single application of a nominal 0.75 kg spinoxamine/ha as a as an emulsifiable concentrate (EC) was performed to bare soik on 4th May 1994 (40097/1 @Im Farm) and 26th April 1994 (40099/8, Old Hall Farm). A single application of a notional 103 kg sprioxantine/ha as a as an emulsifiable concentrate (EC) as performed to base soil on 4th May 1994 (40100/5, Elm Farm), 26th April 1994 (40101/3, Old Hall Farm) and 29th April 1994 (40493/5, Touffreville) Soil dissipation of spiroxamine was studied for a ×, maximum of 244 days

Weather data was collected at a location near to the site during the study period; this data includes the mean air temperature, rainfall and supshine hours. The soft cultivation and the agronomic and maintenance activates on the test plots were conducted according to the usual local agricultural practise. During the studies on covered soils plant protection products were used on the treated and on the control plot for maintenance.

# 2. Sampling

Twenty soil core samples were taken from the treated and control plots directly post application and at different intervals up to 244 days after the treatment. Core samples were taken to a depth of 30 cm (except frial 40193/5 which from 419-234 DAT was sampled to 50 cm depth, diameter 50 mm) and segmented into 10 cm soil avers prior to homogenisation and analysed. Samples were taken at the Elm Farm⁷(trial 40097/1 and 40100/6)⁷ site, at 0, 7, 94, 28, 56, 90, 121, 149, 182 and 244 days after treatment (DAT), for the Mid Hall Farm (trial 40097/10 and 40101/3) site, at 0, 7, 14, 28, 55, 90, 120, 150, 181 and 240 DAT and for the Touffeeville (trial 40193/5) at 0, 7, 14, 28, 56, 88, 119, 146, 182 and 234 DAT. The control plots were sampled at the beginning and end of the study.

At each sampling point 20 cores were taken using a pushing sampling system (Wacker Hammer) down to a depth of 00 cm (diameter 50 mm) per sampling interval. Locations of sampling were statistically distributed over the plot of get representative samples. Samples were transported in a cooler box containing dry ice, before being stored at -18°C until analysis at the laboratory.

The frozen soil cores were cut into 10 cm segments. Ten (control sample) to twenty (treated samples) of such segment of one later were milled and carefully homogenised.



### **3.** Analytical Procedures

Soil samples were analysed for spiroxamine and the metabolites M01 (spiroxamine-desethyl) and  $M^{02}$ (spiroxamine-despropyl). Replicate sub-samples were analysed by Method 00374 (RA-607/94) (M-607/94) 019207-02-1, involving liquid chromatography.

In summary, the method involved Soxtec extraction with refluxing methanol water/ammonia (25) (8:2:0.1, v/v/v). After solvent evaporation to the aqueous remainder the internal standard over added LOQ (5  $\mu$ g/kg)of the method was 2  $\mu$ g/kg for parent and metabolites.

Procedural recovery samples were analysed. Untreated sort samples were fortified with known amounts of spiroxamine, M01 and M02 and carrying these samples through the procedure alongside the treate samples.

### 4. Determination of degradation kinetics

The DT₅₀ and DT₉₀ of spiroxamine determined in the study was reported for each site. However, a reevaluation of the degradation kinetics in accordance with DOCUS guidance dominant on degradation kinetics (20142) and the EFSA guidance or deriving Deg 1% values from laboratory and field dissipation studies (EFSA 20145), was performed in the report presented under point KC 27.1, 2.2.1/12 (M-769140-01-1).

Results and Discussion

### A. Analytical Methodology

Ø Full details and acceptable vandation data to support this method (Method 00374 (RA-607/94)) are presented in Document M-CA 4, Section 4.1.2 (M-019007-02-1). The method complies with the EU regulatory requirements outlined within SANCO/3029/99 rex, 4 and is suitable for the determination of spiroxamine and its metabolites in soil samples by HPLC/MS/MS.

1

Analytical performance was determined by analysing known amounts of spiroxamine and internal standards. The mean recovery of spirovamine, M01 and M02 was  $7.1 \pm 0.3\%$ ,  $89.8 \pm 5.8\%$  and  $91.1 \pm 6.7\%$ 

Ľ **B. Data** The concentration of the total residues of spiroxamine and its metabolites are presented in the report. The concentrations of the single compounds are simmatised in Table CA 7.1.2.2.1-32 to Table CA

situes of spiroxamine and situes of spiroxam



Table CA 7.1.2.2.1-32: Residues of spiroxamine in 0-30 cm horizons of soil at Trial 400971/1	
(Elm Farm) expressed as µg/kg	

	``		, <b>-</b>		r-8 [,] 8						<u>_</u>	$\sim$
Depth	Repli-					DA	АT					
[cm]	cate	0	7	14	28	56	90	121	<b>~149</b>	182	244	9
	Α	516	125	122	83.8	93.0	77.1	52.9	43.0	38.5⁄	3608	
	В	474	127	119	87.3	89.2	72.1	<u>47</u> .9	45.2	A.1	28.9	6
0-10	С	504	121	-	-	ĉa -	- /	<u>~</u> -	- "	> - `^	- 2	
	D	421	142	-	- «	- 37	@	° –	- Č 44.1		<u>Ø</u>	o ^r
	Mean	479	129	121	85.6	91.1	74.6	50.4	44.1	A1.8		0
	Α	7.6	n.d.	n.d.	STAS	<loq< td=""><td>Q.d.</td><td>9n.d. /</td><td>Ç n.d. _L</td><td>5.8 Ĉ</td><td>n.d</td><td>V</td></loq<>	Q.d.	9n.d. /	Ç n.d. _L	5.8 Ĉ	n.d	V
10-20	В	7.0	n.d.	n.d. 🗸	8.3	n.d.	n.d.	n.d.	n.d [©]	<løq< td=""><td>n.Q.</td><td></td></løq<>	n.Q.	
	Mean	7.3	n.d.	n.¢.	5. <b>4</b> )°	<lqq< th=""><th>n%d.</th><th><b>.</b></th><th>and.</th><th>≫¥ OQ</th><th>Kn.d.</th><th></th></lqq<>	n%d.	<b>.</b>	and.	≫¥ OQ	Kn.d.	
	Α	n.d.	n.d.		m.d.	<b>A</b> LOQ	M.d.	h.d.	Ön.d. "	n.d.	, n.d. ∘	
20-30	В	n.d.	n.d. 🖌	,~n.d. ∞	Øn.d.~	n.d. *	n.d.	n.d.	n.d.	n.et	nØ.	
	Mean	n.d.	n.d. 🖇	n.d.	n.d.	<loq< td=""><td>n d. "</td><td>'n,d.</td><td></td><td><b>≪ŋ.d.</b></td><td>"n.d.</td><td></td></loq<>	n d. "	'n,d.		<b>≪ŋ.d.</b>	"n.d.	

DAT: days after treatment, LOQ (limit of quadritation) = 5 µg/g, LOD (limit of detection) = 2 µg/kg, n. 6 = not detected above LOD

Table CA 7.1.2.2.1-33: Residues of Mol (spipoxamula - desethyl) in 0-30cm hopizons of soil at Trial 400971/1 (Elm-Farm) expressed as age/kg

		*	<u> </u>	Ci ^V	<del>Y </del> ℓ	<u> </u>	/ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	()			
Depth	Repli-	\$ (		y R	,		AT S		L.S.		
[cm]	cate "	0-	7	JA [®]	28	<b>Š</b> 6	en 90	×121	<b>149</b>	182	244
	Â	<b>29</b> .8	\$90.2	87.1	A2.3	<b>%</b> 86.2 (	52.7%	39.2	27.9	24.4	18.7
	B C VO	(, 27.§ Ĉ	⊳്95.8€	₹ 74.9 [~]	74 2	75Ø	55.4	38.2	29.2	27.1	18.5
(	Ç Ç	28.6		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			<i>Õ</i> - ^	Ş-	-	-	-
	<u> </u>	<u>3</u> 0.6	3.8		Ú- (	- 4 1		-	-	-	-
		[×] 31.6	92.6	81,0	73,5		54.A	38.7	28.5	25.8	18.6
	A 🖉	nd	n 🕡 🎽 , n.d.	n.d.	p,d.	∧n.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	s fr.d.		"An.d. 🦕	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	n d 🤇	n.d	n.d.	n.ď	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
(	A A	n de	n d.	, n.d.	n.d.	Ø.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	A B V	<u>m</u> .d. ·	. fr.d.	On.d. 👡	Ôn.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
4 N N N N N N N N N N N N N N N N N N N	Mean 🎓	n.d.	n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

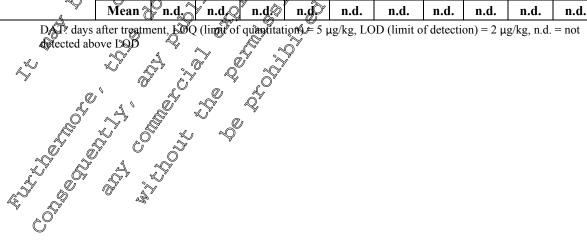




Table CA 7.1.2.2.1-34: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of s	soil at
Trial 400971/1 (Elm Farm) expressed as µg/kg	an°

					· -						Ø	ð
Depth	Repli-					DA	АT				N.	S
[cm]	cate	0	7	14	28	56	90	121	<del>)</del> -149	182 _@	244	U
	А	36.5	119	89.5	82.4	89.4	67.6	46.8	34.8	30.7/	255	
	В	25.9	123	80.3	84.1	78.6	70.6	48.2	35.7	\$3.1	<b>_Q4</b> .7	Ô
0-10	С	26.7	124	-	-	ča -		<u>~</u> _	- , '	الأ الأ		j [*]
	D	27.9	120	-	- «	r -		-	- () 35.3		<u> </u>	Ó
	Mean	29.3	121	84.9	83 A	84.0	6901	47.5	35.3	<u>3</u> 1.9	$\bigcirc$	K //
	А	n.d.	n.d.	n.d.	≤ĽQQ	<loq< td=""><td>Qn.d.</td><td>∘n.d.</td><td>🕻 n.d. 🦼</td><td>n.d. 🤇</td><td>n.d</td><td>2</td></loq<>	Qn.d.	∘n.d.	🕻 n.d. 🦼	n.d. 🤇	n.d	2
10-20	В	n.d.	n.d.	n.d. 🗸	LOQ	<u></u>	× .	n.d.	n.d.O	n.¢	n.Ø.	
	Mean	n.d.	n.d.	n.¢	<lqq< td=""><td><lqq< td=""><td>p‰d.</td><td>"n.d.</td><td>æð.</td><td>`^ŋ.d.</td><td>≪n.d.</td><td></td></lqq<></td></lqq<>	<lqq< td=""><td>p‰d.</td><td>"n.d.</td><td>æð.</td><td>`^ŋ.d.</td><td>≪n.d.</td><td></td></lqq<>	p‰d.	"n.d.	æð.	`^ŋ.d.	≪n.d.	
	А	n.d.	<loq< td=""><td>n.a.</td><td>m.d.</td><td><b>₹</b>LOQ</td><td></td><td>n.d.</td><td>Øn.d. "</td><td>n.d. 🕰</td><td>n.d ∘</td><td></td></loq<>	n.a.	m.d.	<b>₹</b> LOQ		n.d.	Øn.d. "	n.d. 🕰	n.d ∘	
20-30	В	n.d.	n.d. 👷	A.d. 🗞	Øn.d.∧		n.d	n.dC	n.d.	n.đ	n@. 	
	Mean	n.d.	<loø< td=""><td>n.d.</td><td>n.d.</td><td><l00< td=""><td>પ્રસ.</td><td>ĵn≱d.</td><td>n.d.</td><td><b>≪ŋ.d</b>.</td><td>An.d.</td><td></td></l00<></td></loø<>	n.d.	n.d.	<l00< td=""><td>પ્રસ.</td><td>ĵn≱d.</td><td>n.d.</td><td><b>≪ŋ.d</b>.</td><td>An.d.</td><td></td></l00<>	પ્રસ.	ĵn≱d.	n.d.	<b>≪ŋ.d</b> .	An.d.	

DAT: days after treatment, LOQ (limit of quadration)  $\neq$  5 µg/g, LOP (limit of detection) = 2 µg/kg, n  $d \neq$  not detected above LOD

Table CA 7.1.2.2.1-35: Residues of spiroxamine in 9-30 cm horizons of soil at Trial 40099/8 (Old Hall Farm) expressed as µg/kg Ĩ Ô

		$\sim$	&		Ÿ ₹	~ ~		Ô	~		
Depth	Repli-			y k	-		AT ∕S΄		C.		
[cm]	cate "	04	7	14	28	~k,j¥	§ 90	×120 į	<b>150</b>	181	240
	A	693	<b>39</b> 8	288	چ211 _م	Non a	€ 196	123	79.7	88.8	52.4
	B C	c 634 Ĉ	457-C	278 ~	212	210	197	118	77.3	81.5	59.4
0.10		714	426	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		S.	<i>©</i> - ^	Ç.	-	-	-
	<u> </u>	694	<b>3</b> 57		ý- (	- 2	× -	-	-	-	-
Ro.	Mean	^{KU} 684 @	, 434 ₃	283	21	217	197	120	78.5	85.1	55.9
	A 🖉	33.4	120	<loq< td=""><td>19.3</td><td></td><td>∼n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	19.3		∼n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
10-20	, <b>K</b>	s,€.1	13.7		Q16.2	LOO	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∛32.2 √	13.5	<loq∕< th=""><th>17</th><th><loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th><loq< th=""></loq<></th></loq<></th></loq∕<>	17	<loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th><loq< th=""></loq<></th></loq<>	n.d.	n.d.	n.d.	n.d.	<loq< th=""></loq<>
20-30	A A	<lqq< td=""><td>n d.</td><td>⊾n.d.</td><td>n.d.</td><td>Q.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></lqq<>	n d.	⊾n.d.	n.d.	Q.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	B	).d		On.d. 👡		Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Mean 🎓	LOQ			n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

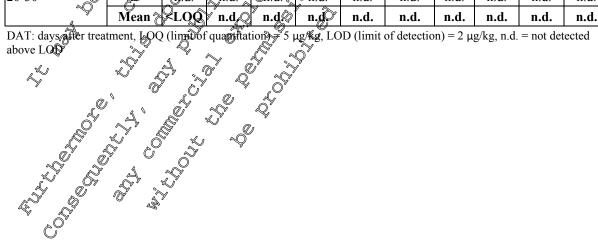




Table CA 7.1.2.2.1-36: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soi	l at
Trial 40099/8 (Old Hall Farm) expressed as µg/kg	a,°

						_	_	-			Q	ð
Depth	Repli-					DA	АT				N.	S
[cm]	cate	0	7	14	28	55	90	120 (~150	181 _@	240	U
	А	17.5	76.9	103	88.8	89.0	85.8	57.	46.4	46.2	31Q8	
	В	15.1	81.2	96.9	90.7	90.0	78.1	<u>5</u> 6.7	44.6	Å 1.6	~ \$4.9	Ô
0-10	С	36.9	78.3	-	-	õa -		<u>, </u>	- , '	× - ×		ŕ
	D	15.6	84.8	-	- 4	F -		-	- 0 43 .9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>	Ó
	Mean	21.3	80.3	99.9	89.8	82.0	570	45.5	43.9	33.9	\bigcirc	£ //
	А	n.d.	<loq< td=""><td>n.d.</td><td>nd.</td><td>n.d.</td><td>Qn.d.</td><td>∘n.d. ∥</td><td>Ç n.d. 🔬</td><td></td><td>n.d</td><td><i>v</i></td></loq<>	n.d.	nd.	n.d.	Qn.d.	∘n.d. ∥	Ç n.d. 🔬		n.d	<i>v</i>
10-20	В	n.d.	<loq< td=""><td>n.d. 🗸</td><td>n.d.</td><td>n.d.</td><td>n.d.Ø</td><td>n.d.</td><td>n.d.O</td><td>n.¢</td><td>nØ</td><td></td></loq<>	n.d. 🗸	n.d.	n.d.	n.d.Ø	n.d.	n.d.O	n.¢	nØ	
	Mean	n.d.	<loq< td=""><td>n.¢.</td><td>n.¢,°</td><td>n.d.</td><td>p‰d.</td><td>"n.d.</td><td>æd.</td><td>`^p.d.</td><td>Kn.d.</td><td></td></loq<>	n.¢.	n.¢,°	n.d.	p‰d.	"n.d.	æd.	`^p.d.	Kn.d.	
	А	n.d.	n.d.	n.a.	sn,d.	m.d.		n.d.	Ön.d. A	n.d. 🕰	, n.d. ∘	
20-30	В	n.d.	n.d. 👷	~n.d. ∞	Øn.d.∼	n.d.	n.d	n.dC	n.d.	n.đ	nØ.	
	Mean	n.d.	n.d 🖇	n.d.	n.d.	n.d.	પ્રસ.	ĵn,∕d.	n.d.	≪ŋ.d.	An.d.	

DAT: days after treatment, LOQ (limit of quartitation) $\neq 5 \mu g (g, LOD (limit of detection) = 2 \mu g (g, n, g) = not detected$ above LOD

Table CA 7.1.2.2.1-37: Residues of M02 (spiroxamure-despropyly in 0-30 cm borizons of soil at Trial 40099/8 (Old Hall Farm) expressed as µg/kg \bigcirc

		•	<u> </u>	Ci 4	∑ 	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1 🔊	Ś	^		
Depth	Repli-	\$ (y "Q	,	D	AT ∕S		Ż		
[cm]	cate "	0	7	1ª	28	r k ≥	90	×120	A150	181	240
	A A	A 6.2	% 1.4	108	N N		90.2	63.8	51.7	48.1	33.4
	B C V	(14.9 Ĉ	85.6	105 ~	101	95 B	84.1	62.8	49.7	43.5	39.6
(Ç VO	33.2	81.4	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			<i>Q</i> -	¢-	-	-	-
	P	₫5.7	88.5		ý - V	ر الم	- 1	-	-	-	-
		[©] 20.0 ©	84.2	106~	99,7	95.8	87.2	63.3	50.7	45.8	36.5
	A 🖑	nd	<lqq< td=""><td>n.d.</td><td><loq< td=""><td>S G OQ</td><td>∧n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></lqq<>	n.d.	<loq< td=""><td>S G OQ</td><td>∧n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	S G O Q	∧n.d.	n.d.	n.d.	n.d.	n.d.
10-20	Ŗ	s, fP.æ.	< LOQ	Çn.d. 🦕	QLOQ	LOQ () n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∛n.d. ∢	×LOQ	n.d.	<l00< th=""><th></th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></l00<>		n.d.	n.d.	n.d.	n.d.	n.d.
(n 🎝	nd.	nd.	n.d.	Ø.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	B	<u>m</u> .d.	M.d.	On.d. 👡		Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Mean 🎓	on.d.	n.d _/ Q	n.d.Q	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

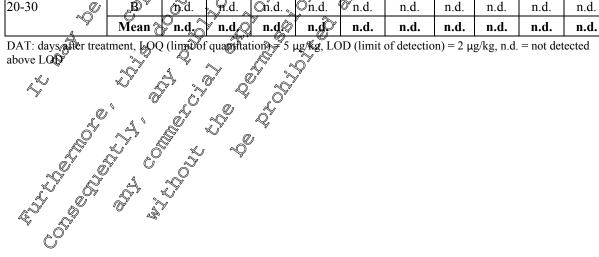




Table CA 7.1.2.2.1-38: Residues of spiroxamine in 0-30 cm horizons of soil at Trial 4010	0/5 (Elm
Farm) expressed as µg/kg	°

		· •									Ŵ	ð
Depth	Repli-					DA	٩T					
[cm]	cate	0	7	14	28	56	90	121	_{&gt;} 149	182 🖉	244	0
	Α	226	149	130	87.7	81.2	82.8	64.8	52.2	54.6⁄	540	
	В	253	143	126	84.0	81.5	74.5	64.1	57.5	\$7.4	\$8.2	Ô
0-10	С	267	155	-	-	ĉa -	-	$\mathcal{L}^{\frac{n}{2}}$	- /	لاً - الأ	2 <u>-</u> ×	ĺ
	D	240	144	-	- 4	<b>F</b> -		-	- () <b>54</b> .9	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<b>55.1</b>	Ľ
	Mean	246	148	128	85.8	81.4	7807	64.4	\$4.9	56.0	\$ <b>5</b> .1 ¢	0″
	А	7.6	<loq< td=""><td>n.d.</td><td><b>SV</b>Q</td><td><loq< td=""><td>Q.d.</td><td>n.d.</td><td>Ç n.d. 🔬</td><td>n.d. 🕻</td><td>n.d</td><td>V</td></loq<></td></loq<>	n.d.	<b>SV</b> Q	<loq< td=""><td>Q.d.</td><td>n.d.</td><td>Ç n.d. 🔬</td><td>n.d. 🕻</td><td>n.d</td><td>V</td></loq<>	Q.d.	n.d.	Ç n.d. 🔬	n.d. 🕻	n.d	V
10-20	В	8.9	n.d.	n.d. 🗸	LOQ		<lq< td=""><td>n.d.</td><td>'n.vd.©°</td><td><løq ≈¥µ0Q</løq </td><td>n.Ø.</td><td></td></lq<>	n.d.	'n.vd.©°	<løq ≈¥µ0Q</løq 	n.Ø.	
	Mean	8.3	<loq< th=""><th>n.¢.</th><th><løø< th=""><th><lqq< th=""><th><loq< th=""><th><b>.</b></th><th>æd.</th><th>≫¥j2OQ</th><th>≪n.d.</th><th></th></loq<></th></lqq<></th></løø<></th></loq<>	n.¢.	<løø< th=""><th><lqq< th=""><th><loq< th=""><th><b>.</b></th><th>æd.</th><th>≫¥j2OQ</th><th>≪n.d.</th><th></th></loq<></th></lqq<></th></løø<>	<lqq< th=""><th><loq< th=""><th><b>.</b></th><th>æd.</th><th>≫¥j2OQ</th><th>≪n.d.</th><th></th></loq<></th></lqq<>	<loq< th=""><th><b>.</b></th><th>æd.</th><th>≫¥j2OQ</th><th>≪n.d.</th><th></th></loq<>	<b>.</b>	æd.	≫¥j2OQ	≪n.d.	
	Α	n.d.	n.d.	n.a.	n.d.	m.d.	n.d.	LOQ	Øn.d. "	, n.d. 🛋	<loq<sub>0</loq<sub>	
20-30	В	n.d.	n.d. 🖌	∽n.d. »≈	Øn.d.へ	n.d.	♥ n.d.	n.d.	n.d.	n.đ.	<loqq< td=""><td></td></loqq<>	
	Mean	n.d.	n.d. 🖇		n.d.	n.d.	n dr. "	<body></body>	n.d.	<b>≪ŋ.d.</b>	LOQ	

DAT: days after treatment, LOQ (limit of quaditation) # 5 µg/cg, LOD (limit of detection) = 2 µg/kg, n.d # not detected above LOD

Table CA 7.1.2.2.1-39: Residues of MUI (spitoxamine-desethyl) in 0-30cm hopizons of soil at Trial 40100/5 (Elm Farm) expressed as fig/kg

			<u> </u>	Ci 1	<del>\</del>	<u> </u>		(i)	~		
Depth	Repli-	\$ (		y R	e -	$\mathbf{D}_{A}$	AT S		S.		
[cm]	cate "	0-		L'Ar	<u>_</u> 29	<b>Š</b> 6	<b>90</b>	×120	<b>Å</b> 151	180	258
	A.	<b>2</b> 4.6	<b>43</b> .3	38.0	37.8 x	≫26.6 (	23.4	29. <b>9</b>	20.5	17.3	18.0
	B C V	(, 15.8 Ĉ	¥46.6€	37.8~	35.00	290	25.8	29.3	18.6	15.9	20.4
	Ç VO	15.6	45.3	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		29 <b>&amp;</b>	<i>©</i> - ^	Ç -	-	-	-
	P	₫3.8	ð1.2 g			لا ارا الم		-	-	-	-
		[©] 17.5©		37,9%	36,4	27.9	24.6	29.6	19.5	16.6	19.2
	A 🖉	nd	n 🐨	n.d.	n.d.	A.d.	∼n.d.	n.d.	n.d.	n.d.	n.d.
10-20	Ŗ	∘ <b>_19.2</b> .	n.d.	"An.d. 🦕	On.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∲n.d. ∢	n.d	n.d.	n.d∛	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
(	A A	n	nd.	, m.d.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	B ×	<u>m</u> .d. ·	M.d.	On.d. 👡	Ôn.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Mean 🎓	n.d.	n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

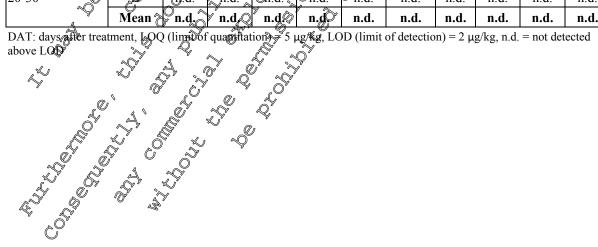




Table CA 7.1.2.2.1-40: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of so	oil at	
Trial 40100/5 (Elm Farm) expressed as µg/kg	°	

				-	-							ð
Depth	Repli-					D	АТ					A.
[cm]	cate	0	7	14	28	56	90	121) 149	182	₽ 244	0
	Α	23.3	49.8	41.9	41.4	29.1	26.3	29.8	22.2	20.4	1903	
	В	15.2	55.8	41.6	39.4	31.5	27.4	29.7	21.9	A8 .4	Q1.0	Ò
0-10	С	15.4	53.2	-	-	ès -	- 1	<u> </u>	- , '	الأ − ا	- 2	·
	D	13.2	41.7	-	- 4	F -		-	- Č \$2.1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		, ô ^y
	Mean	16.8	50.1	41.7	40.4	30.3	26.8	29.8	\$2.1	A 9.4		
	Α	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🗸	n.d. 🤇	20.2 ≬ n.d_℃	7
10-20	В	<loq< td=""><td>n.d.</td><td>n.d. 🗸</td><td>n.d.</td><td>n.d.</td><td>n.d.®</td><td></td><td>n.d.O</td><td>n.¢</td><td>n.Ø.</td><td></td></loq<>	n.d.	n.d. 🗸	n.d.	n.d.	n.d.®		n.d.O	n.¢	n.Ø.	
	Mean	<loq< td=""><td>n.d.</td><td>n.¢k</td><td>n.¢,°</td><td>n.đ.</td><td></td><td>"n.d.</td><td>pd.</td><td>°~19.d.</td><td>Kn.d.</td><td></td></loq<>	n.d.	n. ¢ k	n.¢,°	n.đ.		"n.d.	pd.	°~19.d.	Kn.d.	
	Α	n.d.	n.d.	n.a.	n,d.	ŋ.d.		n.d.	Øn.d. "	n.d. 🛋		
20-30	В	n.d.	n.d. 😵	An.d. 🗞	Øn.d.~		n.ds	n.dÇ	n.d.	n.đ	<løq< td=""><td></td></løq<>	
	Mean	n.d.	n.d 🖇	n.d.	n.d.	n.d.	વ્ર.ચ.	ĵn,∕d.	n.d.	≪ŋ.d.	LOQ	

DAT: days after treatment, LOQ (limit of quaditation) = 5 µg/g, LOD (limit of detection) = 2 µg/kg, n. 4 not detected above LOD

Table CA 7.1.2.2.1-41: Residues of spiroxamine in Q-30 cm horizons of soil at Trial 40101/3 (Old ĵÔ Hall Favm) expressed as µg/kg Ô

		\sim	% .	Ĉ, ×	9 @	<u> </u>		' (<u>)</u>	^		
Depth	Repli-			، بهر بهر	- -	, D A	\T _{\$} \$″		L.		
[cm]	Cale	Ū–	7	14	28	riz≚	e . 90	×120	\$150	181	240
	A	\$ 3 0	≪229	146	©131 ۲	¢∕113 (106	× 57. 7	50.2	43.2	45.4
	B C	, 312 Ĉ	∑ [*] 223	146~	137	89Ø	133	74.1	53.1	44.0	47.7
0.10		346	214	~~		S.	Ø- ;	Ş-	-	-	-
⁰	<u> </u>	300	223		S - C	- 4	· -	-	-	-	-
<i>R</i> ₀	Mean	[©] 327 ⊘	222	146	134	101	120	65.9	51.7	43.6	46.6
10-20	A 🖉	20	<loq< td=""><td><loq< td=""><td>n.d.</td><td>~~3.3</td><td>5.1</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td><td>~~3.3</td><td>5.1</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	n.d.	~~3.3	5.1	n.d.	n.d.	n.d.	n.d.
10-20	, P	∘ <u>_</u> 8%	ÎÌ.2	¢Ê0Q	On.d.	⁶ 5.1%	C-LOQ	n.d.	n.d.	n.d.	n.d.
		§ 9.1 K	× 6.9~	- LOQ	n.d		<loq< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<>	n.d.	n.d.	n.d.	n.d.
	A A	12.00	<l qq<="" td=""><td>⊾n.el.</td><td>n.d.</td><td>J.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></l>	⊾n.el.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
20-30		<u>3</u> .2 ·	∉UOQ	On.d.	©n.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Â.	Mean 🎓	8.6	<loq< td=""><td>n.dØ</td><td>n.d</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	n.dØ	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>

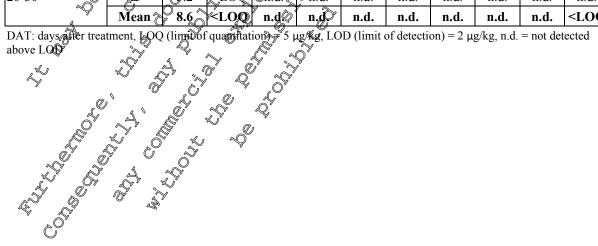




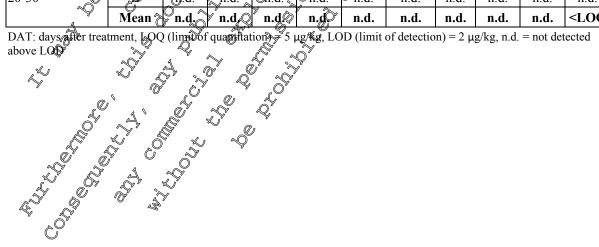
Table CA 7.1.2.2.1-42: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of s	oil at
Trial 40101/3 (Old Hall Farm) expressed as µg/kg	<i>a</i>

					-			-			Ø	"N
Depth	Repli-					D	AT					
[cm]	cate	0	7	14	28	55	90	120	~150	181	240	0
	Α	7.6	30.1	31.4	34.2	26.2	27.9	26,	20.0	17.8⁄	240 1992	
	В	6.5	32.9	30.2	33.3	28.4	36.0	27.8	19.1	A.4	⊴ 9.3	Ô
0-10	С	7.8	31.4	-	-	<u>~</u>		<u>~</u> _	- , '	7 - 7	- 2	Ĩ
	D	6.1	31.2	-	- «	- 12		-	- () 19255	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		Ľ
	Mean	7.0	31.4	30.8	33.8	27.3	320	27.0	19,55	£7.6	A9.3 💡	0″
	Α	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d.	Ç n.d. 🗶	n.d. Ĉ	49.3	V
10-20	В	n.d.	<loq< td=""><td>n.d. 🗸</td><td>n.d.</td><td>n.d.</td><td>n.d.Ø</td><td>n.d.</td><td>n.d.O</td><td>n.¢</td><td>n.d.</td><td></td></loq<>	n.d. 🗸	n.d.	n.d.	n.d.Ø	n.d.	n.d.O	n.¢	n.d.	
	Mean	n.d.	<loq< td=""><td>n.¢</td><td>n.¢</td><td>n.đ.</td><td>pKd.</td><td>"n.d.</td><td>Jand.</td><td>°~ny.d.</td><td>≪n.d.</td><td></td></loq<>	n. ¢	n.¢	n.đ.	pKd.	"n.d.	Jand.	°~ny.d.	≪n.d.	
	Α	n.d.	n.d.	n.a.	n,d.	m.d.		n.d.	Øn.d. "A	n.d. 🛋		
20-30	В	n.d.	n.d. 🖋	着 n.d. 🗞	Øn.d.∼	, n.d. *	n.ds	n.dC	n.d.	n.đ.	n@. Sn.d.	
	Mean	n.d.	n.d 🖴	n.d.	n.d.	n.d.	પ્રસ.	ĵn,∕d.	n.d.	≪ŋ.d.	An.d.	

DAT: days after treatment, LOQ (limit of quadritation) \neq 5 µg/cg, LOD (limit of detection) = 2 µg/kg, n ϕ^2 not detected above LOD

Table CA 7.1.2.2.1-43: Residues of M02 (spiroxamtire-despropyly in 0-30 cm borizons of soil at Trial 40101/3 (Old Hall Farm) expressed as µg/kg \bigcirc

			<u> </u>	Ci 4	∑~ @			()	~		
Depth	Repli-	\$ (y R	-	, D	AT S		L.		
[cm]	cate "	0-	No.	LA .	28	ేసిన	en 90	×120	\$150	181	240
	A	<i>\$</i> .7	×29.3	34.9	39.0 ₁	≫32.5 (31.2	30.8	19.9	18.8	21.4
	B C V	(6.5 Å	31.3	° 33.3 [≈]	38.90	33Ø	38.2	30.8	19.1	19.1	20.6
(7.1	31.3 30.0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		S.	Ĩ- Ĵ	Ç -	-	-	-
	B	6.2	ð0.6 (2 - Q	- 2		-	-	-	-
		[©] 7.0 ©		34,1×	38,9	~	34,7	30.8	19.5	19.0	21.0
	A 🖉	nd	n 🐨	n.d.	n.d.	"M.d.	∕n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	s¢ØQ	5.1	©n.d. »	On.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∕×LOQ	×LOQ		n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
	A	n 🎝	n d.	, n.d.	n.d.	J.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>
20-30	A A B Mean ?	<u>)</u> .d.	M.d.	On.d. 👡		Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	n.d.	n.d _/ Q		n.d	n.d.	n.d.	n.d.	n.d.	n.d.	<loq< td=""></loq<>





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Table CA 7.1.2.2.1-44: Residues of spiroxamine in 0-30 cm horizons of soil at Trial 40193/5
(Touffreville) expressed as μg/kg

	Repli-					DA	АТ				
[cm]	cate	0	7	14	28	56	88	119	⊳ 146	182 _©	234
	А	342	168	98.8	52.7	40.4	21.5	<loq< td=""><td>7.2</td><td><løq< td=""><td><lqq< td=""></lqq<></td></løq<></td></loq<>	7.2	<løq< td=""><td><lqq< td=""></lqq<></td></løq<>	<lqq< td=""></lqq<>
	В	285	156	112	62.8	30.9	22.2	<u>8</u> .2	7.1	\$.1	QLOQ
0-10	С	309	153	94.6	68.1	38.2	22.2	¥0.7		¥ - ^∧	-~
	D	300	148	101	53.9 🐔	31.5	21.1	8.8	- Õ		<u>"</u> Q"
	Mean	309	156	102	59.4	35.3	2107	7.5	- Č ×1,2	≸ĽŎQ	EOQ
	А	9.5	n.d.	5.1	Â.d.	n.d.	QOQ	9n.d. /	Ç n.d. 🗶	,<ĽOQ	
10-20	В	5.8	<loq< td=""><td>8.0 🗶</td><td>LOQ</td><td>n.d.</td><td><lq< td=""><td>n.d.</td><td>n.d.^O″</td><td>n.Ø</td><td>n.C.</td></lq<></td></loq<>	8.0 🗶	LOQ	n.d.	<lq< td=""><td>n.d.</td><td>n.d.^O″</td><td>n.Ø</td><td>n.C.</td></lq<>	n.d.	n.d. ^O ″	n.Ø	n.C.
	Mean	7.7	<loq< td=""><td>6.5</td><td><løq< td=""><td>n.đ.</td><td><loq< td=""><td>..d.</td><td>Rd.</td><td>¥¥jõQ</td><td>≪ĔŎQ</td></loq<></td></løq<></td></loq<>	6.5	<løq< td=""><td>n.đ.</td><td><loq< td=""><td>..d.</td><td>Rd.</td><td>¥¥jõQ</td><td>≪ĔŎQ</td></loq<></td></løq<>	n.đ.	<loq< td=""><td>..d.</td><td>Rd.</td><td>¥¥jõQ</td><td>≪ĔŎQ</td></loq<>	. .d.	Rd.	¥¥jõQ	≪ĔŎQ
	А	<loq< td=""><td>n.d.</td><td><løq< td=""><td>≨LOQ</td><td>m.d.</td><td>m.d.</td><td>LOQ</td><td>Øn.d. A</td><td>, n.d. 🛋</td><td>, n.d. ∘</td></løq<></td></loq<>	n.d.	<løq< td=""><td>≨LOQ</td><td>m.d.</td><td>m.d.</td><td>LOQ</td><td>Øn.d. A</td><td>, n.d. 🛋</td><td>, n.d. ∘</td></løq<>	≨LOQ	m.d.	m.d.	LOQ	Øn.d. A	, n.d. 🛋	, n.d. ∘
20-30	В	5.2	n.d. 🧋	An.d. 🗞	Øn.d.~	n.d. *	n.d.	n.d.	n.d.	n.e	nØ.
	Mean	<loq< td=""><td>n.d 🖉</td><td>⊓.ad.≫</td><td><løø< td=""><td>n.d[°]</td><td>n d.</td><td>'n,d.</td><td>"n.d.</td><td>≪ŋ.d.</td><td>An.d.</td></løø<></td></loq<>	n.d 🖉	⊓.ad.≫	<løø< td=""><td>n.d[°]</td><td>n d.</td><td>'n,d.</td><td>"n.d.</td><td>≪ŋ.d.</td><td>An.d.</td></løø<>	n.d [°]	n d.	'n,d.	"n.d.	≪ŋ.d.	An.d.
	А	-	Q	×.	2	<u> </u>	× -	Ön.d. K	Øn.d.	n.d.	n.d.
30-40	В	-	- - -	<i>®</i> - `	≫	V`_~	- ~	n.d	n.c	n/d.	n.d.
	Mean	- ~	\$ - @	- - 0	A	- AN	17 28 - 28 -			h h	n.d.
	А	- S	₹ \$	~ ~	ð	\$.	ŝ-	n.d.	n.d.	∀ n.d.	n.d.
40-50	В	<u></u>	~ ·	- °	S - 6	- ^	-~~	n,d?	n.d.	n.d.	n.d.
	Mean	P - () - Ø	- - 2	Ŕ	~^`	L'	'n,d.	Ăr∕d.	n.d.	n.d.
Ĉ			D I 4.			S. S.		S.			
								, S			
								5			
40-50 DAT: days after treat above LOD								, S			



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Table CA 7.1.2.2.1-45: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soil a	at
Trial 40193/5 (Touffreville) expressed as µg/kg	

Depth [cm]	Repli-					D.	AT				
[•····]	cate	0	7	14	28	56	88	119	~146	182	234
	Α	18.2	25.9	17.8	20.0	11.3	8.9	n.d	<loq< td=""><td>n.đ.</td><td><lqq< td=""></lqq<></td></loq<>	n.đ.	<lqq< td=""></lqq<>
	В	13.5	21.5	22.1	13.7	10.3	8.2	< <u>k</u> OQ	<loq< td=""><td>æd.</td><td>QLOQ</td></loq<>	æd.	QLOQ
0-10	С	18.0	27.4	18.2	13.9	12.1ھ	8.5	LOQ		y - x	
	D	16.1	25.7	16.6	14.8 🖗	710.3	7.9	<loq< td=""><td>-0</td><td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td><td><u> </u></td></loq<>	-0	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>
	Mean	16.4	25.1	18.7	15.6	11.0	89	<loq< td=""><td>⊴LÕQ</td><td>m.d.</td><td>EOQ</td></loq<>	⊴LÕQ	m.d.	EOQ
	Α	5.7	n.d.	n.d.	nd.	n.d.	Qn.d.	on.d. ⊿	Ç n.d.	n.d. 🤇	<loq< td=""></loq<>
10-20	В	<loq< td=""><td><loq< td=""><td>n.d. 🗸</td><td>h.d.</td><td>n.d.</td><td>n.d.@</td><td>n.d.</td><td>n.d^O</td><td>n.¢</td><td>n.Q.</td></loq<></td></loq<>	<loq< td=""><td>n.d. 🗸</td><td>h.d.</td><td>n.d.</td><td>n.d.@</td><td>n.d.</td><td>n.d^O</td><td>n.¢</td><td>n.Q.</td></loq<>	n.d. 🗸	h.d.	n.d.	n.d.@	n.d.	n.d ^O	n.¢	n.Q.
	Mean	<loq< td=""><td><loq< td=""><td>n.¢</td><td>n.¢°</td><td>n.¢</td><td>p‰d.</td><td>"n.d.</td><td>ત્રુતે.</td><td>°~19.d.</td><td>₹ŁOQ</td></loq<></td></loq<>	<loq< td=""><td>n.¢</td><td>n.¢°</td><td>n.¢</td><td>p‰d.</td><td>"n.d.</td><td>ત્રુતે.</td><td>°~19.d.</td><td>₹ŁOQ</td></loq<>	n.¢	n.¢°	n.¢	p‰d.	"n.d.	ત્રુતે.	°~19.d.	₹ŁOQ
	А	n.d.	n.d.	n.d.	≼LØQ).d.	@n.d. 泠	n.d.	Øn.d. 🔬	n.d. 🛋	n.d. ∘
20-30	В	n.d.	n.d.	, 🗍 a.d. 🦕	(non		n.d.	n.dC	n.d.	n.¢	nØ.
	Mean	n.d.	n.d 🖇	n.d.	<l00< td=""><td>n,d</td><td>n d.</td><td>ìn,d.</td><td>"n.d.</td><td>≪ŋ.d.</td><td>"m.d.</td></l00<>	n,d	n d.	ìn,d.	"n.d.	≪ŋ.d.	"m.d.
	А	-	Q		Ž			n.d. "	n.d.	n.d.	n.d.
30-40	В	-	\$-	<i>®</i> - `	×- *	V - ू	¥ - 🔿	n.d	n.c	n.d.	n.d.
	Mean		× - ¢	- 0		5	4	And.	a.d.	n.d.	n.d.
	А	- S	Å,		Ø	~- ~	R-	n.d.	n.d.	∀ n.d.	n.d.
40-50	В	<u>v</u>	& - "	8-	§ - q	× - 4	۲ - ^۲ ∼۲	n d	n.d.	n.d.	n.d.
	Mean	ê - (- 0, '0	- Ç	, 	ā. [\]		n.d.	ăn∕d.	n.d.	n.d.
_(Ĵ a.	s,	& ,	\searrow	L	S.	Å Å	Ş			
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								5			
								<u> </u>			
40-50 DAT: days after trea above LOD								<i>S</i>			



	Tri	al 40193	3/5 (Toi	uffrevil	le) expr	ressed a	s µg/kg				Ŵ	~
Depth	Repli-					D	AT				N.	S
[cm]	cate	0	7	14	28	56	88	119	<b>~146</b>	182	234	0
	А	19.4	28.6	20.3	17.2	12.5	9.8	<lqq< td=""><td><loq< td=""><td><loq< td=""><td><lqq< td=""><td></td></lqq<></td></loq<></td></loq<></td></lqq<>	<loq< td=""><td><loq< td=""><td><lqq< td=""><td></td></lqq<></td></loq<></td></loq<>	<loq< td=""><td><lqq< td=""><td></td></lqq<></td></loq<>	<lqq< td=""><td></td></lqq<>	
	В	14.2	23.3	23.5	13.5	12.1	10.3	< <u>k</u> OQ	5.6	<b>≤</b> ©OQ	<b>ADOQ</b>	Ô
0-10	С	20.5	29.8	19.2	14.2	12.8	10.1	LOQ	<ul> <li></li> </ul>	الا لا	- ~	Į
	D	17.2	28.4	17.9	14.8 🖄	<b>7</b> 11.5	9.4	<loq< td=""><td>- کُ حِ<b>لِیO</b>Q</td><td></td><td>× Q^v</td><td>6</td></loq<>	- کُ حِ <b>لِیO</b> Q		× Q ^v	6
	Mean	17.8	27.5	20.2	14 <b>.</b>	12.2	<b>99</b>	<loq< td=""><td><b>≪LÕQ</b></td><td><b>₹</b>OQ</td><td><b>Æ</b>ÕQ</td><td></td></loq<>	<b>≪LÕQ</b>	<b>₹</b> OQ	<b>Æ</b> ÕQ	
	А	7.0	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d. ⊿	Ç n.d. _A		/ <loq< td=""><td></td></loq<>	
10-20	В	<loq< td=""><td><loq< td=""><td><loq4< td=""><td>n.d.</td><td>n.d.</td><td>ndÕ</td><td>n.d.</td><td>n.d.^{O°}</td><td>n.Ø</td><td><løq< td=""><td></td></løq<></td></loq4<></td></loq<></td></loq<>	<loq< td=""><td><loq4< td=""><td>n.d.</td><td>n.d.</td><td>ndÕ</td><td>n.d.</td><td>n.d.^{O°}</td><td>n.Ø</td><td><løq< td=""><td></td></løq<></td></loq4<></td></loq<>	<loq4< td=""><td>n.d.</td><td>n.d.</td><td>ndÕ</td><td>n.d.</td><td>n.d.^{O°}</td><td>n.Ø</td><td><løq< td=""><td></td></løq<></td></loq4<>	n.d.	n.d.	ndÕ	n.d.	n.d. ^{O°}	n.Ø	<løq< td=""><td></td></løq<>	
	Mean	<loq< th=""><th><loq< th=""><th></th><th>n.¢., °</th><th>n.¢</th><th>p‰d.</th><th>"n.d.</th><th>æd.</th><th>°~19.d.</th><th><b>₹</b>ĽOQ</th><th></th></loq<></th></loq<>	<loq< th=""><th></th><th>n.¢., °</th><th>n.¢</th><th>p‰d.</th><th>"n.d.</th><th>æd.</th><th>°~19.d.</th><th><b>₹</b>ĽOQ</th><th></th></loq<>		n.¢., °	n.¢	p‰d.	"n.d.	æd.	°~19.d.	<b>₹</b> ĽOQ	
	А	n.d.	n.d.	n.Q.	≼LOQ	<u>m</u> .d.	@n.d. 🤌	n.d.		<loq<sup>1</loq<sup>	<loq.< td=""><td></td></loq.<>	
20-30	В	n.d.	n.d.	📬 a.d. 🦻	©n.d.∼	n.d.	n.ds	n.dC	n.d.	n.¢	nØ.	
	Mean	n.d.	n.d.	n.d.	<lqq< th=""><th>n,d</th><th>વર્ત થ.</th><th>n,d.</th><th>n.d.</th><th>≪LOQ</th><th></th><th></th></lqq<>	n,d	વર્ત થ.	n,d.	n.d.	≪LOQ		
	А	-	Ŕ	L.	26		× -		n.d.	n.d.	n.d.	
30-40	В	-	<u> </u>	<i>°</i> - <i>°</i>	≫ [™] - [™]	- ``	¥ -````	n.d.	n.¢	n.d.	n.d.	
	Mean	- "	× - ĝ	- [©]		- S	~	god.	a.d.	n.d.	n.d.	
	А	Ś	°≈∕~		Ø,	~- ~	Q-	n.d.	Ön.d.	∀ n.d.	n.d.	
40-50	В	SX II	& - <u> </u>	0-	Ş - q	r - 4		n.d	n.d.	n.d.	n.d.	]
	Mean	<b>P</b> - , [©]	P - ĝ	-5		,		n.d.	ħ.d.	n.d.	n.d.	]

Table CA 7.1.2.2.1-46: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of soil at Trial 40193/5 (Touffreville) expressed as µg/kg

DAT: days after treatment, LOQ (limit of quantitation) = 5  $\mu$ g/g, LQDQ limit of detection) = 2  $\mu$ g/g, n.d. = not detected above LOD

### C. Residues

No residue concentration of spiroxamine, Mol and Mo2 above LOQ (5 µg/kg) of the analytical method could be found in the control samples.

Starting from an application rate of 15 (0.75) kg spiroxardine/ha and a soil density of 1.5 kg/L the theoretical total conceptration in a 10 cm layer is 6000 (500) µg/kg soil. The concentration of spiroxamine in the 0-10 cm layer found immediately after application were 479, 684, 246, 327 and 309 µg/kg for Elm Farm (4009)/1), Old Half Farm (4009)/8), Ebn Farm (40100/5), Old Hall Farm (40101/3) and Touffreville (40193/5) trial sites, respectively. This equates that at day zero 47.9%, 68.4%, 49.2%, 65.4% and 61.8% of the applied amount was recovered from each site, respectively.

For the Elm Farm (trial site 400971/1) the mean residue concentration in the 0-10 cm soil segment decreased from 479 µg/kg at 0 PAT to 29.9 µg/kg in 244 DAT. In the 10-20 cm layer spiroxamine was found on two occasion at values greater than the DOD, with the maximum value of 7.3 µg/kg found at 0 DAT. In the 20-30 cm layer spiroxamine was not found at levels great than LOQ (5 µg/kg) at any time point. For the metabolite M01 in the 0-10 cm soil segment concentrations reached a maximum of 92.6 µg/kg at 7 DAT and decreased to 18 µg/kg at 244 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 121 µg/kg at 7 DAT and decreased to 25.2 µg/kg at 244 DAT. In both the 40-20 cm and 20-30 cm layer for the metabolites M01 and M02, no residues were found at levels greater than LOQ (5 µg/kg) at any time point.

For the Old Harl Farm (trial site 40099/8) the mean residue concentration in the 0-10 cm soil segment decreased from  $684 \mu g/kg$  at 0 DAT to 55.9  $\mu g/kg$  at 240 DAT. In the 10-20 cm layer spiroxamine was found on three occasion at values greater than the LOD, with the maximum value of 32.2  $\mu g/kg$  found at 0 DAT. In the 20-30 cm layer spiroxamine was not found at levels great than LOQ (5  $\mu g/kg$ ) at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of 99.9  $\mu g/kg$  at 14 DAT and decreased to 33.3  $\mu g/kg$  at 240 DAT. For the metabolite, M02 in the 0-10 cm



soil segment concentrations reached a maximum of 106  $\mu$ g/kg at 14 DAT and decreased to 36.5  $\mu$ g/kg at 240 DAT. In both the 10-20 cm and 20-30 cm layer for the metabolites M01 and M02, no residues were found at levels greater than LOQ (5  $\mu$ g/kg) at any time point.

For the Elm Farm (trial site 40100/5) the mean residue concentration in the 0-10 cm soil segreent decreased from 246 µg/kg at 0 DAT to 55.1 µg/kg at 244 DAT. In the 10-20 cm and 20-30 cm lacer spiroxamine was not found at levels great than LOQ (5 µg/kg) at any time point. In the 10-20 cm/ayer spiroxamine was found on one occasion at values greater than the LOD, with the maximum value of 8.30 µg/kg found at 0 DAT. In the 20-30 cm layer spiroxamine was not found at levels great than LOQ µg/kg) at any time point. For the metabolite, M01 in the 10 cm soil segment concentrations reached a maximum of 44.1 µg/kg at 7 DAT and decreased to 192 µg/kg at 240DAT. For the metabolite, M02 in C the 0-10 cm soil segment concentrations reached a maximum of 56 y µg/kg at 7 DAT and decreased to 20.2 µg/kg at 244 DAT. In both the 10-20 cm and 20230 cm layer for the metabolites A01 and M02 pro residues were found at levels greater than LOQ (5 µg/kg)at any time point.

For the Old Hall Farm (trial site 40101/3) site the measuresidine concentration in the 0-10 cm soil segment decreased from 327 µg/kg at 0 DAT to 46.6 µg/kg at 240 DAT. In the 10°20 cm layer pirox mine was found on three occasions at values greater than the LQD, with the maximum value of 9.1 µg/kg found at 0 DAT. In the 20-30 cm layer spiroxamine was found on one occasion at values greater than the LOD, with the maximum value of 8.6 µg/kg found at 0 pAT. For the pletabolite, Mo1 in the 0-10 cm soil segment concentrations reached a maximum of 33x8 µg/kg at 28 DAF and decreases to 19,3 µg/kg at 240 DAT. For the metabolite, M02 in the 0-10 gm soil segment concentrations reached a maximum of 38.9 µg/kg at 28 DAT and decreased to 21.0 µg/kg at 240 DAT on both the 10, 20 cm and 20-30 cm layer for the metabolites M0k and M02, no residues were found a level greater than POQ (5 µg/kg) at any time point. ()

For the Touffreville (trial site 40193/5) the mean residue concentration in the 10 cm soil segment decreased from 309 µg/kg at DAT to <5 µg/kg 234 DAT. In the 10-20 cm/layer spiroxamine was found on two occasions at values greater than the LOD with the maximum value of 7.7 µg/kg found at 0 DAT. In the 20,30, 30,40,50 cm layer spiroxamine was not found at levels great than LOQ (5 µg/kg) at any time point. For the metabolite, M01 in the 0-10 cm soil segment concentrations reached a maximum of  $25.1 \mu g/cg$  at 7 DAT and decreased 45 < LOQ at 234 DAT. For the metabolite, M02 in the 0-10 cm soil segment concentrations reached a maximum of 27.5  $\mu g/kg$  at 7 DAT and decreased to <LOQ at 234 DAT. In both the 10-20020-30, 30-40 and 40 50 em layer for the metabolites M01 and M02, no residues were found at levels greater than OLOQ (5 µg/kg) at any time point.

# F. Degradation kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.1.2.2.1/12 ( $\sqrt{2763}$ )  $\sqrt{-01-0}$ .

# Conclusion

Spiroxatoine was applied at a single application at two different applications rates of either 3.0 L/ha (1.5 kg a.s./ha) or 1.5 L/ha (0.75 kg a.s./ha) in opring 1994 to spring cereal crops. The decline of spiroxamine and the formation and destine of its metabolity's M01 and M02 was followed for up to 244 days after application at 5 gites in Great Britain and France.

During the test duration, nearly all residues remained in the 0-10 cm layers of the soil. However, spiroxamine was also found in the 19-20 cm layer in four of the trial sites investigated, the maximum value of 32.2 µg/kg found at DAT 0 at the Old Hall Farm trial site (40099/8, 1.5 kg a.s./ha application). In the 20-30 cm layer spiror amine was found on one occasion at values greater than the LOQ, with the maximum value # 8.6 pp/kg found at 0 DAT at the Old Hall Farm trial site (40101/3, 0.75 kg a.s./ha application). No mobility into soil layers below 30 cm was observed. The metabolites M01 and M02 were detected at all sites. The metabolite M01 reached a maximum of 99.9 µg/kg at 14 DAT in the Old Hall Farm trial site (40099/8, 1.5 kg a.s./ha application) in the 0-10 cm layer. The metabolite M02 reached a maximum of 121 µg/kg at 7 DAT in the Elm Farm trial site (400971/1, 1.5 kg a.s./ha application) in the 0-10 cm layer.



A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in KCA 7.1.2.2.1/12 (M-763140-01-1).

### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study is considered valid to assess the dissipation of spiroxamine under field conditions is soil. The study meets the requirements to assess field persistence of spiroxamine and its metabolities and to derive parent soil DegT_{50matrix} values for legacy field studies as defined by EFSA (2004). It is not spirable for assessing metabolite soil DegT_{50matrix} values as the design the not minimise soil surface processes immediately after application as required by EFSA (2014).

Data Point:	KCA 7.1.2.2.1/04 & 6 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Report Author:	
Report Year:	
Report Title:	Dissipation of KWG 4168 in soils under field conditions (France and Italy)
Report No:	RA-2048/94 %
Document No:	<u>M-0061280Y-1 5 5 5 5 5 5 6 6</u>
Guideline(s) followed in	<u>M-006128@Y-1</u> <u>Y</u>
study:	
Deviations from current	Vesatteter below) 7 / 2 / 2 / 2
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in
	study symmary) Q ^y Qy
Previous evaluation:	yes, evaluated and accepted 4 and a construction of the second se
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities.	
Acceptability/Reliability;	Yes y y y y y

### Executive Summary

Soil dissipation of spiroxamine was studies after application as an EC formulation containing 491.4 g/L to bare soil plots under field conditions for up to 240 days at two trial sites in Laudun, France and Filetto, Italy.

A single application of a nominal 400 g spiroxamine/la as an emulsifiable concentrate formulation was performed to bare soil on 21st tone 1994 (Laudun, France) of 22nd August 1994 (Filetto, Italy).

The initial dissipation of spiroxamme was rapid for both sites, showing a slower dissipation phase after 7 DAT. Residues of spiroxamme were detected mainly in the 0-10 cm soil horizon throughout the trial. Residues of spiroxamme were found above the LOO (5  $\mu$ g/kg) in the 10-20 cm horizon once at Laudun at 0 DAF, and once in the 20-30 cm horizon at Filetto at 7 DAT.

M0f (spiroxamine-deseth) was only detected above LOQ once at Laudun (6.86  $\mu$ g/kg at 7 DAT in the 0-10 cm horizon only). At Filetto, M@I (spiroxamine-desethyl) was detected above LOQ at 14, 31 and 60 DAT in the 0-10 cm horizon only. Peak levels of 8.39  $\mu$ g/kg were found at 31 DAT before declining below LOQ at 91 DAT. No residues of proxamine were found above the LOQ (5  $\mu$ g/kg) in 10-20 or 20-30 cm porizons on either site.

M02 (spiroxanine-desprop)) was detected above LOQ at Laudun at 0 and 7 DAT before dropping below LOQ at 16 DAT (peak of 7.55  $\mu$ g/kg at 7 DAT in the 0-10 cm horizon only). At Filetto, M02 (spiroxanine-despropyl) was detected above LOQ at 14, 31 and 60 DAT in the 0-10cm horizon only. Peak levels of 8.72  $\mu$ g/kg were found at 31 DAT before declining below LOQ at 91 DAT. No residues of spiroxamine were found above the LOQ (5  $\mu$ g/kg) in 10-20 or 20-30 cm horizons on either site.

The DT₅₀ and DT₉₀ of spiroxamine determined in the study was reported for each soil. However, a re-



 $\overline{a}$ 

evaluation of the degradation kinetics in accordance with the FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT50 values from laboratory and field dissipation studies (EFSA 2014), was performed in the report presented under point KCA 7.1.2.2.1/12 763140-01-1).

> I. **Materials and Methods**

I. Materials and Methods
A. Materials
I. Test Items
Spiroxamine (KWG 4168 500 EC), emulsifiable concentrate (491.4cd, spiroxamine)
Image: Product no.:
Product no.:
Product no.:
O122945
Batch no.:
FL 94023/0089A
Certificate of analysis:
FAR 240 (16 December 1993)
C. Trial locations & soils
The study was performed at two different trial sites in Laudum-1' artorise, France (wam) and Filetto, Italy (silty clay loam). Site soil is characterized for Table CA 7.1.2.2.147. The field soil dissipation trial con-(silty clay loam). Site soil is characterized the Table CA 7, 1.2.2. 1e47. The field soil dissipation trial consisted of one treated and one untreated plot on each site. Plot measurements in the report given as 228 m² and 480m² in Laudun and Filetto, respectively (it was not specified if this referred to the entire area used for the trial or the treated area oddy). No pesticide history was given for previous years before the trial for either site. L,

Table CA 7.	1.2.2	47:Noc	ation. s	site des	cription	and	climatic	data	of test sites
		$\sim$	- Y '	×,	~ [*]	$\sim$	- /	$\supset$	s s s s s s s s s s s s s s s s s s s

Trial designation S 0 0 40198/G	40424/1
Soil Designation	Filetto
Vegetation O S & Mines S	Vines
Geographic Location	Filetto, Ravenna
Country St Pratoe	Italy
Textural Classification ( $6$ SDA) Sand [50 - 2009 $\mu$ m] (%) Silt [2 - 50 $\mu$ m] (%) Clay [< 201m] (%)	Silty clay loam
Textural Classification (6SDA) Solution (6SDA)	9.5
Sand $[50 - 2000 \mu\text{m}]$ (%) Silt $[2 - 50 \mu\text{m}]$ (%) Clay $[<20 \text{m}]$ (%)	51.2
	39.3
pH in CaCl ₂	7.6
Organic Matter (%) $\mathcal{T}$ $\mathcal{T}$ $\mathcal{Q}$ $\mathcal{T}$ 1.34	2.22
Organic carbon (%)	1.29
Cation Exchange Capacity 10	17
(meq/100 g) (meq/1	
Soil Moissure capacity (gl 00g sol) 37.0	46.8

# B. Study Design

# 1. Experimental Conditions

A single application of a nominal 400 g spiroxamine/ha as an emulsifiable concentrate (EC) formulation was performed to bare soil on 21st June 1994 at Laudun and 22nd August 1994 at Filetto. Application confirmation was performed by calculation using the DAT 0 samples.



During the trials, soil cultivation and maintenance was performed according to the usual local agricultural practice. At Laudun, applications of glyphosate, copper, sulphur and azoxystrobin were used for maintenance of the vines. Application of mancozeb only was made for maintenance of vines at Fighto. No irrigation was carried out on either site. Products used for maintenance were listed, with none containing active substances in the same chemical family as spiroxamine.

Average temperatures, rainfall and sunlight are given for sampling dates themselves and time periods between sampling points at each site from weather stations an unknown distance from the trial sites. Total rainfall for Laudun is 513 mm for 11th June – 31st December 1994 and 83 mm for 1st January 20th February 1995. Total rainfall for Filetto from 22nd August – 19th December 1994 is 23^o mm and 138 mm between 21st December 1994 – 19th April 1995. Temperatures and rainfall for both sites cepter.

Soil dissipation of spiroxamine was studies for 240 days.

### 2. Sampling

At 0, 7, 16, 28, 58, 91, 119, 149, 175 and 240 days after meatment (DAP) at Laudun and 0, 7, 14, 41, 60, 91, 119, 150, 182 and 240 days at Filetto, 20 cores were taken at locations around the plot (statistically distributed to ensure representative samples), down to a depth of 30 cm (diameter of approximately 50 mm) using a 'Wacker Hammer'. Soll cores were split into 10 cm sections, homogenised and frozen (-18°C) before storage and analysis. Control plots were sampled at the beginning and the end of the study.

# **3. Analytical Procedures**

Soil samples were extracted at using a Soctec extractor with boiling methanol/water/ammonia (25%), 80/20/1 (v/v/v). Extracts were re-dissolved in methanol and quantified using HPLC/MS/MS. Specific details of the method are given in MCA Section 4 (Method no. 00374 (RA-607/94) (M-019207-02-1)). The limit of quantification (MOQ) is given as 5  $\mu$ g/kg and limit of detection (LOD) of 2  $\mu$ g/kg for spiroxamine and metabolites.

Method validation was performed separately with a mixture of standard soils (soil 2.1/soil 2.2/soil 2.3, 1/1/1, v/v/v), fortified with spiroxamine, M01 (spiroxamine-describyl) or M02 (spiroxamine-despropyl). The mean recoveries were 98.8% (relative standard deviation, RSD 3.96%) for spiroxamine, 99.7% (RSD 2.72%) for M01 (spiroxamine-describyl) and 101% (RSD 2.74%) for M02 (spiroxamine-despropyl).

In addition, concurrent recoveries were run with soil from control plots from each site fortified with spiroxamine, M04 (spiroxamine desetbyl) or M02 (spiroxamine-despropyl). Mean spiroxamine recoveries were 88.7 and 83.8% (RSD 18.9 and 18.4%) for baudun and Filetto, respectively. Mean M01 (spiroxamine desetbyl) recoveries were 94.3 and 86.5% (RSD 8.4 and 9.0%) for Laudun and Filetto, respectively. Mean M02 (spiroxamine-despropyl) recoveries were 95.7 and 93.1% (RSD 9.3 and 9.6%) for Lauduf and Filetto, respectively.

# 4. Determination of degradation kinetics

The  $DT_{50}$  and  $DT_{80}$  of sphroxappine determined in the study was reported for each site. However, a reevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2010) and the EFSS guidance on deriving DegT50 values from laboratory and field dissipation studies (EFSA 2014), was performed in the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

### II. Results and Discussion

# A. Analytical Methodology

Full details and acceptable validation data to support this method (Method 00374 (RA-607/94)) are presented in Document M-CA 4, Section 4.1.2 (M-019207-02-1). The method complies with the EU regulatory requirements outlined within SANCO/3029/99 rev. 4 and is suitable for the determination of



spiroxamine and its metabolites in soil samples by HPLC/MS/MS.

### B. Data

The results for spiroxamine and its metabolites are presented below as soil residue concentrations on a  $\mu$ g/kg dry weight basis) for each of the treated plots in Table CA 7.1.2.2.1-55 to Table CA 7.1.2.2.1-48: Mean residues of spirozential in C

Table CA 7.1.2.2.1-48: Mean residues of spirox	amine in 0-30 cm	horizons of soil	l at Laga	
pressed as µg/kg	~	L.	$\sim$	

	I -		-99			Ĉħ	6	۶Ŭ	*			
Depth	Repli-				~	<b>D</b>	AT 🖉	, j	, î	~? ~	L.	, de la companya de l
[cm]	cate	0	7	16	28	58	99	119	149	.đ.75		
	А	65.6	45.0	14.0	29.7	13.3	Q1.1	8.69	Ç 7.28 (	, <loq< td=""><td>5.55</td><td>þ″</td></loq<>	5.55	þ″
	В	63.4	33.0	15.8 🗸	26.6	15 7	1210	9.77	7.20	<løq< td=""><td>&lt;<b>L</b>ØQ</td><td></td></løq<>	< <b>L</b> ØQ	
0-10	С	59.0	31.4	-&	-©3°	13.	×,	<i>*0</i> *	£	°∼,-	<i>К</i> ⁷ -	
	D	55.0	23.5	0	2	<u>0</u> -	6- 6	6 -	6 - L	- 2	°.,- «	
	Mean	60.8	33.2 💥	<b>∱14.9</b> ‰	28.2	14,5	11.6	9.23	7.24	<lqq< th=""><th><løq< th=""><th></th></løq<></th></lqq<>	<løq< th=""><th></th></løq<>	
	Α	6.96	<loo< td=""><td><lqq< td=""><td><løø< td=""><td><lqq< td=""><td>p.d.</td><td><i>≤</i>bØQ</td><td>m.d.</td><td>≪n.d.</td><td>an.d.</td><td></td></lqq<></td></løø<></td></lqq<></td></loo<>	<lqq< td=""><td><løø< td=""><td><lqq< td=""><td>p.d.</td><td><i>≤</i>bØQ</td><td>m.d.</td><td>≪n.d.</td><td>an.d.</td><td></td></lqq<></td></løø<></td></lqq<>	<løø< td=""><td><lqq< td=""><td>p.d.</td><td><i>≤</i>bØQ</td><td>m.d.</td><td>≪n.d.</td><td>an.d.</td><td></td></lqq<></td></løø<>	<lqq< td=""><td>p.d.</td><td><i>≤</i>bØQ</td><td>m.d.</td><td>≪n.d.</td><td>an.d.</td><td></td></lqq<>	p.d.	<i>≤</i> bØQ	m.d.	≪n.d.	an.d.	
10-20	В	6.36	p Q	<b>≪Ľ</b> ØO	₹ÇQ0	QU QU	n.d.	Ôn.d.	n.d.	n.d.	n.d.	
	Mean	6.66	<b>LOQ</b>	<b>QLOQ</b>					n d	n≾d.	n.d.	
	Α	<loq< td=""><td>[™]<lqø< td=""><td><lqq< td=""><td><lqq< td=""><td><lon LOQ</lon </td><td>n.d.</td><td>≪<b>g</b>QQ</td><td>3.4</td><td>n.d.</td><td>n.d.</td><td></td></lqq<></td></lqq<></td></lqø<></td></loq<>	[™] <lqø< td=""><td><lqq< td=""><td><lqq< td=""><td><lon LOQ</lon </td><td>n.d.</td><td>≪<b>g</b>QQ</td><td>3.4</td><td>n.d.</td><td>n.d.</td><td></td></lqq<></td></lqq<></td></lqø<>	<lqq< td=""><td><lqq< td=""><td><lon LOQ</lon </td><td>n.d.</td><td>≪<b>g</b>QQ</td><td>3.4</td><td>n.d.</td><td>n.d.</td><td></td></lqq<></td></lqq<>	<lqq< td=""><td><lon LOQ</lon </td><td>n.d.</td><td>≪<b>g</b>QQ</td><td>3.4</td><td>n.d.</td><td>n.d.</td><td></td></lqq<>	<lon LOQ</lon 	n.d.	≪ <b>g</b> QQ	3.4	n.d.	n.d.	
	В	<body></body>	ñ.d.	<u></u> LÕQ	< QÓQ	<b>KLOQ</b>	w.d.	n.d.	©n.d.⊙	∛ n.d.	n.d.	
20-30	С	5.45	S - 🔍	0 - 6	§ - N	· ·		Ţ.	<lqq< td=""><td>-</td><td>-</td><td></td></lqq<>	-	-	
	D 🔊	5.31	- 6	-6	Ż				ð.d.	-	-	
	Mean	<loq< td=""><td><kol></kol></td><td>&lt;00Q</td><td><b>SOQ</b></td><td><b>Ł</b>OQ</td><td>&amp; §⁄n.d._{(k}</td><td>n.d.</td><td><b>≫LOQ</b></td><td>n.d.</td><td>n.d.</td><td></td></loq<>	<kol></kol>	<00Q	<b>SOQ</b>	<b>Ł</b> OQ	& §⁄n.d. _{(k}	n.d.	<b>≫LOQ</b>	n.d.	n.d.	

DAT: days after treatment LOQ (limit of quantitation) =  $5 \frac{1}{2} \frac{1}{\sqrt{2}} \frac{1}{\sqrt{2}$ above LOD \Ó

Table CA 7.1.202.	1-49 Mean residu	es of MO1 (spirox)	amine-desethvl) i	n 0-30 cm horizons of soil
<u> </u>	Sat Isandun ovn	rossed of pa/log		
Č	10° at Laduun Exp	nesseu as µg/kg		

		$\checkmark$	<u> </u>	<del>}                                    </del>	. "0"	<i>.</i>					
Depth	Repli-	ĭ <		., 0	, Cr	N DA	<u>۱۳</u>				
[cm]	cate	A CON	7	.J6	~~2 [°] 28	58	⁰ ≽91	119	149	175	240
	, A	6.02	Ş <b>7</b> .77 🕅	LOQ	LO	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<>	<loq< th=""><th>n.d.</th><th>n.d.</th></loq<>	n.d.	n.d.
	B A	€.03 5.©5	6.40	<L $OO$	<lqq< th=""><th>&lt;<b>b</b>Q</th><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>nd</th></loq<></th></loq<></th></loq<></th></loq<></th></lqq<>	< <b>b</b> Q	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>nd</th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th>nd</th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th>nd</th></loq<></th></loq<>	<loq< th=""><th>nd</th></loq<>	nd
0-10	CO,	5.65	2,06	~ ⁰ ″ .		Ø_	-	I	-	-	-
	D	SEOQ.		Q ⁷ - 🖉		¢ -	-	-	-	-	-
	Mean	<loq< th=""><th></th><th><lqq< th=""><th><løq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<></th></loq<></th></løq<></th></lqq<></th></loq<>		<lqq< th=""><th><løq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<></th></loq<></th></løq<></th></lqq<>	<løq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<></th></loq<></th></løq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th>n.d.</th><th>n.d.</th></loq<></th></loq<>	<loq< th=""><th>n.d.</th><th>n.d.</th></loq<>	n.d.	n.d.
	AC	n d.	'n⊾d.	Ay.d.	~9a.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, В	Jn.d.	~n.d. 4	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
0	Mean	<loq< th=""><th></th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<>		n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Á	A	n d.	nd.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	≪₿	A.d.	ر n.d. م	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	Mean	-LOQ	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

DAT: days after reatment LOQ (himit of quantitation) = 5  $\mu$ g/kg, LOD (limit of detection) = 2  $\mu$ g/kg, n.d. = not detected above LOD 



Table CA 7.1.2.2.1-50: Mean residues of M02 (spiroxamine-despropyl) in 0-30 cm horizo	ns of
soil at Laudun expressed as µg/kg	

			1		• •	8						ð
Depth	Repli-					D	АТ				. 🖉	
[cm]	cate	0	7	16	28	58	91	119	<b>⊳149</b>	175	240	U
	Α	6.51	8.60	5.03	<loq< td=""><td><loq< td=""><td><loq< td=""><td><lqq< td=""><td>n.d.</td><td>n.đ.</td><td>240. .n.Q.</td><td></td></lqq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><lqq< td=""><td>n.d.</td><td>n.đ.</td><td>240. .n.Q.</td><td></td></lqq<></td></loq<></td></loq<>	<loq< td=""><td><lqq< td=""><td>n.d.</td><td>n.đ.</td><td>240. .n.Q.</td><td></td></lqq<></td></loq<>	<lqq< td=""><td>n.d.</td><td>n.đ.</td><td>240. .n.Q.</td><td></td></lqq<>	n.d.	n.đ.	240. .n.Q.	
	В	6.50	7.15	<loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>áv.d.</td><td>∼Qn.d.</td><td>Ô</td></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>áv.d.</td><td>∼Qn.d.</td><td>Ô</td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>áv.d.</td><td>∼Qn.d.</td><td>Ô</td></loq<></td></loq<></td></loq<>	<loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>áv.d.</td><td>∼Qn.d.</td><td>Ô</td></loq<></td></loq<>	< <u>k</u> OQ	<loq< td=""><td>áv.d.</td><td>∼Qn.d.</td><td>Ô</td></loq<>	áv.d.	∼Qn.d.	Ô
0-10	С	5.88	7.33	-	-	es -	- 1	<u>, -</u>	^	ا∕ - ا∕م		į
	D	<loq< td=""><td>7.13</td><td>-</td><td>_ 4</td><td>- 7</td><td></td><td>-</td><td>- () xa.d.</td><td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td><td>J.</td><td></td></loq<>	7.13	-	_ 4	- 7		-	- () xa.d.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	J.	
	Mean	5.35	7.55	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>nd.</th><th>m.d.</th><th></th><th>6.0</th></loq<></th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th>nd.</th><th>m.d.</th><th></th><th>6.0</th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th>nd.</th><th>m.d.</th><th></th><th>6.0</th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th>nd.</th><th>m.d.</th><th></th><th>6.0</th></loq<></th></loq<>	<loq< th=""><th>nd.</th><th>m.d.</th><th></th><th>6.0</th></loq<>	nd.	m.d.		6.0
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d. ∥	Ç n.d. 🔬	, n.d. 🔇	n.d	7
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.Ø	n.d.	n.d ^{O°}	n.¢	n.d.	
	Mean	n.d.	n.d.	n. <b>k</b>	n.¢_°	n.C	ŋ‰d.	"n.d.	æd.	`~p.d.	Kn.d.	
	Α	n.d.	n.d.	n.a.	n.d.	<u>m</u> .d.		n.d.	Øn.d. "	. n d 🗳	n.d_∘	
20-30	В	n.d.	n.d. 💡	A.d. 🦻	©n.d.∼	n.d.	n.ds	n.dC	n.d.	n.đ	n@. 	
	Mean	<loq< td=""><td>n.d.</td><td></td><td>n.d.</td><td>n,đ</td><td>n dt.</td><td>'n,d.</td><td>"n.d.</td><td><b>≪p.d.</b></td><td>an.d.</td><td></td></loq<>	n.d.		n.d.	n,đ	n dt.	'n,d.	"n.d.	<b>≪p.d.</b>	an.d.	

DAT: days after treatment, LOQ (limit of quaditation) = 5 µg/g, LOD (limit of detection) = 2 µg/kg, n. 4 not detected above LOD

Table CA 7.1.2.2.1-51: Mean residues of spiroxamine in 630 cm horizons of soil at Filetto expressed as µg/kg Ô Ô 

				ð í	6	<u> </u>	<u> </u>	<u>Ó</u>			
Depth	Repli-	\$ C		y R	, °C (	, DA			L.		
[cm]	cate 🏷		7		<u>s</u>	S≰A	91	119	\$150	182	240
	A.	<b>\$</b> 2.9	<b>×63</b> .4	72.3	A1.9	≫40.0 €	O -	22.5	16.2	21.0	29.5
	B A	( 107.2Ĉ	66.4	🖗 62.6 🖗	67 0	388	28.9	25.0	16.5	21.1	28.5
0-10	B C C	,107.2 920	68.1	~"		S.	Ø- j	25.0 S-	-	-	-
	Ę,	<u>&amp;</u> 9.2	ð7.1 g		ÿ- 2	- 4	× - ~	-	-	-	-
	Mean	[©] 97.8©	68.8	67,5%	69,5	39.4	27.5	23.8	16.4	21.1	29.0
10-20	A 🔊	< L Q Q	< L O O	n.d.	n.d.	"A.d.	n.d.	n.d.	<loq< td=""><td>n.d.</td><td><loq< td=""></loq<></td></loq<>	n.d.	<loq< td=""></loq<>
10-20	ķ	sấ¢ÔQ	<loq< td=""><td>©n.d. ∞</td><td></td><td>n.d.</td><td>n.d.</td><td><loq< td=""><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<></td></loq<>	©n.d. ∞		n.d.	n.d.	<loq< td=""><td><loq< td=""><td>n.d.</td><td>n.d.</td></loq<></td></loq<>	<loq< td=""><td>n.d.</td><td>n.d.</td></loq<>	n.d.	n.d.
	Mean			n.d.	<lqq< th=""><th>n.đ.</th><th>n.d.</th><th><loq< th=""><th><loq< th=""><th>n.d.</th><th><loq< th=""></loq<></th></loq<></th></loq<></th></lqq<>	n.đ.	n.d.	<loq< th=""><th><loq< th=""><th>n.d.</th><th><loq< th=""></loq<></th></loq<></th></loq<>	<loq< th=""><th>n.d.</th><th><loq< th=""></loq<></th></loq<>	n.d.	<loq< th=""></loq<>
(		n.d.	6,45	< <b>E</b> ØQ		Ø.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20.30		).d.		On.d. 👡	Ôn.d. '	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	C 🇞		∕ 5.16Q	- 0°		-	-	-	-	-	-
	D	, n.d.	988	N.		-	-	-	-	-	_
	Mean	₄ n.d.	6.00	È SLOQ	Şn.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

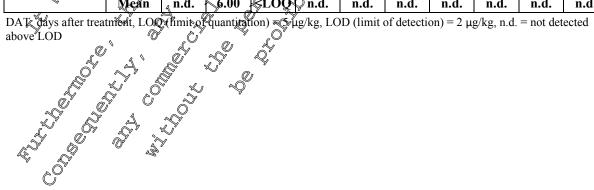




Table CA 7.1.2.2.1-52: Mean residues of M01 (spiroxamine-desethyl) in 0-30 cm hori	zons of soil
at Filetto expressed as µg/kg	°

			L	1.9	8						, O	×
Depth	Repli-					D	АТ				N.	
[cm]	cate	0	7	14	31	60	91	119 (	-150	182 _@	240	0
	А	<loq< td=""><td><loq< td=""><td>7.09</td><td>8.35</td><td>5.01</td><td><loq< td=""><td><lqq< td=""><td><loq< td=""><td><loq< td=""><td></td><td></td></loq<></td></loq<></td></lqq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td>7.09</td><td>8.35</td><td>5.01</td><td><loq< td=""><td><lqq< td=""><td><loq< td=""><td><loq< td=""><td></td><td></td></loq<></td></loq<></td></lqq<></td></loq<></td></loq<>	7.09	8.35	5.01	<loq< td=""><td><lqq< td=""><td><loq< td=""><td><loq< td=""><td></td><td></td></loq<></td></loq<></td></lqq<></td></loq<>	<lqq< td=""><td><loq< td=""><td><loq< td=""><td></td><td></td></loq<></td></loq<></td></lqq<>	<loq< td=""><td><loq< td=""><td></td><td></td></loq<></td></loq<>	<loq< td=""><td></td><td></td></loq<>		
	В	<loq< td=""><td>5.15</td><td>7.56</td><td>8.43</td><td>5.78</td><td><loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>\$©OQ</td><td><b>C</b>LOQ</td><td>Ô</td></loq<></td></loq<></td></loq<>	5.15	7.56	8.43	5.78	<loq< td=""><td>&lt;<u>k</u>OQ</td><td><loq< td=""><td>\$©OQ</td><td><b>C</b>LOQ</td><td>Ô</td></loq<></td></loq<>	< <u>k</u> OQ	<loq< td=""><td>\$©OQ</td><td><b>C</b>LOQ</td><td>Ô</td></loq<>	\$©OQ	<b>C</b> LOQ	Ô
0-10	С	<loq< td=""><td><loq< td=""><td>-</td><td>-</td><td><u>r</u>a -</td><td>- "</td><td>×<u>-</u></td><td>- 🦿</td><td>× - ×</td><td>2 - 2 2 - 2</td><td>Ĩ</td></loq<></td></loq<>	<loq< td=""><td>-</td><td>-</td><td><u>r</u>a -</td><td>- "</td><td>×<u>-</u></td><td>- 🦿</td><td>× - ×</td><td>2 - 2 2 - 2</td><td>Ĩ</td></loq<>	-	-	<u>r</u> a -	- "	× <u>-</u>	- 🦿	× - ×	2 - 2 2 - 2	Ĩ
	D	<loq< td=""><td>7.13</td><td>-</td><td>_ 《</td><td>-</td><td>@</td><td>-</td><td>- 0</td><td></td><td></td><td></td></loq<>	7.13	-	_ 《	-	@	-	- 0			
	Mean	<loq< th=""><th><loq< th=""><th>7.33</th><th>8.39</th><th>5.40</th><th><loq< th=""><th><loq< th=""><th><b>≪LÕQ</b></th><th>₹ĴŎQ</th><th><b>∕£OQ</b></th><th>, O'</th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th>7.33</th><th>8.39</th><th>5.40</th><th><loq< th=""><th><loq< th=""><th><b>≪LÕQ</b></th><th>₹ĴŎQ</th><th><b>∕£OQ</b></th><th>, O'</th></loq<></th></loq<></th></loq<>	7.33	8.39	5.40	<loq< th=""><th><loq< th=""><th><b>≪LÕQ</b></th><th>₹ĴŎQ</th><th><b>∕£OQ</b></th><th>, O'</th></loq<></th></loq<>	<loq< th=""><th><b>≪LÕQ</b></th><th>₹ĴŎQ</th><th><b>∕£OQ</b></th><th>, O'</th></loq<>	<b>≪LÕQ</b>	₹ĴŎQ	<b>∕£OQ</b>	, O'
	А	n.d.	n.d.	n.d.	nd.	n.d.	Qn.d.	∘n.d. ∥	Ç n.d. 🗶	, n.d. (		, ^w
10-20	В	n.d.	n.d.	n.d. 🗸	n.d.	n.d.	n.d.Ö		n.d ^O	n.¢	n.Ø.	
	Mean	n.d.	n.d.	n. <b>d</b> k	n.¢	n.C	ŋ‰d.	"n.d.	A.d.	°~19.d.	≪n.d.	
	А	n.d.	n.d.	n.a.	n,d.			n.d.	On.d. A	n.d. 🛋		
20-30	В	n.d.	n.d. 💡	着 a.d. 🦻	©n.d.∧		♥ n.d₄	n.dC	n.d.	n.đ.	n@. 	
	Mean	n.d.	<loo< td=""><td>n.d.</td><td>n.d.</td><td>n,đ</td><td>n d.</td><td>'n,d.</td><td>n.d.</td><td><b>≪ŋ.d</b>.</td><td>An.d.</td><td></td></loo<>	n.d.	n.d.	n,đ	n d.	'n,d.	n.d.	<b>≪ŋ.d</b> .	An.d.	

DAT: days after treatment, LOQ (limit of quadratation)  $\neq$  5 µg/kg, LOD (limit of detection) = 2 µg/kg, n.  $f \neq$  not detected above LOD

Table CA 7.1.2.2.1-53: Mean residues of M@ (spiroxamine-despropyl) n 0-30 cm horizons of soil at Filetto expressed as µg/kg

		$\sim$	<u>&amp;</u> .	CV 4	<del>y a</del>			Ô	^		
Depth	Repli-			y k	-	<b></b>	AT S		L.		
[cm]	cate	04.	7	14°	<u>s</u>	60	<b>9</b> 1	[≪] ¥19 į	<b>\$150</b>	182	240
	A	< <b>A</b> DOQ	≪LOQ	7.30	A.87 🚽	\$5.36 (	) <loø≁< td=""><td><lqq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></lqq<></td></loø≁<>	<lqq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></lqq<>	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
	^B ^C C	€ <rol> </rol>	LOQ	7.47~	8.56	5.99	<loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
(		<lqq< td=""><td><loq< td=""><td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td><td></td><td>5.9<b>9</b></td><td>Ũ- Ĵ</td><td>Ş -</td><td>-</td><td>-</td><td>-</td></loq<></td></lqq<>	<loq< td=""><td>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</td><td></td><td>5.9<b>9</b></td><td>Ũ- Ĵ</td><td>Ş -</td><td>-</td><td>-</td><td>-</td></loq<>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		5.9 <b>9</b>	Ũ- Ĵ	Ş -	-	-	-
	, P	<i>≤</i> <b>b</b> OQ	<b>6</b> .47	<u>, 0 -</u> ;	ý- (	7 - 2		-	-	-	-
	Mean	K⊂LOQ	<loq< th=""><th>7.39</th><th>8.72</th><th>5.68</th><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<></th></loq<></th></loq<>	7.39	8.72	5.68	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""></loq<></th></loq<>	<loq< th=""></loq<>
10-20	A 🖑	nd	n Ø n.d.	n.d.	n.d.	And.	∕n.d.	n.d.	n.d.	n.d.	n.d.
10-20	, P	s <b>, I</b> P.ď.	n.d.	©n.d. »,	On.d.	n.d.s	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	∮n.d. ∢	n.d.	n.d 🖉	n.d.	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.
(	A A	n.đ	n d.	⊾n.d.	n.d.	d.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	A B	<u>)</u> .d.	, fr.d.	On.d. 👡	Ôn.d.	Øn.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean 🎓	on.d.^	∕×LO@	n.d.Q	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

DAT: days ther treatment, LOQ (limit of quantitation) 5  $\mu$ g/kg, LOD (limit of detection) = 2  $\mu$ g/kg, n.d. = not detected above LOD

# C. Residues

Analysis of compol samples showed to residues above the limit of quantification (LOQ) of 5  $\mu$ g/kg at either site.

The average initial concentration of sphoxamine in soil samples taken immediately after application was 60.8 and 92.8  $\mu$ g/kg in Loudun and Filetto respectively. Within the report, an application rate of 400 g/ka, assuming a soil density of 1.5 g/cm3 and depth of 10 cm, is given as 267 mg/kg soil. Therefore, according to the report, the measured soil concentrations at 0 DAT were 12 and 20% of nominally applied sphoxamine for Laudun and Filetto sites, respectively.

The inftial dissipation of spiroxamine was rapid for both sites, showing a slower dissipation phase after 7 DAT. Residues of spiroxamine were detected mainly in the 0-10 cm soil horizon throughout the trial. Residues of spiroxamine were found above the LOQ (5  $\mu$ g/kg) in the 10-20 cm horizon once at Laudun



at 0 DAT, and once in the 20-30 cm horizon at Filetto at 7 DAT.

M01 (spiroxamine-desethyl) was only detected above LOQ once at Laudun (6.86  $\mu$ g/kg at 7 DAT in the 0-10 cm horizon only). At Filetto, M01 (spiroxamine-desethyl) was detected above LOQ at 14, 37 and 60 DAT in the 0-10cm horizon only. Peak levels of 8.39  $\mu$ g/kg were found at 31 DAT before declining below LOQ at 91 DAT. No residues of spiroxamine were found above the LOQ (5  $\mu$ g/kg) in 10-20 or 20-30 cm horizons on either site.

M02 (spiroxamine-despropyl) was detected above LOQ at Laudun at 0 and 7 DAT before dropping below LOQ at 16 DAT (peak of 7.55  $\mu$ g/kg at 7 DAT in the 0-10 cm horizon only). At Frietto, M02 (spiroxamine-despropyl) was detected above LOQ at 14, 31 and 60 DAT in the 0-10 cm horizon only. Peak levels of 8.72  $\mu$ g/kg were found at 31 DAT before declining below LOQ at 31 DAT before declining below LOQ at 31 DAT. No residues of spiroxamine were found above the LOQ (5  $\mu$ g/kg) in 10-20 or 20-30 cm horizons on either site.

### **D.** Kinetic Analysis

Degradation rates determined in the report are superseded by the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

# J. Conclusion

Following a single application of spirovamine at a rate of nominal rate of 400 g ha to bare soil applied on 21st June 1994 (Laudun) and 22^{pc} August 1994 (Filette), decline of spirovamine, and the formation and decline of M01 (spirovamine-desetbyl) and M02 (spirovamine-desproy)) was followed for up to 360 days after application at 2 trial sites in Haudun France and Effetto, Haly. A re-evaluation of the degradation kinetics in accordance with FQCUS guidance document or degradation kinetics (2014) is performed in KCA 7.1.2.2.1/12 (M-763149-01-1)

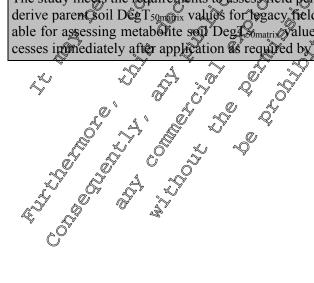
M01 (spiroxamine-desethyl) was detected at a peak level of \$39 µg/kg in the 0-16 cm horizon at Filetto. M02 (spiroxamine-despropyl) was detected at a peak level of \$.72 µg/kg in the 0-10 cm horizon at Filetto.

Filetto. No residues of spiroxamine or its metabolites were found above the LOO (5  $\mu$ g/kg) in 10-20 or 20-30 cm horizons on either site.

# Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283 2013.

The study is considered valid to assess the dusipation of priroxamine under field conditions in soil. The study meets the requirements to assess field persistence of spiroxamine and its metabolites, and to derive parent soil Deg  $T_{50}$  with a studies for tegacy field studies as defined by EFSA (2014). It is not suitable for assessing metabolite soil Deg  $T_{50}$  matrix values as the design did not minimise soil surface processes included by EFSA (2014).





Data Point:	KCA 7.1.2.2.1/05
Report Author:	
Report Year:	1996
Report Title:	Dissipation of KWG 4168 in soils under field conditions (France and Italy)
Report No:	RA-2127/95
Document No:	<u>M-006129-01-1</u>
Guideline(s) followed in	BBA Guideline IV-4.1 (1986)
study:	
Deviations from current	Yes (refer below)
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in study summary)
Previous evaluation:	yes, evaluated and accepted $\mathbb{Q}^{\vee}$
	RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GQP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes O' O' A A A

#### **Executive Summary**

Soil dissipation of spiroxamine was studied after application as an EC formulation containing 498.5 g/L to bare soil plots under field conditions for up to 560 days at two trial sites in Lauran, France and Nogarole Rocca, Italy.

A single application of a nominal 400 g spirox mine/ha as an omulstrable concentrate formulation was performed to bare soil in spring summer 1925.

The initial dissipation of spiroxamine was tapid for both sites, with Landun showing eslower dissipation phase after 14 DAT, whilst Nogarole Rocca showed continued rapid dissipation. Residues of spiroxamine were detected in the 0-10 cm soil horizon throughout the trial. No residues of spiroxamine were found above the LOQ (5  $\mu$ g/kg) in 10-20 or 20-30 cm horizons on either site  $\chi$ 

M01 (spiroxamine deseth) was formed initially rapidly as spiroxamine desipated, and then declined throughout the study. Peak levels of 27.9 µg/kg were found at 7.0 AT at Laudun and 15.7 µg/kg at the same time point at Nogarol Rocca, before declining below 500 at 180 and 91 DAT, respectively. Residues of M01 (spiroxamine-desethyl) were detected in the 0-10 cm soil horizon throughout the trial. No residues of spiroxamine were found above the LOQ (5 µg/kg) in 10-20 or 20-30 cm horizons on either site.

M02 (spiroxamine despropyl) was formed initially rapidly as spiroxamine dissipated, and then declined throughout the study. Peak levels of 20.0 µg/kg were found at 7 DAT at Laudun and 15.8 µg/kg at the same time point at Nogarole Rocca, before declining below LOQ at 180 and 91 DAT, respectively. Residues of M02 (spiroxamine despropyl) were detected in the 0-10 cm soil horizon throughout the trial. No residues of spiroxamine were found above the LOQ (5 µg/kg) in 10-20 or 20-30 cm horizons on eithe site.

The  $DT_{50}$  and  $DT_{9}$  of spiroxamine determined in the study was reported for each site. However, a reevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT50 values from laboratory and field dissipation studies (EFSA 2014), was performed in the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

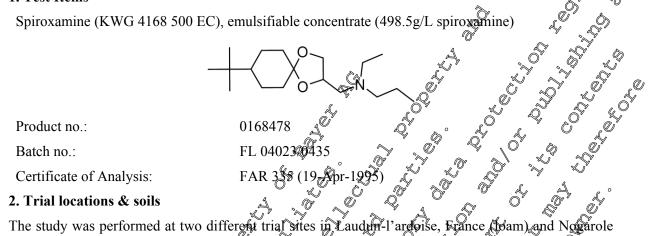


#### I. **Materials and Methods**

#### A. Materials

#### 1. Test Items

Spiroxamine (KWG 4168 500 EC), emulsifiable concentrate (498.5g/L spiroxamine)



The study was performed at two different trial sites in Laudre-l'ardoise, France (beam) and Novarole Rocca, Filetto, Italy (sandy loam). Site soil is characterized in Table CA 7.1.22.1-54. The field soil dissipation trial consisted of one treated and one untreated plot on each site. Plot measurements in the report given as 300 m² and 768m² on Laudun and Nogarole Rooca, respectively (it was not specified if this referred to the entire area used for the triabor the treated area only). No pesticide history was given for previous years before the that for either site.

Trial designation	<u>م</u> کې 50136/0
Soil Designation	Nogarole Rocca
Vegetation S S & S Bare Soil & S	Bare soil
	Nogarole Rocca, Filetto
Geographic Location	/ Italy
Textural Classification (USDA) $\downarrow$ $\uparrow$ Loam $\downarrow$	Sandy loam
Textural Classification (USDA)     Sand [590, 2000 μm] (%)     Sand [590, 2000 μm] (%)     Sand [590, 2000 μm] (%)	74.3
Textural Classification (USDA) $\sim$ Loam $\sim$ Sand [56 2000 $\mu$ m] (%) $\sim$	19.9
$ \operatorname{Clay}  < 2 \mu\mathrm{m} (\%) \gg \sqrt{2} \mu\mathrm{m} (\%) \approx 19 \mu\mathrm{m}$	5.8
$\frac{\text{Clay} [< 2  \mu\text{m}] (\%)}{\text{pH in CaCl}_2} \xrightarrow{\text{Q}} \xrightarrow{\text{Q}$	7.7
Organic Matter (%)	0.65
Organic cathon (%)	0.38
Cation Exchange Capacity Q 45.0 (meq/100 g)	10.0
(meg/100  g)	
Soil Moisture capacity (g/100g soil) 40.5	38.4

# Table CA 7.1.2.2.1-54: Location, site description and climatic data of test sites

# B. Study Design

# 1. Experimental Condition

A single application of a nominal 400 g spiroxamine/ha as an emulsifiable concentrate (EC) formulation was performed to bard soil of 5th October 1995 at Laudun and 7th March 1995 at Nogarole Rocca. Application confirmation was performed by calculation using the DAT 0 samples.

During the trials, soil cultivation and maintenance was performed according to the usual local agricultural practice. At Laudun, 3 applications of glyphosate were used to keep the site free of weeds. No plant protection products were used during the trial at Nogarole Rocca. No irrigation was carried out on either site.



Monthly average temperatures, rainfall and sunlight are given for time periods close to sampling points at each site from weather stations an unknown distance from the trial sites. In addition, temperature, rainfall and sunlight data were taken on sampling dates. Total rainfall for Laudun is 659 mm for  $21^{\text{st}}$  April –  $31^{\text{st}}$  December 1995 and 2984 mm for  $1^{\text{st}}$  January –  $31^{\text{st}}$  May 1996. It is noted in the report that the rainfall in January, February and March 1996 was extraordinarily heavy in the south of France. Total rainfall for Nogarole Rocca from 7th March –  $28^{\text{th}}$  December 1995 is 185.4 mm and 338.8 mm between  $29^{\text{th}}$  December 1995 –  $27^{\text{th}}$  June 1996. Temperatures for both sites and rainfall for Nogarole Rocca represent broadly typical conditions.

Soil dissipation of spiroxamine was studied for 360 days

### 2. Sampling

At 0, 7, 14, 30, 62, 91, 120, 180, 308 and 358 days after treatment (DAT) at Laudun and 0, 7, 14, 30, 60, 91, 120, 178, 268 and 360 days at Nogarole Rocca, 20 cores were taken at locations around the plot (statistically distributed to ensure representative samples), down to a depth of 30 cm (diameter of 50 mm) using a 'Wacker Hammer'. At 0 DAT a replicate was also aken with an RA Piercer' Hown to 10 cm). Soil cores were split into 10 cm sections, from genised and frozen (48°C) before storage and analysis. The control plots were sampled at the beginning and end of the study.

### **3. Analytical Procedures**

Soil samples were extracted at using a Soxtec extractor with boiling methanol/water/ammonia (25%), 80/20/10 (v/v/v). Extracts were re-dissolved in methanol and quantified using HPb C/MS/MS. Specific details of the method are given in MCA Section 4 (Method no. 09374 (RA-60794),  $M^{2019207-02-1}$ ). The limit of quantification (EOQ) is given as 5 µg/kg and limit of detection (COD) of 2 µg/kg for spiroxamine and metabolites.

Method validation was performed separately with a mixture of standard soils (soil 2.1/soil 2.2/soil 2.3, 1/1/1, v/v/v), fortified with spiroxamine, M01 (spiroxamine-deschyl) or M02 (spiroxamine-despropyl). The mean recoveries were 84.3% (relative standard eviation, RSD, 11.8%) for spiroxamine, 89.4% (RSD 5.7%) for M01 (spiroxamine-deschyl) and 91.4% (RSD 6.3%) for M02 (spiroxamine-despropyl).

In addition, concurrent recoveries were ran with soil from control plots from each site fortified with spiroxamine. M01 (spiroxamine-desethyl) or M02 (spiroxamine-despropyl). Mean spiroxamine recoveries were \$7.3 and \$1.3% (RSD 23.5 and 11.3%) for Laudan and Sogarole Rocca, respectively. Mean M01 (spiroxamine-desethyl) becoveries were 86. Dand \$8.7% (RSD 18.4 and 3.9%) for Laudan and Nogarole Rocca, respectively. Mean M02 (spiroxamine-despropyl) recoveries were 90.2 and 96.1% (RSD 14.5 and 5.6%) for Laudan and Nogarole Rocca, respectively.

# 4. Determination of degradation kinetics

The  $DT_{50}$  and  $DT_{90}$  of spreasanine determined in the study was reported for each site. However, a reevaluation of the degradation knetics in accordance with FOCUS guidance document on degradation kinetics (2014²) and the EFSA guidance on deriving DegT50 values from laboratory and field dissipation studies (EFSA 2014⁶) was performed in the report presented under point KCA 7.1.2.2.1/12 (M-763140-01-1).

# Results and Discussion

# A. Analytical Methodology

Full details and acceptable vabilition data to support this method are presented in Document M-CA 4, Section A.1.2 Method, no. 20374 (RA-607/94), <u>M-019207-02-1</u>). The method complies with the EU regulatory requirements on lined within SANCO/3029/99 rev. 4 and is suitable for the determination of sphexamine and its metabolites in soil samples by HPLC/MS/MS.

# B. Data

The results for spiroxamine and its metabolites are presented below as soil residue concentrations (on a  $\mu g/kg$  dry weight basis) for each of the treated plots in Table CA 7.1.2.2.1-55 to Table CA 7.1.2.2.1-60



Table CA 7.1.2.2.1-55: Residues of spiroxamine in 0-30 cm horizons of soil at Laudun	expressed
as µg/kg	a,°

			• •	8								Q	. 8
Depth	Donligato						DA	Т				<u> </u>	S
[cm]	Replicate	0	А	7	14	30	62	91	120	<b>A80</b>	308	358	U
	А	295	206	53.3	46.0	49.9	35.9	19.5	19.8	10.2	<loq< td=""><td><lqq< td=""><td></td></lqq<></td></loq<>	<lqq< td=""><td></td></lqq<>	
	В	207	233	71.0	67.9	53.0	22.0	19.3	23,9	9.30	<rbody><k@q< p=""></k@q<></rbody>	<b>≥©</b> ŁOQ	Ô
0-10	С	296	233	56.7	-	-	Ĉa,	-	Į,	-	°∼ - °∧		j° _
	D	287	217	73.3	-	-	- Tr	-	<i>©</i> ′-	- (		<u> </u>	Ő
	Mean	271	222	63.6	57.0	51.4	Ç 28.9	<b>19.4</b> Ô	^{Se} 21.9	9.76	<fqo< th=""><th></th><th><b>K</b> //</th></fqo<>		<b>K</b> //
	А	n	.d.	n.d.	n.d.	n.d 🏒	<loq< td=""><td>n.Q.</td><td>n.d. Øn.d.</td><td>6,16</td><td></td><td>n.d</td><td>,v</td></loq<>	n.Q.	n.d. Øn.d.	6,16		n.d	,v
	В	<l< td=""><td>OQ</td><td>n.d.</td><td>n.d.</td><td>1200.</td><td>n.d.</td><td>_n.d. ∘</td><td>Øn.d.</td><td>[¶]n.d.∖[®]</td><td>n.dô</td><td>n Ø.</td><td></td></l<>	OQ	n.d.	n.d.	1200.	n.d.	_n.d. ∘	Øn.d.	[¶] n.d.∖ [®]	n.dô	n Ø.	
10-20	С		-	-	-	& - <i>Q</i>	° - 《	- %	× 7	n	Ž,	£)-	
	D		-	-	-	° - L	² 0	Ð	- A	Ø.d.	L - L	- 0	
	Mean	<l< th=""><th>OQ</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th><loq< th=""><th>n.d.</th><th>n.d. 🏾</th><th>Ç≺LOQ[®]</th><th>n.d</th><th><b>n@.</b></th><th></th></loq<></th></l<>	OQ	n.d.	n.d.	n.d.	<loq< th=""><th>n.d.</th><th>n.d. 🏾</th><th>Ç≺LOQ[®]</th><th>n.d</th><th><b>n@.</b></th><th></th></loq<>	n.d.	n.d. 🏾	Ç≺LOQ [®]	n.d	<b>n@.</b>	
	А	n	.d.	n.d.	< <b>E</b> ØQ	N d	n.d.		n.ð.y	nd	sa.d.	J.d.	
	В	n.	.d.	n.d.	Qn.d.	× n.d × n.d ×	nd	n.d.	n.đ.y	d.d.	n.d.	n.d.	
20-30	С		-	- ~~ ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<loq<sup>2</loq<sup>		Ŵ.	×- (	8°- 2			-	
	D		-	_	fêd.	<u></u>	) - Ó	- ^C	_ _₹	. 0	, 'Y	-	
	Mean	n	.d. 🔹	Çn.d. '	≽̃LOQ	n.d.®	n.d.	n d.	n.d.	W.d.	[≫] n.d.	n.d.	

A two samples for 0 DAT only (one using 'Warter Hammaer' and one using 'RA Piercer' poshing sampling system) DAT: days after treatment, LOQOIImit objuantitation) = Lug/kg, LOD (limit of detection) = 2 µg/kg, n.d. = not detected above LOD

above LOD Table CA 7.1.2.2.1-56: Residues of M01(spiroxamine desethyl) in 0-30 cm horizons of soil at Laudun expressed as ug/kg

-	Ô										
Depth [cm]	Replicate		7	¥4	30	DA G62	0 91 <u>(</u>	ي 120	180	308	358
	^~A	5.80K <loq< td=""><td>33.5</td><td></td><td>D° 16.2</td><td>12.<b>D</b></td><td>6,30</td><td>8.45</td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loq<>	33.5		D° 16.2	12. <b>D</b>	6,30	8.45	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
	B	<loqq <loqq<="" td=""><td>31.9</td><td>20.9</td><td>165</td><td>12.22 \$09</td><td><b>©</b>42</td><td>7.61</td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></loqq>	31.9	20.9	165	12.22 \$09	<b>©</b> 42	7.61	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
0-10	C .		\$27.7	Õ-	£ <del>7</del> -	Ky - 1ª	Ś -	-	-	-	-
	D	5.77 <u>4</u> <lqq< td=""><td>18.4</td><td>- ~</td><td>Ø - (</td><td>- `</td><td>-</td><td>-</td><td>-</td><td>-</td><td>-</td></lqq<>	18.4	- ~	Ø - (	- `	-	-	-	-	-
	Mean	5,8% < <b>≤</b> 60Q	27.9	19,0	138	16.7	6.40	8.03	<loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""></loq<></th></loq<>	<loq< th=""></loq<>
	Ŕ		11.u.	n.d.		⊳n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	B C		n.d	n.d	r 11.04	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10-20	C 🖏	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u> </u>			-	-	-	n.d.	-	-
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	D		b ⁷ -	<u></u>	~~~- ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	-	-	-	n.d.	-	-
	Mean	W.d. O	n.d.	[⊗] n.d.C	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	A	🗛 💊 n.d. 🖉	^ાદ્રિત.	n.Q.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	A	y n Q	n.d.	©n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	Č Č		-	n.d.	-	-	-	-	-	-	-
a K	G C G D D D D D D D D D D D D D D D D D	1-~	-	n.d.	-	-	-	-	-	-	-
	Mean	Sn.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

A & two samples for 0 DAT only (one using 'Wacker Hammer' and one using 'RA Piercer' pushing sampling system) DAT: day after treatment, LOQ (limit of quantitation) = 5 µg/kg, LOD (limit of detection) = 2 µg/kg, n.d. = not detected above LOD



	Laudun expressed as µg/kg													
Depth	Darkasta						DA	Т						
[cm]	Replicate	0	Α	7	14	30	62	91	120	A80	308 🥡	358	0	
	А	5.90	<loq< td=""><td>34.4</td><td>18.7</td><td>16.0</td><td>12.1</td><td>7.13</td><td>8.38 (</td><td>LOQ</td><td><loq⁄< td=""><td><LQQ</td><td></td></loq⁄<></td></loq<>	34.4	18.7	16.0	12.1	7.13	8.38 (LOQ	<loq⁄< td=""><td><LQQ</td><td></td></loq⁄<>	< LQ Q		
	В	<loq< td=""><td><loq< td=""><td>32.9</td><td>21.1</td><td>14.1</td><td>10.1</td><td>7.58</td><td>7.83</td><td><loq< td=""><td><LOQ</td><td>∧GŁOQ</td><td>Ô</td></loq<></td></loq<></td></loq<>	<loq< td=""><td>32.9</td><td>21.1</td><td>14.1</td><td>10.1</td><td>7.58</td><td>7.83</td><td><loq< td=""><td><LOQ</td><td>∧GŁOQ</td><td>Ô</td></loq<></td></loq<>	32.9	21.1	14.1	10.1	7.58	7.83	<loq< td=""><td><LOQ</td><td>∧GŁOQ</td><td>Ô</td></loq<>	< L OQ	∧ GŁOQ	Ô	
0-10	С	5.93	<loq< td=""><td>28.0</td><td>-</td><td>-</td><td><u></u></td><td>-</td><td>Ź</td><td>-</td><td>ĵ∼y °≈</td><td>- 2</td><td>ľ .</td></loq<>	28.0	-	-	<u></u>	-	Ź	-	ĵ∼y °≈	- 2	ľ .	
	D	<loq< td=""><td><loq< td=""><td>20.5</td><td>-</td><td>-</td><td>₹</td><td></td><td><i>©</i>′-</td><td>- (</td><td></td><td></td><td>\sim</td></loq<></td></loq<>	<loq< td=""><td>20.5</td><td>-</td><td>-</td><td>₹</td><td></td><td><i>©</i>′-</td><td>- (</td><td></td><td></td><td>\sim</td></loq<>	20.5	-	-	₹		<i>©</i> ′-	- (\sim	
	Mean	<loq< th=""><th><loq< th=""><th>29.0</th><th>19.9</th><th>15.1</th><th>Ç₇ 11.1</th><th>7.36Ĉ</th><th>[≫]8.11</th><th><løq< th=""><th><fqo< th=""><th></th><th>***</th></fqo<></th></løq<></th></loq<></th></loq<>	<loq< th=""><th>29.0</th><th>19.9</th><th>15.1</th><th>Ç₇ 11.1</th><th>7.36Ĉ</th><th>[≫]8.11</th><th><løq< th=""><th><fqo< th=""><th></th><th>***</th></fqo<></th></løq<></th></loq<>	29.0	19.9	15.1	Ç ₇ 11.1	7.36Ĉ	[≫] 8.11	<løq< th=""><th><fqo< th=""><th></th><th>***</th></fqo<></th></løq<>	<fqo< th=""><th></th><th>***</th></fqo<>		***	
	Α	n.	d.	n.d.	n.d.	n.d	n.d.	n Q	n.d. Øn.d.	h.d.		n.d		
	В	n.	d.	n.d.	n.d.	Ø.d.	n.d.	∕≫n.d. "	Øn.d.	[™] n.d.√	Ď́n.dÔ	n Ø.		
10-20	С	-	-	-	- 🗶	- (° - "	÷ - ×	~	n Q`	×,	£.		
	D		-	-	_0`	Ł	Ê Û	1 AV	1 A	Ø.d.	L - A	- 0		
	Mean	n.	d.	n.d.	∦n d.	"n.d.	~n.d. ∕	n .d.		🖓 n.d. 🥈	n.d	nØ.		
	А	n.	d.	n.d.	∲ n.d»	n.d.	n.d.		n.đ.y	nd	sa.d.	an.d.		
	В	n.	d.	n.Q	n, di	n	nd	n.el.	nd.	d.d.	n.d.	n.d.		
20-30	С	-	-	\$-	Ø.d.	۳ مربع	_≪ <u>́</u>		8 - é	ð - Z	r "V	-		
	D			۶- ۷	🗘 n.d. 🖉	- (þ - ć) - L			, 'Y	-		
	Mean	n.	.d. 🕎	n.d	n.d.	n.@	n.d.	n de	n.d.	Ŵ.d.	n.d.	n.d.		

Table CA 7.1.2.2.1-57: Residues of M02 (spiroxamine-despropyl) in 0-30 cm horizons of soil at Laudun expressed as ug/kg

A two samples for 0 DAT only (one using 'Watter Hammer' and one using 'RA Piercer' fushing sampling system) DAT: days after treatment, LOOOlimit of quantitation) = $\frac{1}{4}$ ug/kg, LOD (limit of detection) = $\frac{1}{4}$ ug/kg, n.d. = not detected above LOD

Table CA 7.1.2.2.1-58: Residues of spir@amine in 0-39 cm horizons of soft at Nogarole Rocca ex-, î Î S pressed as µg/kg L Ø

-	~~~		L	~	<u> </u>	¥		~~~			
Depth	Repricate	$\hat{\mathcal{O}}$		14		🔊 ĎA	TS	\checkmark'			
[cm]		\$ ⁷ 0 ⁴ ~	7	14			Õ 91 🖉	》120	178	268	360
	°∼ A			52.5	©31.6	9.80	<l.cq< td=""><td>n.d.</td><td><loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<></td></l.cq<>	n.d.	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
, and the second s	B			34.1	300	9094	. ≪DÓQ	n.d.	<loq< td=""><td><loq< td=""><td><loq< td=""></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""></loq<></td></loq<>	<loq< td=""></loq<>
0-10	C 🛒	211 182		, O ^V		ky - é	Š -	-	-	-	-
	D 🔊	1741167	&4 .7 ĸ)- _v		-0	-	-	-	-	-
	Mean	184 171		43.3 [°]	31.0	9 6 42	<loq< th=""><th>n.d.</th><th><loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<></th></loq<>	n.d.	<loq< th=""><th><loq< th=""><th><loq< th=""></loq<></th></loq<></th></loq<>	<loq< th=""><th><loq< th=""></loq<></th></loq<>	<loq< th=""></loq<>
	Ŕ	C _{<lq< sub=""></lq<>}	md	n d.		⊳n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
10-20	B B	<loq< td=""><td>39.d.</td><td>n.d. 🦻</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td><td>n.d.</td></loq<>	39.d.	n.d. 🦻	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
la l	A B Mean	ُخ LOQ ا	n.d.	n.d 🖉	n.d.	n.d.	n.d.	n.d.	n.d.	<loq< th=""><th>n.d.</th></loq<>	n.d.
20-30	A 🐇	n.d	ņ.@	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	В	n.đ.	(D.d.	n.d.	© [™] n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	_{. ຊ} n.d. ຼູ 🦉	n.d.	n.d.Q	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

A two samples for ODAT on (one using 'Wasker Hammer' and one using 'RA Piercer' pushing sampling system) A two samples for 0.5 AT only (one using 'Wacker Hammer' and one using 'KA Piercer' pushing sampling system) DAT: days after treatment, LOO (limit of quantitation) = 5 μ g/kg, LOD (limit of detection) = 2 μ g/kg, n.d. = not detected above LOD



				- r							<u>_</u>	ð
Donligato						DA	Т					
Replicate	0	A	7	14	30	60	91	120	₫78	268	360	J
А	<loq< td=""><td><loq< td=""><td>11.7</td><td>14.7</td><td>14.7</td><td>6.39</td><td>n.d.</td><td>n.d. (</td><td>n.d.</td><td>n.d. 🗇</td><td>n.Q.</td><td></td></loq<></td></loq<>	<loq< td=""><td>11.7</td><td>14.7</td><td>14.7</td><td>6.39</td><td>n.d.</td><td>n.d. (</td><td>n.d.</td><td>n.d. 🗇</td><td>n.Q.</td><td></td></loq<>	11.7	14.7	14.7	6.39	n.d.	n.d. (n.d.	n.d. 🗇	n.Q.	
В	<loq< td=""><td><loq< td=""><td>17.8</td><td>15.0</td><td>11.4</td><td>5.90</td><td><loq< td=""><td>n.d.</td><td>n.d.</td><td>प्रस.</td><td>_Q¥.d.</td><td>ò</td></loq<></td></loq<></td></loq<>	<loq< td=""><td>17.8</td><td>15.0</td><td>11.4</td><td>5.90</td><td><loq< td=""><td>n.d.</td><td>n.d.</td><td>प्रस.</td><td>_Q¥.d.</td><td>ò</td></loq<></td></loq<>	17.8	15.0	11.4	5.90	<loq< td=""><td>n.d.</td><td>n.d.</td><td>प्रस.</td><td>_Q¥.d.</td><td>ò</td></loq<>	n.d.	n.d.	प्रस.	_Q¥.d.	ò
С	<loq< td=""><td><loq< td=""><td>14.1</td><td>-</td><td>-</td><td>Č.s.</td><td>-</td><td>Ż</td><td>-</td><td>^~ - [^]</td><td>¥ - &</td><td></td></loq<></td></loq<>	<loq< td=""><td>14.1</td><td>-</td><td>-</td><td>Č.s.</td><td>-</td><td>Ż</td><td>-</td><td>^~ - [^]</td><td>¥ - &</td><td></td></loq<>	14.1	-	-	Č.s.	-	Ż	-	^~ - [^]	¥ - &	
D	<loq< td=""><td><loq< td=""><td>19.0</td><td>-</td><td>-</td><td>¢,</td><td>- 4</td><td><i>©</i>′-</td><td>- (</td><td></td><td></td><td>é</td></loq<></td></loq<>	<loq< td=""><td>19.0</td><td>-</td><td>-</td><td>¢,</td><td>- 4</td><td><i>©</i>′-</td><td>- (</td><td></td><td></td><td>é</td></loq<>	19.0	-	-	¢,	- 4	<i>©</i> ′-	- (é
Mean	LOQ	LOQ	15.7	14.8			<loq< th=""><th>🖗 n.d.</th><th>n.d.</th><th>pd.</th><th></th><th></th></loq<>	🖗 n.d.	n.d.	pd.		
А	<l< td=""><td>OQ</td><td>n.d.</td><td>n.d.</td><td></td><td>n.d.</td><td>n.Q</td><td>n.d.</td><td>h.d.</td><td>6.33 (</td><td>n.d</td><td>4</td></l<>	OQ	n.d.	n.d.		n.d.	n.Q	n.d.	h.d.	6.33 (n.d	4
В	<l< td=""><td>OQ</td><td>n.d.</td><td>n.d.</td><td></td><td>n.d.</td><td></td><td>Øn.d.</td><td>n.d.</td><td>Ď″n.dÔ</td><td>n Ø.</td><td></td></l<>	OQ	n.d.	n.d.		n.d.		Øn.d.	n.d.	Ď″n.dÔ	n Ø.	
Mean	<l< td=""><td>OQ</td><td>n.d.</td><td>n.dk</td><td></td><td>﴾ n.d.</td><td>n.d,×</td><td>n.d.</td><td>n d</td><td><body> k Q d ></body></td><td>≪n.d.</td><td></td></l<>	OQ	n.d.	n.dk		﴾ n.d.	n.d,×	n.d.	n d	<body> k Q d ></body>	≪n.d.	
Α	n.	.d.	n.d.	n.Ø.	n _s d	n.đ	nzd.	B.C.	Ø.d.	Lan.d.		
В	n.	.d.	n.d. 👷		n.d.	~n.d. ,	n.d.	n.d. 🏾	🖓 n.d. 🥈	n.d	nØ.	
Mean	n	.d.	n.d	n.d.	n.d.	n.d.)" n.d 🖇		n d.	sa,d.	Jn.d.	
	B C D Mean A B Mean A B	ReplicateAACBCCCDCDCDCDCDCDCC </td <td>BReplicate0^AA$< LOQ$$< LOQB< LOQ$$< LOQC< LOQ$$< LOQD< LOQ$$< LOQ$Mean$LOQ$$LOQB< LOQ$Mean$< LOQ$Mean$< LOQA< LOQA< LOQA< LOQAn.d.Bn.d.$</td> <td>Replicate$0^A$$7$A<math><loq< math=""><math><loq< math="">11.7B<math><loq< math=""><math><loq< math="">17.8C<math><loq< math=""><math><loq< math="">14.1D<math><loq< math=""><math><loq< math="">19.0Mean$LOQ$$LOQ$$15.7$A<math><loq< math="">n.d.B<math><loq< math="">n.d.Mean<math><loq< math="">n.d.A<math><loq< math="">n.d.B<math><loq< math="">n.d.</loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></td> <td>Provide the second sec</td> <td>Replicate 0^A 7 14 30 A <loq< td=""> <loq< td=""> 11.7 14.7 14.7 B <loq< td=""> <loq< td=""> 17.8 15.0 11.4 C <loq< td=""> <loq< td=""> 14.1 - - D <loq< td=""> <loq< td=""> 19.0 - - Mean LOQ LOQ 15.7 14.8 13.1 A <loq< td=""> n.d. n.d. n.d. B <loq< td=""> n.d. n.d. n.d. A <loq< td=""> n.d. n.d. n.d. A <loq< td=""> n.d. n.d. n.d. B <loq< td=""> n.d. n.d. n.d. A n.d. n.d. n.d. n.d.</loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></td> <td>Replicate 0^{A} 7 14 30 60 A $<$LOQ $<$LOQ 11.7 14.7 14.7 6.39 B $<$LOQ $<$LOQ 17.8 15.0 11.4 5.90 C $<$LOQ $<$LOQ 14.1 - - D $<$LOQ $<$LOQ 19.0 - - \checkmark^2 Mean LOQ LOQ 15.7 14.8 13.1 6.15 A $<$LOQ n.d. n.d. n.d. n.d. n.d. B $<$LOQ n.d. n.d. n.d. n.d. n.d. B $<$LOQ n.d. n.d. n.d. n.d. n.d. B n.d. n.d. n.d. n.d. n.d. n.d. n.d.</td> <td>DAT DAT 0^A 7 14 30 60 91 A <math><loq< math=""> <math><loq< math=""> 11.7 14.7 14.7 6.39 n.d. B <math><loq< math=""> <math><loq< math=""> 11.7 14.7 6.39 n.d. B <math><loq< math=""> <math><loq< math=""> 17.8 15.0 11.4 5.90 <math><loq< math=""> C <math><loq< math=""> <math><loq< math=""> 14.1 - - - D <math><loq< math=""> <math><loq< math=""> 19.0 - - - Mean LOQ <math><loq< math=""> 19.0 - - - Mean LOQ 100 15.7 14.8 13.1 6.15 <math><loq< math=""> A <math><loq< math=""> $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$ B <math><loq< math=""> $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$ B $n.d.$ n</loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></loq<></math></td> <td>DAT DAT 0^A 7 14 30 60 91 120 A $<$LOQ $<$LOQ 11.7 14.7 6.39 n.d. n.d. B $<$LOQ $<$LOQ 17.8 15.0 11.4 5.90 $<$LOQ n.d. C $<$LOQ $<$LOQ 14.1 - - - - D $<$LOQ $<$LOQ 19.0 - - - - Mean LOQ $<$LOQ 15.7 14.8 13.1 $<$6.15 $<$LOQ n.d. A $<$LOQ n.d. n.d. n.d. n.d. n.d. Mean LOQ n.d. n.d. n.d. n.d. n.d. n.d. B $<$LOQ n.d. n.d. n.d. n.d. n.d. n.d. n.d. A $<$LOQ n.d. n.d. n.d. n.d. n.d. n.d.</td> <td>DAT DAT 0^{A} 7 14 30 60 91 120 578 A < LOQ 11.7 14.7 14.7 6.39 n.d. n.d. n.d. B LOQ 17.8 15.0 11.4 5.90 LOQ n.d. n.d. B LOQ I.0Q 17.8 15.0 11.4 5.90 LOQ n.d. n.d. C LOQ I.0Q 17.8 15.0 11.4 5.90 LOQ n.d. n.d. D LOQ I.0Q 19.0 -<td>DAT DAT 0^{A} 7 14 30 60 91 120 78 268 A <loq< td=""> <loq< td=""> 11.7 14.7 14.7 6.39 n.d. <t< td=""><td>DAT DAT 0^A 7 14 30 60 91 120 78 268 360 A $< LOQ < LOQ$ 11.7 14.7 14.7 6.39 n.d. n.d.</td></t<></loq<></loq<></td></td>	B Replicate 0^A A $< LOQ$ $< LOQ$ B $< LOQ$ $< LOQ$ C $< LOQ$ $< LOQ$ D $< LOQ$ $< LOQ$ Mean LOQ LOQ B $< LOQ$ Mean $< LOQ$ Mean $< LOQ$ A $< LOQ$ A $< LOQ$ A $< LOQ$ A $n.d.$ B $n.d.$	Replicate 0^A 7 A $11.7B17.8C14.1D19.0MeanLOQLOQ15.7An.d.Bn.d.Meann.d.An.d.Bn.d.$	Provide the second sec	Replicate 0 ^A 7 14 30 A <loq< td=""> <loq< td=""> 11.7 14.7 14.7 B <loq< td=""> <loq< td=""> 17.8 15.0 11.4 C <loq< td=""> <loq< td=""> 14.1 - - D <loq< td=""> <loq< td=""> 19.0 - - Mean LOQ LOQ 15.7 14.8 13.1 A <loq< td=""> n.d. n.d. n.d. B <loq< td=""> n.d. n.d. n.d. A <loq< td=""> n.d. n.d. n.d. A <loq< td=""> n.d. n.d. n.d. B <loq< td=""> n.d. n.d. n.d. A n.d. n.d. n.d. n.d.</loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<></loq<>	Replicate 0^{A} 7 14 30 60 A $<$ LOQ $<$ LOQ 11.7 14.7 14.7 6.39 B $<$ LOQ $<$ LOQ 17.8 15.0 11.4 5.90 C $<$ LOQ $<$ LOQ 14.1 - - D $<$ LOQ $<$ LOQ 19.0 - - \checkmark^2 Mean LOQ LOQ 15.7 14.8 13.1 6.15 A $<$ LOQ n.d. n.d. n.d. n.d. n.d. B $<$ LOQ n.d. n.d. n.d. n.d. n.d. B $<$ LOQ n.d. n.d. n.d. n.d. n.d. B n.d. n.d. n.d. n.d. n.d. n.d. n.d.	DAT DAT 0^A 7 14 30 60 91 A $ 11.7 14.7 14.7 6.39 n.d. B 11.7 14.7 6.39 n.d. B 17.8 15.0 11.4 5.90 C 14.1 - - - D 19.0 - - - Mean LOQ 19.0 - - - Mean LOQ 100 15.7 14.8 13.1 6.15 A n.d. n.d. n.d. n.d. n.d. n.d. B n.d. n.d. n.d. n.d. n.d. n.d. n.d. B n.d. n$	DAT DAT 0^A 7 14 30 60 91 120 A $<$ LOQ $<$ LOQ 11.7 14.7 6.39 n.d. n.d. B $<$ LOQ $<$ LOQ 17.8 15.0 11.4 5.90 $<$ LOQ n.d. C $<$ LOQ $<$ LOQ 14.1 - - - - D $<$ LOQ $<$ LOQ 19.0 - - - - Mean LOQ $<$ LOQ 15.7 14.8 13.1 $<$ 6.15 $<$ LOQ n.d. A $<$ LOQ n.d. n.d. n.d. n.d. n.d. Mean LOQ n.d. n.d. n.d. n.d. n.d. n.d. B $<$ LOQ n.d. n.d. n.d. n.d. n.d. n.d. n.d. A $<$ LOQ n.d. n.d. n.d. n.d. n.d. n.d.	DAT DAT 0^{A} 7 14 30 60 91 120 578 A < LOQ 11.7 14.7 14.7 6.39 n.d. n.d. n.d. B LOQ 17.8 15.0 11.4 5.90 LOQ n.d. n.d. B LOQ I.0Q 17.8 15.0 11.4 5.90 LOQ n.d. n.d. C LOQ I.0Q 17.8 15.0 11.4 5.90 LOQ n.d. n.d. D LOQ I.0Q 19.0 - <td>DAT DAT 0^{A} 7 14 30 60 91 120 78 268 A <loq< td=""> <loq< td=""> 11.7 14.7 14.7 6.39 n.d. <t< td=""><td>DAT DAT 0^A 7 14 30 60 91 120 78 268 360 A $< LOQ < LOQ$ 11.7 14.7 14.7 6.39 n.d. n.d.</td></t<></loq<></loq<></td>	DAT DAT 0^{A} 7 14 30 60 91 120 78 268 A <loq< td=""> <loq< td=""> 11.7 14.7 14.7 6.39 n.d. <t< td=""><td>DAT DAT 0^A 7 14 30 60 91 120 78 268 360 A $< LOQ < LOQ$ 11.7 14.7 14.7 6.39 n.d. n.d.</td></t<></loq<></loq<>	DAT DAT 0^A 7 14 30 60 91 120 78 268 360 A $< LOQ < LOQ$ 11.7 14.7 14.7 6.39 n.d. n.d.

Table CA 7.1.2.2.1-59: Residues of M01 (spiroxamine-desethyl) in 0-30 cm horizons of soil at Nogarole Rocca expressed as µg/kg

A two samples for 0 DAT only (one using Wacker Mammer and one using RA Piercer' pushing sampling system) DAT: days after treatment, LOQ (limit of quantitation) = 5 µg/kg, LQD (limit of detection) = 2 µg/kg, red. = not detected above LOD

Table CA 7.1.2.2.1-60: Residues of M02	(spiroxamine	-despropy)	in 0-30	cm horizons of soil at
Nogarole Rocca ex	pressed as µg	∮kg ́ ∿́		\$ 6

Depth	Replicate		9		ат [©]	, S	- C		
[cm]	Replicate		<u>9</u> 7 P4	30 60	M	<u>%</u> 120	× 178	268	360
	A	&LOQ <loq< th=""><th>12.0 14.6</th><th>3.4 55.39</th><th>LOQ</th><th>⊃″_{n.d.}</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></loq<>	12.0 14.6	3.4 55.39	LOQ	⊃″ _{n.d.}	n.d.	n.d.	n.d.
	В	<l@@ <l@@<="" th=""><th>18.4 14.6</th><th>A (T) A</th><th></th><th>n</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></l@@>	18.4 14.6	A (T) A		n	n.d.	n.d.	n.d.
0-10		COQ <loq< th=""><th>43.8</th><th></th><th><u>A</u></th><th>Z<u>-</u></th><th>-</th><th>-</th><th>-</th></loq<>	43.8		<u>A</u>	Z <u>-</u>	-	-	-
	Ø,	LOQ CLOQ	18.9 - 🔬	Q - Q -	0 - 0	U -	-	-	-
	Mean	LQQ LQQ	15,8 14.0		/ <l000< th=""><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></l000<>	n.d.	n.d.	n.d.	n.d.
L.	A		M.d. n.d.	nga. nga.	_گ ، @ď.	n.d.	n.d.	6.35	n.d.
10-20	В	S <kôd th="" x<=""><th>n.d.</th><th>n.d. Kn.d.</th><th>🛆 n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th><th>n.d.</th></kôd>	n.d.	n.d. Kn.d.	🛆 n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	KLOO O	n.d. n.d.	n.d. n.do	n.d.	n.d.	n.d.	<loq< th=""><th>n.d.</th></loq<>	n.d.
	Ą	n.d.≫	Jr.d. n.d.	pre. pre.	n.d.	n.d.	n.d.	n.d.	n.d.
20-30	уD		n.d n.d.	h.d. n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean	n.d. 3	n.d. n.d.	n.d. n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

A two samples for 0 DAF only (see using 'Wacks' Hamper' and one using 'RA Piercer' pushing sampling system) DAT: days after treatment LOO (limit of grantitation) = 5 ug/kg, LOD (limit of detection) = 2 μ g/kg, n.d. = not detected above LOD

C. Residues

Analysis of control samples from the Nogarole Rocca site, showed no residues above the limit of quantification (LOQ) $0.5 \ \mu g/kg$. However, control samples from the Laudun site, showed a single analytical replicate value $0.81 \ \mu g/kg$ of spiroxamine at 0 DAT at 0-10 cm depth. All other samples taken from the control plot at Laudun showed no detectible residues of spiroxamine or its metabolites.

The average initial concentration of spiroxamine in soil samples taken immediately after application was 247 and 178 μ g/kg in Laudun and Nogarole Rocca respectively. Within the report, an application rate of 400 g/ha, assuming a soil density of 1.5 g/cm³ and depth of 10 cm, is given as 267 μ g/kg soil. Therefore, according to the report, the measured soil concentrations at 0 DAT were 93 and 67% of nominally applied spiroxamine for Laudun and Nogarole Rocca sites, respectively.



The initial dissipation of spiroxamine was rapid for both sites, with Laudun showing a slower dissipation phase after 14 DAT, whilst Nogarole Rocca showed continued rapid dissipation. Residues of spiroxamine were detected mainly in the 0-10 cm soil horizon throughout the trial. No residues of spiroxatione were found above the LOQ (5 μ g/kg) in 10-20 or 20-30 cm horizons on either site.

M01 (spiroxamine-desethyl) was formed initially rapidly as spiroxamine dissipated, and then declined throughout the study. Peak levels of 27.9 µg/kg were found at 7 DAT at Laudun and 15.7 µg/kg at the same time point at Nogarole Rocca, before declining below LOQ at 180 and 91 DATOrespectively. Residues of M01 (spiroxamine-desethyl) were detected majnly in the 0-40 cm soil horizon throughout the trial. No residues of spiroxamine were found above the LOQ (5 µg/kg) in 10-20 or 20-30 cm horizons on either site.

M02 (spiroxamine-despropyl) was formed initially rapidly as spiroxamine dissipated, and then declined throughout the study. Peak levels of 29.0 µg/kg were found at 7DAT at Laudun and 15.8 µg/kg at the same time point at Nogarole Rocca, before declining below LOQ at 180 and 91 DAT, respectively. Residues of M02 (spiroxamine-despropyl) were detected mainly in the 0-10 cm soil horizon throughout the trial. No residues of spiroxamine were found above the WOQ (Sug/kg) in 10-20 or 20-30 conhorizons on either site.

D. Kinetic Analysis

report presented inder point KCA Degradation rates determined in the report are superseded , B , Ô 7.1.2.2.1/12 (<u>M-763140-01-1</u>).

Conclusions

Following a single application of proxamine at a rate of nominal rate of 400 g/ha to bare soil in spring/ summer, 1995, the decline of spiroxamine and the formation and decline of M01 (spiroxamine-desethyl) and M02 (spiroxamine despropyl) was followed for up to 360 days after application at 2 trial sites in Laudun, France and Mogarole Rosca, Ital A resevaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is presented in KCA 7.1.2.2.1/12 (M-763140-01-1).

M01 (spiroxamine-desethy) was detected at a peak lever of 27.9 µg/kg in the 0-10 cm horizon.

M02 (spirovamine-despropyl) was detected at a peak level @29.0 @g/kg in the 0-10 cm horizon.

were found above the LOQ (5 µg/kg) in 10-20 or 20-30 No residues of spiroxamine or its metabolates cm horizons on either site.

Assessment and conclusion by applicant

Study meets the current guidance and the requirements in 283/2013.

The study is considered valid to assess the dissipation of spiroxamine under field conditions in soil. The study meets the requirements to assess field persistence of spiroxamine and its metabolites, and to derive parent soil DegT matrix values for legar field studies as defined by EFSA (2014). It is not suitable for assessing metabolite soil Der T50mper values as the design did not minimise soil surface processes immediately after application as required by EFSA (2014).



Data Point:	KCA 7.1.2.2.1/06
Report Author:	;
Report Year:	2000
Report Title:	Dissipation of spiroxamine in soils - survey of results from studies conducted un-
	der field and laboratory conditions
Report No:	MR-251/00
Document No:	<u>M-036125-01-1</u>
Guideline(s) followed in	BBA: Part IV, 4-1
study:	
Deviations from current	None 🖓 🖉 🖉 🖉
test guideline:	
Previous evaluation:	yes, evaluated and accepted $\sqrt[n]{2}$
	RAR (2010), RAR (2017)
GLP/Officially recog-	No, not conducted under VILP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes O' O' Z' Z' Z' Z' Z'

The details of this study are fully summarised under point KCA 7.1.2.1.1/06.

	Q' Q'<
Data Point:	KCAØ.1.2.2. W07 0 2 0 0 0 4
Report Author:	
Report Year:	4996 Storage stability of KWG 4168 and the metabolites & WG 4557 (desethyl-KWG 4168) in soil MR-535/96 MR-53/
Report Title:	Storage stability of KWG 4168 and the metabolites KWG 4557 (desethyl-KWG
<u> </u>	4168) and KWG 4609 (decoropylat WG 468) in soil
Report No:	MR-535(96 @ 5 2 2 0 4
Document No:	<u>M-006092-01</u>
Guideline(s) followed in	None quoted in the state of the
study:	
Deviations from current	None , , , , , , , , , , , , , , , , , , ,
test guideline:	
Previous evaluation:	yes evaluated and accepted
	DAR (1997), RAR (2010), RAR (2017)
GLP/Officially reco	Ves, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability	$\frac{1 \operatorname{Yes}}{2} + \frac{2}{3} + \frac{2}{3}$
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
.1	
T D	
° Y	
Ó A	
29° 2° 1	
	Ap96 Storage stability of KWG 4168 and the metabolites KWG 4557 (desethyl-KWG 4168) and KWG 4669 (despropyl-KWG 4168) in soil MR-535406 A100602-017 None duoted None yes evaluated and accepted DAR (1997), RAR (2010) RAR (2017) Afes, conducted under GIP/Officially recognised testing facilities Yes Yes Yes Yes Yes Yes Yes Y
õ	



Data Point:	KCA 7.1.2.2.1/08
Report Author:	
Report Year:	1997
Report Title:	Storage stability of KWG 4168 and the metabolites desethyl-KWG 4168 (KWG 4557) and despropyl-KWG 4168 (KWG 4669) in soil
Report No:	MR-3/97
Document No:	<u>M-006079-01-1</u>
Guideline(s) followed in study:	None quoted
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q
GLP/Officially recog- nised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes v v v v v A
Data Point:	KCA7122 MA

Data Point:	KCA 7.1.2.2 109 2 0 2 0 2 0 2 2 2
Report Author:	KCA 7.1.2.2.6/09 ~ 0 ~ 7 ~ 7 ~ 7 ~ 7 ~ 7 ~ 7 ~ 7 ~ 7 ~ 7
Report Year:	
Report Title:	Storage stability of KWG 4168 and the metabolites desethyly WG 4168 (KWG
	45579 despropyl-KWG 4168 (KWG 4669) and KWG 4168 N-oxfde (WAK
	6301) in soil
Report No:	6301) in soil
Document No: ²	
Guideline(s) followed in	None $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$
study:	
Deviations from current	
test guideline: 🔊 🕔	
Previous evaluation:	yes, evaluated and accepted RAR (2016), RAR (2016)
The second se	RAR (2010), RAR (2016)
GLP/Officially recog-	Yes, conducted under OLP/Or cially recognised testing facilities
Previous evaluation: GLP/Officially recog- nised testing facilities:	
Acceptability/Reliability.	YO V V O
Exacutive Summer	

# Executive Summary

The storage stability of priox mine and metabolites M01 M02 and later also M03 in soil was investi-gated under frozen conditions over 3 studies.

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Untreated soil samples were fortified with spirs amine and metabolites M01, M02 and M03 and stored A frozen for period up to 2 years

Storage stability of residues of spiroxamine and metabolites M01, M02 and M03 in soil under frozen conditions was shown to be acceptable for storage periods of up to 2 years.



### I. Materials and Methods

Study	Details Q D
KCA 7.1.2.2.1/07 ( <u>M-006082-01-1</u> ), 535/96	CoA 920522ELB01 (4-Mar 94); parity 99.0% (isomer A 53%, isomer B 46%)
KCA 7.1.2.2.1/08 (M-006079-01-1) MR 3/97	
KCA 7.1.2.2.1/09 ( <u>M-006074-01-1</u> ), MR 38/98	
KCA 7.1.2.2.1/07 ( <u>M-006082-0021</u> ), 535/96	CoA 921103ELB02 (24-Nøv-94), pu- rife 98.0% (isomer A 56%, isomer B
KCA 7.1.2.2.1/08 (*1-006079-01-1), MR@997 ~ @	
KCA 7.1.2.2.109 (M206074-01-1)	CoA 921-03ELS02 (24 Nov 94); pu- rity 980% (isomer A 56%, isomer B
	CoA 921203ELB02 (5 Pan-98); purity 98.0% (150mer A 56%), isomer B 42%)
5 ^{35/96} 5 ^{35/96}	[*] CoA 921103ELB03 (24-Nov-94); pu- rfy 98.0% (isomer A 55%, isomer B 43%)
CA DI.2.2.009 ( <u>Ma 2006074-01-</u> 0); MR <u>3</u> 8/98	CoA 921103ELB03 (24-Nov-94); pu- rity 98.0% (isomer A 55%, isomer B 43%)
	©A 921103ELB03 (12-Dec-97); pu- rity 98.0% (isomer A 55%, isomer B 43%)
RČA TÃ.2.24/09 ( <u>N2006074-01-1</u> ), MR 28/98	CoA 950209ELB01 (2-May-95); pu- rity 93.0%
	CoA M00190 (6-Feb-97)
study was performed using a mixture of t	he BBA 2.1, 2.2 and 2.3 soils below (1:1:1
	KCA 7.1.2.2.1/07 (M-006082-01-1), 535/96 KCA 7.1.2.2.1/08 (M-006079-01-1), MR 3/97 KCA 7.1.2.2.1/09 (M-006074-01-1), MR 38/98 KCA 7.1.2.2.1/07 (M-006082-04-1), 535/96 KCA 7.1.2.2.1/09 (M-006079-01-1), MR 38/98 KCA 7.1.2.2.1/09 (M-006074-01-1), MR 38/98 KCA 7.1.2.2.1/07 (M-06082-01-1), MR 38/98 KCA 7.1.2.2.1/07 (M-06079-01-1), MR 3/97 KCA 7.1.2.2.1/08 (M-006079-01-1), MR 3/97 KCA 7.1.2.2.009 (M-006079-01-1), MR 3/97



Parameter		S	_ پ	
Soil Designation:	BBA 2.1 (sp 149)	BBA 2.1 (sp 1121)	BBA 2.2	BBA 23
Batch	Sp 149	Sp 1121	Sp 2110	Sp\$121
Used for study(s):	KCA 7.1.2.2.1/07 ( <u>M-006082-01-</u> <u>1</u> ), 535/96	KCA 7.1.2.2.1/08 ( <u>M-006079-01-</u> <u>1</u> ), MR (297) KCA 7.1.2.2.1/09 ( <u>M-066074-01-</u> <u>1)</u> MR 38/98	KC& 7.1.2.2.1/08 MR & CA 7.1.2.2.1	$(\underbrace{M-006082-01-1}_{5/96}),$ (M-006059-01-16) (M-006074-01-1), (M-006074-01-1), 38/98
Textural Classification (USDA)	Loamy sand	Sand O	boamy sand	Sanudy loans
Sand [50 - 2000 µm] %	85.9 C	89.4	S. 2 S. 2	م 66 <b>گ</b> ه
Silt [2 – 50 µm] %	8.8	~ 1Q	7.7 \$	° 2.4 °
Clay [< 2 μm] %	5.3	<u>y</u> <u>y</u> .1 <u>v</u>	6A 6	10.8
pH in 0.01M CaCl ₂	5.Q ( V	5.3	K 6.2 K	6.6
Organic Matter (%)	Q.98 0	× 0.98 ~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	L.48
Organic Carbon (%)	0.57	Q Q.57 5	2,50° C	*≫1.44

#### Table CA 7.1.2.2.1-61: Physico-chemical properties of test soil

Other soils were also used for method validation purposes.

### B. Study Design

# 1. Experimental Conditions

Samples (25 g, except 30 g for study KCA7.1.2, 21/09 (M-006074-010), MR 38/98) of soil (a mixture of BBA 2.1, 2.2 and 2.3) were for ified with the test substances and stored frozen (-18 to -25°C), see Table CA 7.1.2, 21-62. In studies KCA 7.1.2, 21/07 (M-006082-41-1), 535/96 and KCA 7.1.2.2.1/08 (M-006079-01-9), MR 3/97 each sample was treated with spirosymme and metabolites M01 and M02. However, for study KCA 7.1.2.2.1/09 (M-006024-01-9), MR 98/98 one sample was treated with spiroxamine and a further samples was treated with metabolite M01. M02 and M03.

The storage stability of spiro tamine and metabolites M01, M02 and M03 were investigated for at least 639 days.

### 2. Sampling

The sampling intervals taken for the various studies are detailed in Table CA 7.1.2.2.1-68. At each sampling occasion whole beated samples were taken for analysis along with untreated controls.

# 3. Analytical Procedures

Details of analytical procedures for the three subles are presented in Table CA 7.1.2.2.1-63. An overview of the concurrent recoveries conducted during the course of the analysis of the storage stability samples is provided in Table CA 7.1.2.2.1-68.

# . 🖉 Results and Discussion

# A. Analytical Methodology

Full details and acceptable validation data to support the methods used in these studies are presented in Document  $M^2$ CA 47 Section 4.1.2 (Method 00352 (M-090916-01-1); 00374 (RA-607/94) (M-019207-02-47); 00433 (M-015066-01-2)). The methods comply with the EU regulatory requirements outlined within SANCO/3029/99 rev. 4 and is suitable for the determination of spiroxamine and its metabolites in soil samples by GC/MS and HPLC-MS/MS.

Details of the recovery data generated during method validation are provided in Table CA 7.1.2.2.1-63



to Table CA 7.1.2.2.1-67.

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						A	Spiroxamine
Гаble CA 7.1.2.2.1-62: I	Experimental overv	view of soils used a	nd treatment level	s for the various st	G udies t	1 ailo	29 ¹¹ ¹⁰ and
				<b>B</b> reerime	ntal phase 2	stability	- 1 Charles
		Method y	validation	l l	Storage	stabilit	<u>L</u> F.
	Analytical method				Duration offrozen	Stability .	
Study	used	Soil(s) used	Treatment level (µg/kg) recoveries	Som(s) used	storage (days) and no of sampling in- ervats	(µg/kg) of storage stability samples	Treatment level (µg/kg) of concur- tent recoveries
KCA 7.1.2.2.1/07 ( <u>M-</u> 006082-01-1), 535/96	00352	BBA 2.1, BBA 2.3, R 30262.7	$\frac{1}{5}$ $\frac{1}{5}$ $\frac{1}{5}$ $\frac{1}{5}$ $\frac{1}{5}$	Mix 2.1, 22, 2.3	0 ¹ 121 days (28-Jinn-94*)	Spx: 400 M01: 400 M02 400	Spx: 401.6, 418.8 M01: 387.2, 390.4 M02: 400.8, 427.6
	00374	BBA 2.1, BBA 2.2, BBA 2, Höfchen Mis 2.1, 2.2, 2	M02: 4.40 - 804	a repr	0-726 days (n=14)	MO2.3400 The State State	Spx: 116.6 - 534.4 M01: 86.1 - 575.4 M02: 88.1 - 843.2
KCA 7.1.2.2.1/08 ( <u>M-</u> <u>006079-01-1</u> ), MR 3/97	00374	BBA 2.1, OBA 2.2 BBA 23, Höfchen, Mix 2.1, 23, 2.3	Spx: 3.34 534 M00 9.60 - 576 M02: 4.40 - 844	Mix St, ¹ 2.2, 2.3	0 – 726 days (n=14) (22 Dec-94)	Spx: 134 M01: 144 M02: 211	Spx: 86.0 - 234 M01: 86.1 - 172 M02: 85.4 - 211
KCA 7.1.2.2.1/09 ( <u>M-</u> <u>006074-01-1</u> ), MR 38/98	00433	Fresho, Watsenvile, Mix 2 102,2, 2.3	Spx: 5,585 - 262 5 M01 5.850 - 252.7 M02: 5,706 - 287.7 M03: 4682 - 2469	NHX 2.1, 2, 2, 2.3	0 - 699 days (n=10) (24-Apr-96*)	Spx: 165.7 M01: 144.2 M02: 153.8 M03: 158.9	Spx: 114.9 – 165.7 M01: 119.4 – 144.2 M02: 124.6 – 153.8 M03: 107.6 – 158.9
* Treatment date	00374 00374 00433 00433 00433 SUX COMME QUENTIX I QUENTIX I WITTON	DPN documence Publicati Publicati explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explication explicat	on i ci on th Ditation of th Asion and Addited and	yiolate			



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Study	Analytical method used	Method report	Method details	Validation details	and and log
KCA 7.1.2.2.1/07 M-006082-01-1), 535/96 used for sam- bling intervals 0 to 121 days	00352	Method 00352 for gas chroma- tographic determination of KWG 4168 and the metabo- lites KWG 4557 and KWG 4669 in soil. RA-294/94 (1- Jun-94)	Soil samples were extracted with boling methanol. The solvent was evaporated and the osidue was re-dissolved in 2-propanol. Quantitative determination was done by gas chromatography with mass selective detector (MSD) in the single-ion-monitoring-mede.	See Fable CA 7.102.2.1-64 for soils used and fortification revels of recovery samples performed for method validation	Sp& 10 μg/k M01 and M0 20 μg/kg
CA 7.1.2.2.1/07 <u>M-006082-01-1</u> ), i35/96 used for sam- bling intervals 150 to '30 days CCA 7.1.2.2.1/08 <u>M-006079-01-1</u> ), MR 3/97	00374	Chromatographic Detectmina- tion of KWG 4168 and the Metabolites KWG 4557 and KWG 4669 in Soil MR-	Soil samples were extracted in a Soxtec hot extraction equipment with boiling methanol water / ammonia (25%) (800+200 + 20 parts by volume). After solvent evaportion to the aqueous remainder the internal standard was added. The active substance and the metabolites were quantitatively determined by liquid chromatography with	See Table CA 701-2.2.1-65 for sols used and fortification levels of recovery samples performed pror method validation See Table CA 7.1.2.2.1-66 for soils used and fortification levels	Spx, M01 an M02: 5 µg/k
КСА 7.1.2.2.1/09 <u>M-006074-01-1</u> ), ИК 38/98	00433 Th	Method 00433 (MR-248/96) for Liquid Coromatographic Determination of KWG 4168 and the Metabolites Desetsyl- KWG 4168 (KWG 4557), Despropyl-KWG 4168 (KWG 4669) and KWG 4168 N-0x- ide (WAK 6301) in Solf. MR- 248/96 (15-Apr-97)	MS-MS detection Soil samples were extracted with a mixture of methanol/ water / amnonia (25%) (800 + 200 (10 parts by volume) during 60 minutes on a mechanical shake) and filtered. From the filtrate an aliquet was concentrated in a Turbo Vap to the aqueous remainder and internal standard was added. Other centrifugation the quantitative determination of the active substance and the metabolites was done by high performance liquid chromatography using MS/MS detection.	See Table CA 7.1.2.2.1-67 for soils used and fortification levels of recovery samples performed for method validation	Spx, M01 ar M02: 5 μg/k
EUIC	Lermor Leeguer	e' any any al per			



		Spiroxamine					M01 🔊	<u>or</u> i	ſ	08		M02		
Soil	Fortifi- cation level (µg/kg)	Recovery values (%)	Mean re- covery (%)	RSD	Soil	Fortifi- cation level (µg/kg)	Recovery values	Mean re- covery	RSD.	e ^{\$} Soil		Recovery values	Mean re- covery (%)	RSD
2.1	10	84.9, 129.1, 73.3	95.8	31	2.1	20~	91.7, 77.2, 81.9	83.6	<b>2</b> 9 à	Ø 2.1	گ ^ا 20	\$73.9, 63,5\$78.6	72.0	11
	20	102.4, 85.5, 94.6	94.2	9		e ¹⁰⁰	83.0, 85.2, 74.5	-80.9	A	0° 2.1 Dib	100>	87.4, 85.4, 77.5	83.4	6
	100	97.7, 96.8, 84.5	93.0	8	E.I	500	71.9,27.5,77.1 *	75.5			O Yean	<pre></pre>	70.9	5
	500	79.6, 87.9, 85.7	84.4	5		£ Í	m and	-121:05	aV		500 Th			
2.3	10	100.2, 110.7	105.5	7,05	2.3 J	20	96.4, 87.8, 96.0	93.4	D ^{Ob} 5	JIN2.3 JOCULINE	20	07.5, 74.3, 74.7	75.5	2
	20	103.3, 90.1, 104.6	99.3	1008-	Osher -	J (J 00 [°]	85, 67.0, 55,6	<u>(8</u> 2	20 ⁰	ADICE	100 C	77.5, 74.3, 74.7	61.5	18
	100	105.1, 74.6, 71.4	83 70 ^C	2210	16 , ¹	500	88.6, 92, 82.4	87.8	<b>\$</b> 6		\$300	67.2, 72.9, 72.5	73.3	5
	500	101.8, 106.2, 93.5	J100.5	10. ⁶ '	The second secon	+ De	JIA 1014	" the	19	Or				
R 30262/7	10	115.3, 108.9, 93.5	105.9	11 %	R 30262	20	111.1, 104.3, 95.5	\$ 93.4 \$	<u>1</u> 2-8	R\$30262/7	20	93.9, 92.1, 85.5	90.5	5
	20	129.1, 120.6, 109.2	119.6	C ^{to}	¥,\$	Ę @	69.6, 66.4, 692	684	<u>20</u>	<i></i>	100	62.5, 60.4, 62.5	61.8	2
	100	103.8, 88.1, 101.6	97.8	<u> </u>		500	84.3, 62.9, 67.7	<b>%</b> 71.6	\$ 16		500	70.6, 56.7, 62.4	63.2	11
	500	94.3, 88.2, 89.9	<b>GO.8</b>	_ ¬G ^{`}}	The The	Ober	O'TO WICH	E DE						<u> </u>
		Overall means	97.3	14.5			🛇 Overall mean:	<i>©</i> , 8Ĭ.6	16.1			Overall mean:	72.5	14.7
	E UI	103.3, 90.1, 104.6 105.1, 74.6, 71.4 101.8, 106.2, 93.5 115.3, 108.9, 93 129.1, 120.6, 109.2 103.8, 88.1, 101.6 94.3, 88.2, 89.9 Overall means the the thought of the	thout		cats 242101 227011 227011	tati gion gited	of the viola							



		Spiroxamine					M01	921 1	ſ	0 ²		· · · · · · · · · · · · · · · · · · ·		
Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values	Mean re-	© RSD	Fortifi- cation level (µg/kg)	Soil	<b>Recovery values</b>	Mean re- covery (%)	RS
3.34	2.1	98.4, 93.5, 103	103	11.2	3.60	2.1	90.2, \$3.4, 92.3	94.7	5.38		2.1	\$86.5, 94 <i>3</i> \$89.7	94.1	10.
	2.2	132, 115, 99.7			4	2.2 ^E	90.5, 96.4, 86.7	1 ²		A CA	2.2 *	89.40.84.5, 82.6	-	l.
	2.3	101, 94.5, 91.0			i S	2.3	94.7.95.3, 105 ×	1 2 2			02.3	89.6, 98.7, 111	-	I.
5.68	Höfchen Mix 2.1, 2.2, 2.3	149 ^A , 130, 102 84.1, 84.9, 91.2 103, 108, 111	97.0	1220	4.304C	Hötchen Mix 2.1, 2.2, 2.3	135 ⁹ , 95.7, 191 104, 101, 103 98, 96.1, 95.6	100°C	3.92 Č	J100 4.404	Höfchen Mux 2.1, 2.2, 2.30	133 ^A ,401, 108 105, 107, 101 102, 103, 100	103	2.49
5.84	Mix 2.1, 2.2, 2.3	102, 106, 101 99.5, 97.6, 100	18100	2,880	4.977	Mix 2.1, 2.2, 23	83.9, 85 0, 96.8 87 5 91.9, 104	91.5	Ô 8 47 🕯	§ 272	Mix 2.1,	87.4, 89.1, 94.7 92.0, 93.1, 116	95.4	11.0
33.4	2.1	88.0, 86.2, 82.8	84.0	<b>4.40</b>	36.0	2.1	95.6, 87.3, 90.7	£ 88.7	ri ^{jojni}	52.9 ×	2.1	96.9, 93.3, 96.9	92.7	3.93
	2.2	81.1, 76.9, 82.		at V	0	2.2	85,5,92.1, 82,1				2.2	88.5, 85.0, 89.9	-	l.
	2.3	87.9, 89.7, 85.7	i la come		L ^S	2.3	×9¥.9, 90.6, €2.8	~C	L'IS.		2.3	95.4, 94.5, 95.8	-	l.
	Höfchen	83.1, 79.9, 83.3	g JJJO 2	19	TU C	Höfchen	87.2 88.8, 89.2		ŕ			90.5, 92.6, 93.2		
113.6	Mix 2.1, 2.2, 2.3	80.4,88.1, 82.6 77.9, 74.4, 83.3	81.2	5.86	\$6.08	Mix 2.1, 2.2, $2.3^{\circ}$	87.2, 88.8, 89.2 91, 102, 02 98.8, 9(3, 99.7, 87.0, 92.2, 87.3 87.0, 92.2, 87.3 87.3 87.0, 92.2, 87.3 87.3 87.0, 92.2, 87.3 87.0, 92.2, 97.5 87.0, 92.2, 97.5 87.0, 92.5 87.0, 92.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5 87.5	¢ 100	1.75	88.08	Mix 2.1, 2.2, 2.3	101, 101, 101 99.7, 99.9, 102	101	0.92
116.8	Mix 2.1, 2.2, 2.3	101, 100, 101 95,4, 99.0, 100	99.3	0 ² .11 ,		2.2, 2.3	87.0, 92.2, 87, 5 83.5, 85, 3, 86.0	86.9	3.38	105.4	Mix 2.1, 2.2, 2.3	85.7, 88.5, 90.1 87.0, 89.41, 88.1	88.1	1.82
134	2.1	87.6, 80.8, 90.3	×8424	2 J.B.	E7-144	<u>2</u>	93, 85.5, 92.3	89.9	4.20	211	2.1	92., 87.9, 92.5	91.3	3.37
	2.2	87.6, 86.9, 80.3	O'L'I	¥ (		\$\$ <b>2</b> .2	<b>88</b> .9, 87.4, 81.8				2.2	93.6, 90.0, 83.7	-	l.
	2.3	87.1, 82.2 8.8	OFT	1 3 L	2001	<u>,</u> 2,300					2.3	93.3, 94.8, 91.0	-	l.
	Höfchen	78.5 8.7, 83.6 1	1 670		erni	Øöfchen	88.1, 90.1, 94.1				Höfchen	91.1, 90.4, 93.9		
454.4	Mix 2.1, 2.2, 2.3	9 <b>9</b> 5, 92.5, 79.3 85.0, 84 <i>3</i> , 96.6	0198.1 0198.1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	349.3	Mix 2.1, 2.2, 2.3	99.4, 96.0, 98.4	99.2	1.99	352.3	Mix 2.1, 2.2, 2.3	99.5, 95.9, 96.3 103, 104, 99.8	99.8	3.34



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h									Å	T	an ^o	i De	,°	
		Spiroxamine					M01	Ť	G		ป	M020	allos	
Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values	Mean re- covery (%)	RSD
467.2	Mix 2.1, 2.2, 2.3	98.1, 93.9, 92.0 101, 101, 94.6	96.8	3.96	395.2	Mix 2.1, 2.2, 2.3	94.6, 91.2, 88.6 88%, 88.5, 93%	91,2 V	a	° 421.6~Ç	Affx 2.1, 2.2, 2.8	91.2,91.7,97.2	93.6	2.66
534	2.1	80.9, 84.5, 86.1	78.5	7.62	576	2.1	\$90.7, <b>8</b> 9,7, 92.1	86.6	0 ⁹ 5.70	844	2.1	87.1, 87.4, 90.6	86.7	4.83
	2.2	83.1, 77.0, 71.2				2.2	87,0, 81.9, 7,69	l and	r C	3	2.2 3	86.0 84.7, 80.0		1
	2.3	84.4, 83.7, 75.6			¥	D 2.3 , K	92.1, 91.3, 88.1		012	OD	<b>∑</b> \$.3	92.3, 93.6, 86.6		1
	Höfchen	73.1, 72.9, 69.2			. ¢	Hötchen	84.4 83.8, 8 3			t at	Höfchen	81.7, 82.0, 88.0		1
<u></u>		Overall mean:	90.1	12.1 %		0*	C Overall mean:	\$2.0	ð <b>6</b> .82	100 Cher	AU .	Gwerall mean:	93.6	7.40
A Excl	uded from m	ean (identified as an or	utlier)	elle		ġ.	er i			V ⁶⁻ .70	STL O	W P		

Table CA 7.1.2.2.1-66: Method validation of spiroxaminerand soil metabolites M01 and M102 in trozen soil for study KCA 7.1.2.2.1/08 (<u>M-006079-01-1</u>)

		Spiroxamine		C ^K	, \$	Ear		0 ^f	i gh			M02		
Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	covery (%)	RSD	Fortifi cation Jevel (µg/kg)	Soil	Recovery values		RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD
3.34	2.1	98.4, 93 0-103	103	dY.2	C3.60	J. J. Y	90.2, 93.4, <b>9</b> 23	94.7	5.4	4.40	Mix 2.1,	105, 107, 101	103	2.5
	2.2	132, 115, 99.7	6			2.2	^O 90.5, 96 4, 86.7				2.2, 2.3	102, 103, 100		
	2.3	101, 94.5, 91.0	10 ¹⁶	PUDL.	at Q L	\$20 [%]	94,95.3, 105			5.27	2.1	86.5, 94.3, 89.7	94.1	10.0
	Höfchen	149, 130, 102		۶ م	Jore n. C	Möfchen	[©] 135, 95.7, 101				2.2	89.4, 84.5, 82.6		
5.68	Mix 2.1, 2.2, 2.3	84.1, 84.9 91.2 103 008, 111 1	97.0	\$12.2	A.30	Mix 2.1, Q.2, 2.3	104, 104, 103 98.1, 96.1, 95.6	100	3.9		2.3	89.6, 98.7, 111		
5.84	2.2. 2.3	99.5, 97 <b>6</b> , 100	OT WOI	£ 2.8		Mix 2.1, 2.2, 2.3	83.9, 85.0, 96.8 87.5, 91.9, 104	91.5	8.5		Höfchen	133, 101, 108		
	C.	Julie Aran	thout	Ŷ [®]	¥ ·									



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·									~	•	and.		,°	-
	-	Spiroxamine	-			-	M01	T	ŞG		3J	M020	and	
Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	(%)	a P	Fortifi- cation level (µg/kg)	Soil	Recovery values	Mean re- covery (%)	RSD
33.4	2.1	88.0, 86.2, 82.8	84.0	4.4	6.71	Mix 2.1, 2.2, 2.3	86,5,97.8, 89,3	90,2, ³	6.6 5	5.27 s		92.0-93.1, 116.	0.5.4	11.0
	2.2	81.1, 76.9, 82.2				Höfchen	94.5, 51.9, 104		ê ê	0 ⁶ .41	× 2.2, 2,3 Mix 2.1, ≥ 2.2, 2,3×	\$97.7, 92,95,83.0	91.6	5.4
	2.3	87.9, 89.7, 85.7			36.0	2.1	\$95.6, 87.3\$ <b>9</b> 0.7	88.7	A.6		Hötchen	9%, 94.2, 90.0		
	Höfchen	83.1, 79.9, 83.3			19	2.2 >	85.5 82.1, 82 1	10.288.7		52.7 ×	2.1	96.9, 93.3, 96.9	92.7	3.9
86.0	Mix 2.1, 2.2, 2.3	85.5, 82.0, 86.9	79.0	8.4 t UINCID	<u>O</u> PDJ Tr	0 ² .3	091.9, 90.6, 92.8	egyre f	0 ^{54.6}		er 19.2	8.5, 85.0, 89.9		
	Höfchen	71.4, 73.8, 74.6	A*	JIGH	- Ore	Hötchen	« <b>\$</b> \$.2, 88.8, <b>89</b> .2	Leg.	<u> </u>	CUIL	23	95.4, 94.6, 95.8		
114	Mix 2.1, 2.2, 2.3	80.4, 88.1, 82.8 77.9, 74.4, 83.5	802	and let	86.1	Mix 2.1, 2,2,2.3	101, 002, 102 9808, 97.3, 90 P	100	1.8	e la	23 Höfchen	90.5, 92.6, 93.2		
117	Mix 2.1, 2.2, 2.3	101, 100, 104 95.4, 99.0, 100	99.3	2.1						Ç\$				
134	2.1	87.6, 80.8, 90.3	84.6		a∿°	Mix 2.1, 2.2, 23	79.7, 85.5, 88.5	T 85.9	\$ 3.4	85.4	Mix 2.1, 2.2, 2.3	87.4, 86.9, 87.3	85.7	2.1
	2.2	87.6, 86.9, 80.3			0 ^t	Höfchen	7 <i>P</i> .7, 85.5, <b>\$</b> .5	Els.			Höfchen	82.9, 84.6, 85.0		
	2.3	87.1, 82.2 \$5.8	cop		98.9 ⁵	Mix 2, 4,	87.0,92.2, 87.20 ⁵	86.9	4.2	88.1	Mix 2.1, 2.2, 2.3	101, 101, 101 99.7, 99.9, 102	101	0.9
	Höfchen	78, 5, 81.5, 83.6	0 ni ^j ê			2.2, 2, 3	83.5, 85.3, 86.0			105	Mix 2.1, 2.2, 2.3	85.7, 88.5, 90.1 87.0, 89.4, 88.1	88.1	1.8
	EVIT	87.6, 86.9, 80.3 87.1, 82.2 \$5.8 78 \$, 81.5, 83.6 thet note 1	the start		PETON PETUN	39" eð	86.4, 20.4, 91.7 79.7, 85.5, 5.5 87.9, 92.2, 87.3 83.5, 85.3, 86.0							



2021-03-31 Document MCA – Section 7: Fate and behaviour in the environment Spiroxamine

					1				\$		and.		- 	
		Spiroxamine					M01	Ţ	Ç,	<u>, , , , , , , , , , , , , , , , , , , </u>	.00	M020	all ^o	
Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)	RSD	Fortifi- cation level (µg/kg)	Soil	Recovery values (%)	Mean re- covery (%)		Fortifi- cation level (µg/kg)	Soil	Recovery values	Mean re- covery (%)	RSD
384	Mix 2.1, 2.2, 2.3	78.8, 81.3, 80.2 68.7, 72.7, 71.1	75.5	7.0	144	2.1	93 25, 83.5, 92 35	29 89.87 7 C	<b>6</b> 4 2 %	211	2.1 ·	© 92.9, 87, 9, 92.5	91.3	3.4
454	Mix 2.1, 2.2, 2.3	90.5, 92.5, 79.3 85.0, 84.6, 96.6	88.1	7.1		2.2 %	88.9 87.4, 81.8		P 3	O ^{to}		\$93.6, 90 <b>(</b> \$83.7		
467	Mix 2.1, 2.2, 2.3	98.1, 93.9, 92.0 101, 101, 94.6	96.8	4.0	Ť	2.3 × *	94.7, 91.6, 90.8 ×	hird hird			<u></u>	93.3, 94.8, 91.0		
534	2.1	80.9, 84.5, 86.1	78.5	7.6	19	Hölchen	88.1, 90.1, 94.1	aula	AUCU	C'LL		91,4,90.4,93.9		
	2.2	83.1, 77.0, 71.2		7.6 JIRERT	34305	Mix 240 2.2 2.3	99.4 96.0, 98.4 100, 102, 99,2	99.27 ⁽	2.000	342 342	Höfchen Wix 2.1, 2.2, 2.3 Höfchen	^{94.5} , 93.2, 93.6	92.3	2.5
	2.3	73.1, 72.9, 69.2	\$ 3.0 ^C	and lo	3580	Mix 2.1, 2.2,25	92.25 <b>8</b> .9, 96.7	90.7 j	\$ 9	ay	Höfchen	88.9, 93.6, 89.9		
	Höfchen	73.1, 72.9, 69		den K		Höfchen				\$352	Mix 2.1, 2.2, 2.3	99.5, 95.9, 91.5 103, 104, 99.8	99.8	3.3
-	-	-	- - - - - -		395	Mix 2.1, 2.2, 2, 3	94.6, 93.2, 58.6 88.6, 88.5, 93.8 907, 89.7, 931	€ 91.2	\$.3.2	422	Mix 2.1, 2.2, 2.3	95.5, 94.4, 91.5, 91.2, 91.7, 97.2	93.6	2.7
-	-	-	\$- ,	<u>~</u>	\$76	2.1	, <b>e</b> ., <i>e</i> , e		5.7	844	2.1	87.1, 87.4, 90.6	86.7	4.8
-	-		je og	C	20	2.2 C	87.0 <b>80</b> 9, 76.9 K	Ç			2.2	86.0, 84.7, 80.0		
-	-		<u> </u>		c0	25	92.1, 91.3, 88 J				2.3	92.3, 93.6, 86.6		I
-	-	K Ť		-21		Höfchen	© 84.4, 83 8, 81.3				Höfchen	81.7, 82.0, 88.0		ļ
		^w Overall mean:	88.1	J2.6	at Q b	1 O'le	overall mean:	91.5	6.8			Overall mean:	92.9	7.2
	EUII	Unsequential with	-thout	ye ye	PETOD.	ar co	· · · · · · · · · · · · · · · · · · ·							

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		Spirox	amine		0.02	NOP M	01 502 0	J.J. M. C.
Soil	Fortification level (µg/kg)	Recovery values (%)	Mean recovery (%)	KSD 0	Fortification level	Recovery values	Mean recovery	RSD
Fresno	5.585	85.9, 90.0, 96.7	85.2	9.Y	5.850	100.2, 93.7; <b>Q</b> 1.8		©7.4
Watsonville		74.9, 79.2, 84.8				84.2, 82.0, 88.5		f O'L
Mix 2.1, 2.2, 2.3	4.923	99.2, 88.6, 89.1	92.3		C 5.1 B.	92.3, 102, 91.1	\$\$95.1	6.3
Fresno	55.85	79.3, 97.1, 80.8	82.5	£\$ 8.8 }	*21.38.50 *21.38.50	85.3 86.2, 81.3	83:8	2.4
Vatsonville		81.0, 78.8, 77.9	. Ĝ - 6			A 4.1, 01.1402.2	- 0 ²	
Mix 2.1, 2.2, 2.3	105.0	87.5, 84.2, 78.2	83.3 0	2 0 bb 5.7 0 2 bb	AN99.1 30	84.2, 207, 94.1	895	5.6
Mix 2.1, 2.2, 2.3	262.5	91.8, 90.9, 912	<b>1 1 1 1 1 1 1 1 1 1</b>	5° 025	272 7 272 7 7 7 7 7 7 7 7 7 7 7 7 7 7	86,2, 93.7, 92,6	0 90.8	4.5
		OveralOmean:	× 86,1 × S	NV 8.1	²⁰⁵ d	Overall mean:	§ 88.9	6.7
		<u>do dil</u>	<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	2 Der 1		\$	22	
Soil		4						
5011	Fortification level (µg/kg)	Recovery values	Mean recovery	1 1200 12 1 1 1200 12 1 12 12 12 12 1 12 12 12 12 1 12 12 12 1 12 12 12 1 12 1	Fortification level (µg/kg)	Recovery values (%)	Mean recovery (%)	RSD
Fresno	5.700	81.8, 97.1, 96.8	Star - Real	ALL GROUND	4.682 20 20 20 20 20 20 20 20 20 2	98.6, 95.5, 99.0	96.7	2.6
Watsonville		90.7, 85,8, 93.5		and and a second	Pr. R.	97.4, 92.3, 97.0		
Mix 2.1, 2.2, 2.3	5.395	105,01.2, 104,0	E 100 2 3	0 ⁵ 7.70	4.613	106, 104, 87.1	99.0	10
resno	57,00	83.1, 95, 7 ₀ 84.4	CO 84.4 50	of 6.7	46.82	92.1, 91.8, 93.1	92.4	1.5
Vatsonville	1. Š	80.7, 82.4, 83,1				90.3, 92.8, 94.4		
Aix 2.1, 2.2, 2.3	115.1	<b>29</b> 9.2, 89.1, <b>8</b> 9.6	\$8.3 ° °	<b>2</b> 2.7	98.41	93.9, 89.1, 90.7	91.2	2.7
Aix 2.1, 2.2, 2.3	287.7	93.1 98.0, 91.1	94.B	3.8	246.0	97.4, 98.0, 97.7	97.7	0.3
		Overall mean:	\$\$90.5 t	8.0		Overall mean:	95.2	4.9
	and a st	overan sycan.	2 2 88.3 94 0 94 0 95 0 96 0 90.5	0.0		overan mean.	95.2	т.у



D	Spirox	amine	Μ	01	М	02	M	03 0
Duration (days)	Stability (%)	RSD (%)	Stability (%)	RSD (%)	Stability (%)	RSD (%)	Stability (%)	<b>RSD</b> (%)
KCA 7.1.2.2	2.1/07 ( <u>M-00</u>	<u>6082-01-1</u> )		I		×,	, O ^v	
0	118.4	7.9	101.6	6.7	Ö 94.9	\$.1	No.	S - S
30	124.5	1.3	98.8	2.1	92.6	<b>Q</b> 2.4	Q- ^	
59	78.3 ^B	13.3	55.8 ^B	19.90	47.1 ^B	20.7	° - °	
101	128.2	5.7	117.8	120	89,1	<b>9</b> .0		- 4
121	97.0	4.8	87.6	2.4 。	8200	مَّ 4.7	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	, <u>,</u> şç
150	88.6	2.9	89.8	1.80	×89.8 ×	<u>_</u> 2,4	Ş - , [×]	4 -
175	84.7	3.6	86.3	à A	© 88.5Q	9.4		6 - L
240	87.8	2.7	88,0	3.9	96-0	A 3.60°	Q- ,	
300	72.2	2.5	8 ⁽⁴⁾ .1	× 3.1	× 84.6 C	<u>z</u>	<u> -                                   </u>	0-
359	95.6	2.8	096.2	·	\$ 99,00	2.1 ×		Q -
419	90.6	3.0 4	Q 88,7	à ^{1.8}	9502	2.3	8 ⁻ ~	-
479	76.5	3.3 🖉	₹8.0	0° 2.8S	@82.1	2.9 <b>r</b> 1	- &	-
538	81.7	2.2	83.5	1.1	× 84,2	\$2.3	<u>_</u> O*	-
618	89.7	<i>3</i> .0 (	89,4	23.5	90.7		Q-	-
658	90.1	³ ∕ _{4.2} <u>↓</u>	89.3	2.5 [°]	\$90.2	\$3	- S	-
730	84.7	2	\$87.4	Å,	× 88.7×	\$√1.6 °>	-	-
mean	93.3	18.0	890	ి14.2 ఫో	\$7.9	12.4	-	-
Concurrent	1169	9.0 ^D	_99.9 ^c	> 20,99	\$6.2° €	24,1°		
recovery	87.0 ^D	9.0 ^D	88.6 ^D (92.2)		91.9	[∞] €.4 ^D		
$\frac{(\%)^{A}}{KCA712}$	Ø96.0)		4		(967)	@(13.4)		
~	201/08 ( <u>M-00</u>		81.8					
	83.1	0.6	V - V	36°,	89.2	4.1	-	-
34 **	78.6	32	80.6 ³		84.7	3.4	-	-
90	82,55	<u>4.4</u>	80.4	° 7.1 °	<u>85.1</u>	3.3	-	-
120		Q * 14,25°	× 100	<u> </u>	§ 82.1	15.4	-	-
181	~0100 C			<u>`^1.9</u>	98.8	1.4	-	-
243	90.0			6 0.40 •	90.6	0.7	-	-
300	76.8	2.3Q	83.3		83.4	0.8	-	-
361	85.4	84	919.7	× 2.0	86.1	1.8	-	-
441	91.6	@ 3.4 °		6 ² 4.3	91.6	3.9	-	-
481	<b>2</b> .6		\$93.6 ¢	0.7	92.1	1.3	-	-
540	076.0		[©] 787	8.4	80.5	3.2	-	-
601	88.0	03.8 5	88.8	4.5	90.6	4.3	-	-
662	\$6.6	1.90	87.8	4.5	88.7	3.6	-	-
726	89.7	<u>5</u>	94.8	7.4	97.3	9.2	-	-
, ^{or mean}	84.9	\$ 9.3	87.4	9.1	88.4	7.8	-	-
Concurrent recovery (%) ^A	84.1	7.6	87.1	8.6	90.0	7.4	-	-



D	Spirox	amine	М	01	М	02	Μ	03
Duration (days)	Stability (%)	RSD (%)	Stability (%)	RSD (%)	Stability (%)	RSD (%)	Stability (%)	RSD (%)
KCA 7.1.2.2	2.1/09 ( <mark>M-0(</mark>	<u>)6074-01-1</u> )					×.	S '
0	85.5	4.1	92.7	2.4	96.0	1.6	97.5	1.9
30	77.8	6.0	87.6	2.0	88.2	0.8	96.9	2.8
61	78.0	2.1	83.5	2.6	86.4	3(5)	91.4	Q.8 K
120	80.2	3.6	88.1	2.0	© 90.5	£1.9	95,2	3.5
177	72.9	5.5	86.2	1.9	86.3	á [©] 3.7	<b>\$</b> 0.2 å	1.8
268	73.9	4.0	84.4	3.10	86.7	0.8	° 92.7 🔗	9.6
355	78.1	3.2	87.8	201	90,5	A.2 Q	, 989	2.6
427	77.1	2.5	85.0	3.2 °	8507	× 3.7~	89.2 4	5.6°
555	76.4	2.6	85.2	1.80 [°]	×88.0 ×	_h2	\$ 92.9	4 6.2
639	79.7	3.8	85.6	23	×88.0 // Ø 85.4Q	0.8	902	Q 1.2 S
mean	78.0	5.5	86,6	3.6	\$ <b>8</b> 4	$4.0^{\circ}$	≪92.9	43
Concurrent recovery (%) ^A	81.0	9.1	88.2 4 5 88.2 4		88.50°	A.5 5	894 894 2	0 49 6.7

Recovery samples spiked and analysed at the same time as the storage stability samples A

В The mean result presented excluded some outliers

Ô Overall mean and RSD value for concurrent recoveries asing the GC/MS method at sampling interval 0-121 days С

D Overall mean and RSD value for concurrent recoveries using the LC-MS/MS method at sampling interval 150-730 days

### Condusions

Storage stability of residues of spiroxamine and metabolites MQC, M02 and M03 in soil under frozen conditions was shown to be acceptable for storage periods of up to 2 years.

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#### Assessment and condusion by applicant:

Study meets the current gurdance and the requirements in 283/2013.

Ö

Study meets the current gurdance and the requirements in 28372013. The study is considered valid to assess the storage stability of spiroxamine in soil under frozen condi-tions.



#### **Kinetic evaluation**

Data Point:	KCA 7.1.2.2.1/10
Report Author:	
Report Year:	
Report Title:	Kinetic modelling analysis of spiroxamine and its metabolites KWG 4557 and
	KWG 4669 from field soil residue studies conducted in Europe
Report No:	VC/07/007A
Document No:	<u>M-293744-01-1</u>
Guideline(s) followed in	EU Council Directive 91/414/EEC, as amended by Commission Directive 95/36/EC of July 1995, Section 5, Point 7.1.1
study:	95/36/EC of July 1995, Section 5, Point 7.1.1
Deviations from current	None $\sqrt{2}^{\prime}$ $\sqrt{2}^{\prime}$ $\sqrt{2}^{\prime}$
test guideline:	
Previous evaluation:	yes, evaluated and accepted
	RAR (2010), RAR (2017) $\beta^{\circ}$ $\beta^{\circ}$ $\gamma^{\circ}$ $\gamma^{\circ}$ $\gamma^{\circ}$
GLP/Officially recog-	No, not conducted upder GI@/Officially recognise desting facilities
nised testing facilities:	
Acceptability/Reliability:	Yes N N A A O A
<b>Executive Summary</b>	

#### **Executive Summary**

This study was previous considered during the evaluation of spiroxample (RAR (2000), RAR (2017)) and is therefore included again for completeness. The gudy perform Sa kinetic evaluation according to FOCUS 2006⁵ of soil dissipation studies reported in studies KCA 51.2.2. 901 (* 006 (16-01-1)); KCA 7.1.2.2.1/02 (<u>M-006126-01-1</u>) KCA 7.1.2 1/03 (<u>M-006127-01</u>); KCA 7.1.2.2.1/04 (<u>M-006128-01-1</u>); and KCA 7.1.2.2.1/05 (<u>M-006129-01-5</u>). The kinetic evaluation reported in this guidy is superseded by the new kinetic evaluation performed in story KQ 7.122.1/124(M-763140.01-1) on all the same soil dissipation studies

## Assessment and conclusion by applicant

The study and its data are considered as supplementary data with no use in risk assessment

. Q	
Data Point.	KCA7.1.20.1/11
Report Author:	
Report Year:	
	Kinesic modelling analysis of spirovamine and its metabolites KWG 4557 and
Report Litle:	KAYG 4669 from field so fresidue studies conducted in Europe normalised to
	Q0°C and pF2 y and p
Report No	VC/08019
Documeter No:	<u>M_002004-64-1</u>
Guideline(s) followed in study.	not applicable
Deviations from current	
test guideline:	
Previous evaluation:	ses, evaluated and accepted
	RAR (2010), BAR (2017)
GLP/Officially recog- O	No not conducted under GLP/Officially recognised testing facilities
nised testing facilities;	
Acceptability Reliabority:	Ves
	X Y

## Executive Summary

This study was previous considered during the evaluation of spiroxamine (RAR (2010), RAR (2017)) and is therefore included again for completeness. The study performs a kinetic evaluation according to FOCUS 2006⁵ of soil dissipation studies reported in studies KCA 7.1.2.2.1/01 (M-006116-01-1); KCA



7.1.2.2.1/02 ( $\underline{M-006126-01-1}$ ); KCA 7.1.2.2.1/03 ( $\underline{M-006127-01-1}$ ); KCA 7.1.2.2.1/04 ( $\underline{M-006128-01-1}$ ); and KCA 7.2.2.3/05 ( $\underline{M-006129-01-1}$ ). The kinetic evaluation reported in this study is superseded by the new kinetic evaluation performed in study KCA 7.1.2.2.1/12 ( $\underline{M-763140-01-1}$ ) on all the same soil dissipation studies.

#### Assessment and conclusion by applicant:

The study and its data are considered as supplementary data with no useun risk asses

Data Point:	KCA 7.1.2.2.1/12
Report Author:	
Report Year:	
Report Title:	Spiroxamine: Kinetickassessment of field soil dissipation studies
Report No:	0471836-KIN3 O & A A
Document No:	<u>M-763140-01-1</u> A & O Q Q A O O Q A
Guideline(s) followed in	
study:	
Deviations from current test guideline:	None $\mathcal{O}_{\mathcal{A}} \mathcal{O}_{\mathcal{A}} \mathcal{O} \mathcal{O}_{\mathcal{A}} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O} \mathcal{O} $
Previous evaluation:	No, not previously submitted a 2 0 0 0 0
GLP/Officially recog-	not applicable of S a A A
nised testing facilities:	
Acceptability/Reliability:	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

#### **Executive Summary**

The dissipation behaviour of spiroxamine was investigated in the field in five studies at eighteen European sites (see studies KCA 7.1.2.2.1/01 ( $\underline{M}$ -006/16-0.1), KCA 7.1.2.2.1/02 ( $\underline{M}$ -006/126-01-1), KCA 7.1.2.2.1/03 ( $\underline{M}$ -006/127-0.-1), KCA 7.1.2.2.1/04 ( $\underline{M}$ -006/126-01-1) and KCA 7.1.2.2.1/05 ( $\underline{M}$ -006/129-01-1).

The study design for each study did not exclude loss processes such as photolysis or volatilisation; therefore, they are considered to follow the "legacy" study design according to EFSA (2014) guidance. The data from these studies were considered appropriate to derive persistence/trigger and modelling endpoints and were analysed using the CAKE version 3.4 (2020) software package. A kinetic analysis to determine  $DT_{50}$  and  $DT_{50}$  values for comparison with relevant study triggers and persistence/trigger endpoints provided by POCUS (2014). To determine  $DegT_{50}$  matrix values, a kinetic assessment was performed following the flow charts for calculating modelling endpoints provided by POCUS (2014). To determine  $DegT_{50}$  matrix values, a kinetic assessment was performed following the flow charts for calculating modelling endpoints provided by EFSA (2014), and using data that have been normalised to reference conditions (20°C and pF 2 soil moisture content) and subject to timestep normalisation procedures. These endpoints were used for the selection of an appropriate modelling value for use with regulatory Predicted Environmental Concentration (PEC) models.

The derived persistence and modelling endpoints for spiroxamine, M01 and M02 are summarised in Table CA 7.1.2.2.1-69 and Table CA 7.1.2.2.1-70, respectively.

## Materials and Methods

The dissipation behaviour of spiroxamine was investigated in the field in five studies at eighteen European sites (see studies KCA  $(1.2.2.1/01 (M-006116-01-1), KCA 7.1.2.2.1/02 (M-006126-01-1), KCA 7.1.2.2.1/03 (M-006227-01-1), KCA 7.1.2.2.1/04 (M-006128-01-1) and KCA 7.1.2.2.1/05 (M-006129-01-4). It is noted that some studies are performed on sites at the same location at the same time. These have been fitted separately, and the individual endpoints used for persistence/trigger purposes. For modelling, the geomean of <math>DT_{50mod}$  values from the individual fits for these sites have been used for final endpoints.

The study design for each study did not exclude loss processes such as photolysis or volatilisation;



therefore, they are considered to follow the "legacy" study design according to EFSA (2014) guidance.

Daily rainfall, air temperature, soil temperature and soil moisture values were not provided in the stady reports.

#### A. Normalisation to reference conditions

Kinetic analysis to generate persistence/trigger endpoints was initially performed using the data as reported (i.e. not normalised to reference conditions).

Kinetic analysis to generate modelling endpoints was performed with data that have been normalised to reference conditions (20°C and moisture at pF 2), and subject to a timestep normalisation procedure increasing or reducing the length of each day in the study, depending on the soil temperature and moisk ture, according to FOCUS guidance (FOCUS, 2014). These procedures were conducted in KGX 7.1.2.2.1/11 (M-302004-01-1). Daily rainfall and air temperature data were used from weather stations <20km from test sites (summarised in the study report). In order to estimate soil temperature and soil moisture values, the PEARL v2.2.2 model was used @EARL meteorological files were generated from the available daily weather data (minimum and maximum air temperature, rainfall and PET) and input files were set up with van Geneuchten parameters estimated with the HYPRES database, using soil characterisation data obtained for the study. There was no crop chosen for the PEARL simulations as the applications was made to bare soil. The PEARL meteorological data and the estimated daily soil temperature and volumetric moistire content stored in an output file. PEARL input files are available in the study report (Appendix 3). An example of the timestep normalisation is also provided in the study sport (Appendix 5).

#### B. Data handling

Input data were generated according to the data handling recommendation made in the FOCUS guidance for degradation kinetics (FOCUS, 2014)

True individual replicates were not taken in any of the studies. The reported measured concentrations (mg/kg dry soil) were converted to g/ha and handled in accordance with the FOCUS guidance on values below the limit of detection (LOD) or limit of quantification (LOO) according to individual depths and time. Spiroxamme residues in individual korizons at each sampling time were summed before conversion to g/ha, with metabolite values corrected for molecular weight dufferences before conversion.

The handling of values below the LOD and LOO was performed according to the procedure recommended by (FOCUS, 2014) as follows:

- All values between LOD and LOO were set to the actual measured value. If the actual measured concentration was not peptred, 0.5% (LOQ+LOD) was used.
- All samples LODovere set to 0.5 × LOD.
- Aft samples after the first non-detect (<LOD) were omitted unless positive detections above COQ were made later in the experiment. In that case, samples were included up to the first nondetect (<LQD) which is NOT followed by later positive samples above LOQ.

### C. Input data

Sampling interval values in actual days were used for persistence/trigger endpoint kinetics assessments and normalised days were used for modelling endpoint kinetics assessments.

The studies were conducted ocording to the "legacy" design, without measures to eliminate surface loss processes in the modeling endpoint kinetics assessment for these studies, in accordance with EFSA (2014) guidance, the datapoints before 10 mm cumulative rainfall were excluded from the SFO kinetic fit since the study design did not exclude surface processes. The normalised times at which >10 mm cumulative rainfall was measured were determined (see Table 3-6 in the study report).

Sampling interval values in actual days were used for persistence/trigger kinetics assessments. Sampling intervals normalised to soil moisture at pF 2 and a temperature of 20°C were used for the modelling



kinetics assessments. The data used for conversion to g/ha and subsequently input into the kinetic models for each field trial site in the soil dissipation studies are presented in the study report (Table 3-7 to Table 3-24, pages 23-40).

#### **D.** Kinetic modelling

The kinetic modelling of the field data was conducted using CAKE version 3 (2020).

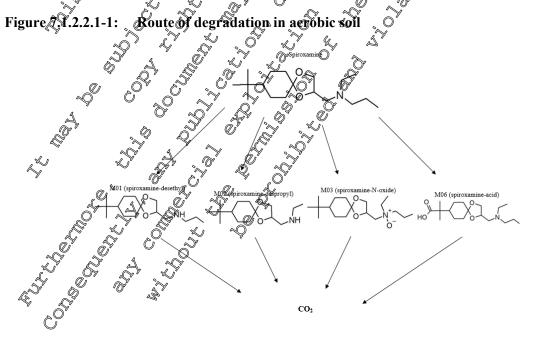
In the first instance, the data were directly fitted, un-weighted, with the complete data for and phonostrained initial concentration (M₀). The acceptability of kinetic fits was judged both visually and according to the  $\chi^2$  error and the t-test functions as recommended by FOCUS (2014). It is recommended that a  $\chi^2$  error of 15% or less indicates an acceptable fit, although for data that may include intrinsically variable data (e.g. field data) higher values can be tolerated if the visual fit is acceptable or good.

The FOCUS Kinetics guidelines state that the confidence that can be assigned to a parameter must be assessed and a t-test probability of greater than 95% (p<0.05) for estimated degradation rate constants indicate robust estimates. When fitting the first-order multi-compartment model (FOMC), the t-test is not appropriate as a measure of confidence (FOCUS, 2014).

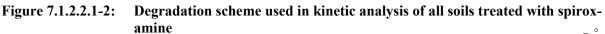
The FOCUS (2014) flowcharts for calculating persistence/fogger and modelling endpoints and the EFSA (2014) flowcharts for calculating modelling endpoints were followed, as appropriate. Each dataset has been considered following the steps in the flowcharts and the considerations are discussed in detail below. The full outputs from the persistence/trigger and modelling kinetic fits (including the initial settings) are shown in the study report (Appendices 6 and 7) respectively). For persistence endpoints, kinetic fits for both spiroxamine and metabolites M01 and M02 were performed following FOCUS (2014), whilst for modelling endpoints fits for spiroxamine were considered according to EFSA (2014). For modelling endpoints of M01 and M02, fitting of the decline curve is performed to derive DT₅₀ values only.

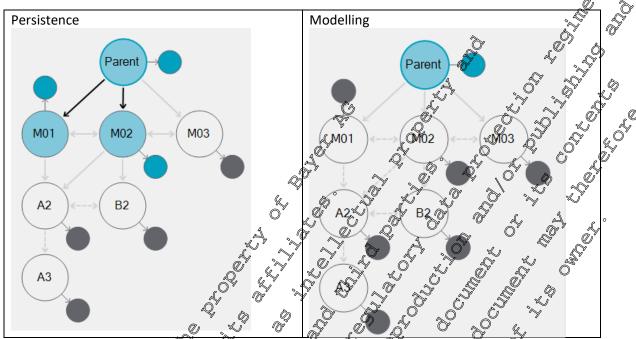
It is noted that some Studies are performed on sites at the same location at the same time. These have been fit separately and the separate endpoints used for persistence/trigger purposes. For modelling, the geomean of  $DT_{5000}$  values from the separate fits for these sites have been fasted for final endpoints.

Kinetic assessments were performed using the degradation schemes presented in Figure 7.1.2.2.1-1 and Figure 7.1.2.2.1-2.









The acceptability of kinetic fits was judged both visually and according to the  $\chi^2$  error and the t-test functions as recommended by FOCUS. The visual assessment is recommended as the main tool for assessing goodness of fit. However, it is also recommended that a  $\chi^2$  error of less than 15% and a t-test probability of greater than 95% (p < 0.05) for estimated degradation rate constants indicate an acceptable fit. The  $\chi^2$  error was not considered as an absolute cut-off criterion as FOCUS guidance indicates that there will be cases where the error is higher than 15%. But the fit still represents a reasonable description of the degradation for systematic error is considered mortant.

The t-test assesses whether degradation tate constants differs significantly from zero (i.e., no degradation). Alternatively, confidence intervals can be examined. In this assessment, the t-test was chosen for assessing confidence in rate constants. When fitting the FOMC model, FOCUS guidance indicates that the t-test is not appropriate as a measure of confidence for the gamma-distribution parameters  $\alpha$  and  $\beta$ . Therefore, if a FOMC fit indicated slow degradation, confidence intervals for  $\beta$  were examined to determine if they were high compared to the parameter estimate, which would indicate that the parameter estimate was not reliable.

When calculating modelling endpoints for a metabolite, it was considered important to derive a formation fraction wherever possible. In the FOCUS flowsheets, if the SFO fit for a metabolite is not considered acceptable, a case-by-case decision is required. The first option given is to assess the decline of the metabolite after its maximum ('top-down' nethod). However, this method does not allow formation fraction assessment. The second option given is to fix the formation fraction to a worst-case value (usually 1) and use this in combination with a worst-case  $DT_{50}$  (usually 1000 days). However, this method almost always results in a clear overestimation of observed metabolite residues. The final option given is to use alternative – but conservative – estimates that describe the observed patterns. In this assessment, alternative – but conservative – estimates were chosen, implemented by fixing the formation fraction to the fitted value and using this in combination with a conservative  $DT_{50}$ , or vice versa. The parameter to amend and its value were chosen based on expert judgement and iterative amendments to give a conservative description of the observed metabolite residue pattern.

The FOCUS (2014) flowcharts for calculating persistence and modelling endpoints were followed.

If necessary, the kinetic endpoints derived for each soil were normalised to FOCUS reference conditions



(soil temperature of 20°C and soil moisture content equal to pF 2) following the procedures recommended by FOCUS.

#### II. Results and Discussion

#### A. Persistence/trigger endpoints

The kinetic evaluation was conducted using CAKE version 3.4 (2020) following the FOCUS (2014) decision flowchart for persistence/trigger endpoints. A summary of the fits achieved and decision taken is provided (Appendix 4.1.) for each soil in Appendix 4.1.4 to Appendix 4.1.18.

The resulting persistence or best-fit endpoints are presented in Table QA 7.1.2.2.1-6

The spiroxamine persistence/trigger  $DT_{50}$  values ranged from 0.5 to 59.6 days and  $DT_{90}$  values Panged from 43.5 to 433 days.

M01 persistence/trigger DT₅₀ values ranged from 17.8 to 223 days and DT ovalues ranged from 39 to 742 days.

M02 persistence/trigger DT₅₀ values ranged from 2 to 16 days and DT₉₀ values ranged from 696 to 533 days.

#### **B.** Modelling endpoints

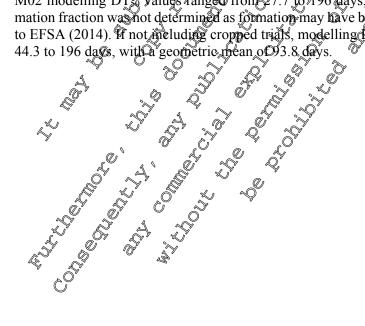
The kinetic evaluation was conducted using CAKE version 3.4 (2020) following the EFSA (2014) decision flowcharts for calculating DegT₅₉ matrix values. A summary of the fits enlieved and decisions taken is provided (Appendix 4.2:) for each soil in Appendix 4.2.1 to Appendix 4.2.18. For modelling endpoints of M01 and M02, fitting of the decline curve is performed to derive DT₅₀ values only.

The resulting modelling endpoints are presented in Table CA 7.1.2.2 1-70

The spiroxamine modelling  $DP_{50}$  values (at 20°C and pF-2) ranged from 16.1 to 133 days, with a geometric mean of 42.9 days. If not including cropped trials, modelling  $DT_{50}$  values (at 20°C and pF 2) ranged from 23.4 to 78 days, with a geometric mean  $DA_{3.8}$  days.  $\mathcal{L}$ 

M01 modelling  $DT_{50}$  values ranged from 23.4 to 1,000 days (default), with a geometric mean of 66.2 days. Formation fraction was not determined as formation may have been affected by photolytic factors according to EFSA (2014). If not including cropped trials, modelling DT₅₀ values (at 20°C and pF 2) ranged from 23.4 to 1,000 days, with a geometric mean of §9.8 days.

M02 modelling DT 3 values ranged from 27.7 to 196 days, with a geometric mean of 69.1 days. Formation fraction was not determined as formation may have been affected by photolytic factors according to EFSA (2014). If not meluding cropped trials, modelling  $5T_{50}$  values (at 20°C and pF 2) ranged from 44.3 to 196 dags, with a geometric mean of 3.8 days.





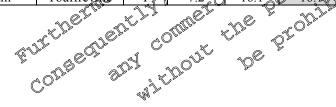
6

John projecties         pil (Ca(L))         Diss Ts (ary)         Diss Ts (day)         PisTs (day)         Diss Ts (day)         PisTs (day)         PisTs (day)<	Soi	l properties			Snirov	amine			M	01	JEN	1,0 ¹	M.	ardia oz	
Sun type         Son name         (CaCl)         (days)         (%)         iss         (days)         (iss         (days)         (%)         iss         (days)         (days)         (%)         iss         (days)         (days)         (%)         iss         (days)         (days)         (%)         (days)			рН	DissT ₅₀			Kinet-			zzerror	Kinet-	DissT50	DEST 90		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Soil type	Soil name						(davs)	• (davs)	(%)	ics_%	(days)	(days)		
Silt loam         Höchen         6.5         13.8         145         11.8         9FOP         48.1         640.2         C47.6         SFO         2.0         560.6         C46.5         SFO           Sandy loam         Elm Farm/ Thurston         7.5         0.8         196         6.3         9FOP         50.3         167.0         11.9         SFO         48.3         160.6         10.8         SFO           Loamy sand         Pakenham         7.3         0.5         132.0         8.2         DFOP         51.4         471         12.0         28FO         577.7         6192         10.7         SFO           CA 7.1.2.2.1/02 (M-006126-01-1) 1995         5         5         5         5         5         5         5         7         SFO         6.9         SFO         13.5         447         7.2         SFO           Sandy loam         Laacher Hof         6.6         20.5         12.5         6.9         SFO         161         533         12.4         SFO           Silt loam         Swistal-Holm         6.3         7.9         6.9         22.3         6.74         2.85         SFO         161         533         12.4         SFO	CA 7.1.2.2.1/01 (M	- <u>006116-01-1</u> ) 1995	5			• • •	* L	K CF	~ Diosi			OUL	H.C.F.		
Sandy loam         Elm Farm/ Thurston         7.5         0.8         197         24         DPOP         514         C71         120         2670         577         592         10.7         SF0           Loamy sand         Pakenham         7.3         0.5         132         8.2         DFOP         574         190         13.0         SF0         6.38         212         13.7         SF0           CA 7.1.2.2.1/02 (M-006126-01-1) 1995	Silt loam	Höfchen	6.5	13.8	145	11.8	<b>DFOP</b>	\$ 98.1	j Co0.2		SFO	21.0	69.6	16.5	SFO
Loamy sand         Pakenham         7.3         0.5         132         8.2         DFQP         574         190         13.0         SFO         63.8         212         13.7         SFO           CA 7.1.2.1/02 (M-006126-01-1) 1995         5         5         5         5         6.9         SFO         6.9         SFO         7.2         SFO           Sandy loam         Laacher Hof         6.6         205         124         95         DEOP         125         446         7.4         5         5         SFO         161         533         12.4         SFO           Sandy loam         Maasen         5.9         584         271         40.6         506         205         447         7.8         500         401         133         1000         SBO         49.2         164         8.8         SFO           CA 7.1.2.2.1/03 (M-006127-01-1)         1995         6.3         DFOP         72.6         248         248         55         SFO         75.9         252         9.7         SFO           Sandy loam         Elm Farm/ Thurston         7.4         446         132         67         5FO         75.9         252         9.7         SFO <tr< td=""><td>Loam</td><td>Laacher Hof</td><td>6.8</td><td>32.6</td><td>196</td><td></td><td>DFQP</td><td>► 50.3 ℃</td><td>167_0</td><td>11.9%</td><td>SFQ</td><td>48,3 C</td><td>1605</td><td>10.8</td><td>SFO</td></tr<>	Loam	Laacher Hof	6.8	32.6	196		DFQP	► 50.3 ℃	167_0	11.9%	SFQ	48,3 C	1605	10.8	SFO
Loamy sand         Pakenham         7.3         0.5         132         8.2         DFQP         574         190         13.0         SFO         63.8         212         13.7         SFO           CA 7.1.2.1/02 (M-006126-01-1) 1995         5         5         5         5         6.9         SFO         6.9         SFO         7.2         SFO           Sandy loam         Laacher Hof         6.6         20.5         127         95         DFOP         422         6.9         SFO         161         533         12.4         SFO           Sandy loam         Maasen         5.9         84.4         271         \$10.6         OPCP         223         742         8.5         SFO         161         533         12.4         SFO           Sandy loam         Maasen         5.9         84.7         7.9         FOM         40         133         1000         SBO         49.2         164         8.8         SFO           CA 7.1.2.2.1/03 (M-006127-01-1) 1995         7.8         63         BFOP         24.8         248         595         SFO         75.9         252         9.7         SFO           Sandy loam         Flarem/ Thurston         7.4         446 <td>Sandy loam</td> <td></td> <td>7.5</td> <td>0.8</td> <td>197</td> <td>R4</td> <td><b>D</b>FOP</td> <td>10 SI.4</td> <td>2<b>9</b>71</td> <td>12.0</td> <td>08F0</td> <td>357.7</td> <td>e 192</td> <td>10.7</td> <td>SFO</td>	Sandy loam		7.5	0.8	197	R4	<b>D</b> FOP	10 SI.4	2 <b>9</b> 71	12.0	08F0	357.7	e 192	10.7	SFO
CA 7.1.2.2.1/02 (M-006126-01-1) 1995       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       X       Y       Y       Y       X       X       X       Y       Y       Y       X       X       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y       Y <thy< th="">       Y       Y</thy<>	Loamy sand	Pakenham	7.3	0.5	132	8,2%	DFOP	57:4	191,0	13.00	SFO	6318	212	13.7	SFO
Sandy loam       Laacher Hof       6.6       29       121       95       DEOP       125       446       74       860       122       406       5.7       SFO         Sandy loam       Maasen       5.9       84.4       271       10.6       0100       223       2742       8.5       SFO       161       533       12.4       SFO         Silt loam       Swistal-Holn       6.7       7.9       84.7       7.9       FOMC       40       133       1000       SFO       49.2       164       8.8       SFO         Clay loam       Albig       7.8       68       74.3       63       960       22.3       974       21.7       SFO       63.3       210       18.7       SFO         CA 7. 1.2.2.1/03 (M-06127-01-1) 1995	CA 7.1.2.2.1/02 (M	-006126-01-1) 1995	5		\$ \$	E.	- Orie	. A	20-	AU	Ň	TO ON I	r o		
Sandy loam       Laacher Hof       6.6       29       121       95       DEOP       125       446       74       860       122       406       5.7       SFO         Sandy loam       Maasen       5.9       84.4       271       10.6       0100       223       2742       8.5       SFO       161       533       12.4       SFO         Silt loam       Swistal-Holn       6.7       7.9       84.7       7.9       FOMC       40       133       1000       SFO       49.2       164       8.8       SFO         Clay loam       Albig       7.8       68       74.3       63       960       22.3       974       21.7       SFO       63.3       210       18.7       SFO         CA 7. 1.2.2.1/03 (M-06127-01-1) 1995	Silt loam	Höfchen	6.4	56.6	393	0 8.1 <u>°</u> C	FOMC	130 0	432	6.9	SFQ	135 @	447	7.2	SFO
Silt loam       Swistal-Hohn       6.7       7.9       84.7       7.9       FOMC       40       133       1000       SEQ       49.2       164       8.8       SFO         Clay loam       Albig       7.8       7.9       FOMC       40       133       1000       SEQ       49.2       164       8.8       SFO         CA 7.1.2.2.1/03 (M-006127-01-1) 1995       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.4       7.5       7.5       7.5       2.52       9.7       SFO         Sandy loam       Elm Farm/ Thurston       7.4       7.4       7.4       7.4       7.4       7.5       9.6       7.5.9       2.52       9.7       SFO         Sandy loam       Elm Farm/ Thurston       7.4       7.4       7.4       7.5       9.6       7.5.9       2.52       9.7       SFO         Sandy loam       Elm Farm/ Thurston       7.4       7.4       7.4       7.4       7.4       7.5       9.6       7.5.9       2.52       14.8       SFO         Sandy loam       Pakenham       7.0	Sandy loam	Laacher Hof	6.6		128	9 <b>\$</b>	DFOP		410				406	5.7	SFO
Sandy loam       Elm Farm/ Thurston       7.4       436       132       properties       74.8       248       248       248       248       252       9.7       SFO         Sandy loam       Pakenham       7.0       9.5       199       6.3       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Elm Farm/ Thurston       9.4       9.1       433       8.7       ØFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       75.2       16.4       SFO       103       342       10.8       SFO         Silt loam       Touffree@le       7.2       43.5       9.2       DFOP       Too few data points       Too few data points       SFO       14.6       SFO         Loam       Laudun       7.6       59.6       295       16.9       DFOP       17.8	Sandy loam	Maasen	5.9	JI 8.4	_ °271 _	\$10.6	DFOP	ات 223 ا	© 742			161		12.4	SFO
Sandy loam       Elm Farm/ Thurston       7.4       436       132       properties       74.8       248       248       248       248       252       9.7       SFO         Sandy loam       Pakenham       7.0       9.5       199       6.3       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Elm Farm/ Thurston       9.4       9.1       433       8.7       ØFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       75.2       16.4       SFO       103       342       10.8       SFO         Silt loam       Touffree@le       7.2       43.5       9.2       DFOP       Too few data points       Too few data points       SFO       14.6       SFO         Loam       Laudun       7.6       59.6       295       16.9       DFOP       17.8	Silt loam	Swisttal-Hohn	6.70	7.9 0	84.7		FOMC						164		
Sandy loam       Elm Farm/ Thurston       7.4       436       132       properties       74.8       248       248       248       248       252       9.7       SFO         Sandy loam       Pakenham       7.0       9.5       199       6.3       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Elm Farm/ Thurston       9.4       9.1       433       8.7       ØFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       75.2       16.4       SFO       103       342       10.8       SFO         Silt loam       Touffree@le       7.2       43.5       9.2       DFOP       Too few data points       Too few data points       SFO       14.6       SFO         Loam       Laudun       7.6       59.6       295       16.9       DFOP       17.8			7.8	<u>i</u>	74.5	<u></u> (0.5	<b>DFOP</b>	\$2.3	x 3074	¢21.7	<b>SFÓ</b>	63.3	210	18.7	SFO
Sandy loam       Elm Farm/ Thurston       7.4       436       132       properties       74.8       248       248       248       248       252       9.7       SFO         Sandy loam       Pakenham       7.0       9.5       199       6.3       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Elm Farm/ Thurston       9.4       9.1       433       8.7       ØFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Pakenham       7.0       11.2       247       9.2       DFOP       75.2       16.4       SFO       103       342       10.8       SFO         Silt loam       Touffree@le       7.2       43.5       9.2       DFOP       Too few data points       Too few data points       SFO       14.6       SFO         Loam       Laudun       7.6       59.6       295       16.9       DFOP       17.8	CA 7.1.2.2.1/03 (M		j p	Out to C	) 6		Obe	<u>} </u>		J. C.	0.		-		
Sandy loam       Pakenham       7.0       9.5       199       6.3       DFQP       72.6       241       5.2       SFO       73.2       243       4.0       SFO         Sandy loam       Elm Farm/ Thurston       9.4       9.1       433       6.7       9FOP       96.8       322       10.2       SFO       75.9       252       14.8       SFO         Sandy loam       Pakenham       7.0       112       247       9.20       DEOP       96.8       322       10.2       SFO       75.9       252       14.8       SFO         Sandy loam       Pakenham       7.0       112       247       9.20       DEOP       96.8       322       10.2       SFO       103       342       10.8       SFO         Silt loam       Touffree the       7.2       6.1       8.4       3.8       DPOP       22.6       75.2       16.4       SFO       21.3       70.7       14.6       SFO         CA 7.1.2.2.1/04 (M-006128-01-1) 1996       7.6       59.6       29.5       16.9       DFOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         Silty clay loam       Filetto       7.6	Sandy loam			^{₭46}		Ear	DEOP	<u>2</u> 4.8	²⁴⁸	6)2195	SFO	75.9	252	9.7	SFO
Sandy loam       Pakenham       7.0       11.2       2470       9.20       DEQP       96.8       322       10.2       SFO       103       342       10.8       SFO         Silt loam       Touffree the       7.2       0.1       88.4       3.8       DPOP       22.6       75.2       16.4       SFO       21.3       70.7       14.6       SFO         CA 7.1.2.2.1/04 (M-006128-01-1) 1996       CA 7.1.2.2.1/04 (M-006128-01-1) 1996       CA 7.1.2.2.1/05 (M-006129-01-1) 1996       Too few data points       Too few data points       Too few data points         Silty clay loam       Filetto       7.6       39.6       295       16.9       0FOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       Image: Second seco	Sandy loam	Pakenham	7.0	° 95 ∡0	້ 100 ຝ	6.3 \$	🚩 DFQP 🔨	1 /2.Q	241 V	5.2	SFO	73.2	243	4.0	SFO
Sandy loam       Pakenham       7.0       11.2       2470       9.20       DEQP       96.8       322       10.2       SFO       103       342       10.8       SFO         Silt loam       Touffree the       7.2       0.1       88.4       3.8       DPOP       22.6       75.2       16.4       SFO       21.3       70.7       14.6       SFO         CA 7.1.2.2.1/04 (M-006128-01-1) 1996       CA 7.1.2.2.1/04 (M-006128-01-1) 1996       CA 7.1.2.2.1/05 (M-006129-01-1) 1996       Too few data points       Too few data points       Too few data points         Silty clay loam       Filetto       7.6       39.6       295       16.9       0FOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       Image: Second seco	Sandy loam		2	<b>%</b> .	433	6.7		<u> </u>	•	7.95	SFO	75.9	252	14.8	SFO
Loam       Laudun       7.6       20       43.9       90.       DFOP       Too few data points       Too few data points         Silty clay loam       Filetto       7.6       59.6       295       16.9       DFOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       7.6       59.6       29.5       16.9       DFOP       30.9       103       17.7       SFO       28.9       96.1       19.1       SFO         Sandy loam       Nogarde Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO         Sandy loam       Nogarde Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO	2	0	7.00%	11,20	2470	9,20 ^{3,6}									
Loam       Laudun       7.6       20       43.9       90.       DFOP       Too few data points       Too few data points         Silty clay loam       Filetto       7.6       59.6       295       16.9       DFOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       7.6       59.6       29.5       16.9       DFOP       30.9       103       17.7       SFO       28.9       96.1       19.1       SFO         Sandy loam       Nogarde Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO         Sandy loam       Nogarde Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO			7.2	0.1°	\$8.4	3.8		22.6	75.2	16.4	SFO	21.3	70.7	14.6	SFO
Silty clay loam       Filetto       7.6       59.6       295       16.9       DFOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       7.7       21       93.3       3.9       DFOP       30.9       103       17.7       SFO       28.9       96.1       19.1       SFO         Loam       Laudun       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO         Sandy loam       Nogarofe Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO	CA 7.1.2.2.1/04 (M					• O	Ĺ,	<u></u>							
Silty clay loam       Filetto       7.6       59.6       295       16.9       DFOP       17.8       59.0       12.5       SFO       18.1       60.1       11.4       SFO         CA 7.1.2.2.1/05 (M-006129-01-1) 1996       7.7       21       93.3       3.9       DFOP       30.9       103       17.7       SFO       28.9       96.1       19.1       SFO         Loam       Laudun       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO         Sandy loam       Nogarofe Rocca       7.7       3.5       43.8       1.9       DFOP       28.8       95.6       3.5       SFO       28.5       94.8       3.3       SFO			J.G	20 ^{yr}	43.9	201							Too few c	lata points	
Loam         Laudun         Top         Open         State         DFOP         30.9         103         17.7         SFO         28.9         96.1         19.1         SFO           Sandy loam         Nogarobe Rocca         17.7         3.5         43.8         1.9         DFOP         28.8         95.6         3.5         SFO         28.5         94.8         3.3         SFO				~Q39.6	£\$ <b>2</b> 95		DFOP	17.8	59.0	12.5	SFO	18.1	60.1	11.4	SFO
Sandy loam         Nogarou Rocca         1.7         3.5         43.8         1.9         DFOP         28.8         95.6         3.5         SFO         28.5         94.8         3.3         SFO           Worst-case         596         430         223         742         161         533															
223 742 161 533		Laudun				·									
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Sandy loam					) ²⁰ 1.9	DFOP			3.5	SFO			3.3	SFO
$\mathcal{N}^{\mathcal{N}} = \mathcal{O}^{\mathcal{N}}$ A dependence: $ \mathcal{N}^{\mathcal{N}} = \mathcal{N}_{\mathcal{N}} =  \mathcal{N}_{\mathcal{N}} =  \mathcal{N}_{\mathcal{N}}$ No		NON KWO	brst-case.	5966						-					
EVEL OF THE P	_~	[©] [∞] _© ¢H dep	endence :	Kr N	8 ⁷			N	0			N	0	J	



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Table CA 7.1.2.	2.1-70: Summa	ary of n	nodelling	endpoin	ts for spire	oxamine	and met	abolites N	/101 ang@M	102		S. D. D.	e O	J'I'lle .	ind.
	Soil properties	6			Spiroxa	mine			€ M0	1	6.5°		M	02_0	
Soil type	Soil name	Crop (Y/N	pH (CaCl2)	In- divid. trial model- ling DegT ₅₀ (days)	Final model- ling DegT50 (days)	χ ² er- ror (%)	Kinet-	In- divid. Trial model Ing DegT ₅₀ (dags)	Final model- ling Org T50 (days)	x ² er- ron⊘ x ² (2%)	Kinet- ies	In- divid frial model ling DegT 50 (days)	[™] ling Deg¶3₀ (days)	Pror (%)	Kinet- ics
CA 7.1.2.2.1/01		1	-			F G	<u>Or</u>		3 I Con	A.	10 ⁴⁰	J.	-Der		
Silt loam	Höfchen	N	6.5	38.7	54.9	kl X	DFQP ³	52.3	72.10	5.2 0		52.3	76.5	9.6	SFO
Loam	Laacher Hof	Y	6.8	44.1	<u>چ</u> 50.2	10.1	SD Ö	\$ <u>9</u> .2	<u>9</u> 90.4	f0.5	SKO	66.3	96.5	9.7	SFO
Sandy loam	Elm Farm/ Thurston	Y	7.5	59 <b>9</b>	78.6	8.4.C		48.9	65.30	3.0	- O, be	56.7 J	£69.7	4.1	SFO
Loamy sand	Pakenham	Y	7.3	<b>43.6</b>	045.1	ð 10.4	<b>SFO</b>	S9.5	<b>A</b> .9	DS.1	<b>SPO</b>	66.0	72	15.8	SFO
CA 7.1.2.2.1/02		í		-10 ³		0		·	¥ <u>,</u> 6	<u></u>		69			
Silt loam	Höfchen	N	6.4	<b>8</b> .0	1 2 m	<b>\$</b> .2	SOO	29.31	L DEL	5.0	SFO y	112	_2	6.3	SFO
Sandy loam	Laacher Hof	N	9 6.6	57.2	<u> </u>	4. <u>3</u>	SFO 💒	ۍ 167 🖉	<u><u><u> </u></u></u>	5.6	<b>₿</b> Ť0	140	_2	4.8	SFO
Sandy loam	Maasen	N	5.9	<u>, 66.4</u>	60.4	J. 1.0	STON.	No fit	1,000 default	ANK 9	NA	196	196	12.2	SFO
Silt loam	Swisttal- Hohn	N		473	4731	10,85	SFQ	53.8	, 53.8 ⁽¹⁾	11.2	SFO	64.4	64.4	10.1	SFO
Clay loam	Albig	N _	7.8	33.7	× 33.7 .	8.2	<b>Ø</b> FOP	O¥5.9	*A5.9	22.2	SFO	70.4	70.4	16.5	SFO
CA 7.1.2.2.1/03	(M-006127-01-1	) 1995	- <u>6</u> 7	OCT.	1 0 kr	, OL	300	× C	1						
Sandy loam	Elm Farm/ Thurston	Y	7.4	C 61.0		8.6	SFO	39.3	_2	8.3	SFO	61	_2	10.5	SFO
Sandy loam	Pakenham	Y	. 20	426	10 ³	7.3	SFO	101.0	_2	4.6	SFO	57.7	_2	3.7	SFO
Sandy loam	Elm Farm/ Thurston	Y	7.4			7.0	DFOP	96.2	_2	10.5	SFO	98	_2	10.0	SFO
Sandy loam	Pakenham	© [®] Y	3.0°	A9.5	. Called to	× 2.0	SFO	96.2	<b>_</b> ²	9.6	SFO	97.3	_2	11.0	SFO
Silt loam	Touffreyil	Y	7.2 °C	16.1	2 16.1	4.8	HS	28.9	28.9	11.6	SFO	28.1	28.1	9.8	SFO
	10ume vite	* 22		e. V	Dile										





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												O.D.O.		i Dl	
	Soil properties				Spiroxa	mine			- Site	)1	1	OS IN	M	12 ^{1/1}	n <u>ò</u> .
Soil type	Soil name	Crop (Y/N	pH (CaCl ₂ )	In- divid. trial model- ling DegT ₅₀ (days)	Final model- ling DegT50 (days)	χ ² er- ror (%)	Kinet- ics	In- divid. trial model- ling Deg Lo (days)	Final model- ling	χ ² er 🛇	e ^{f^kt Kinet- ics}	In- divid. trial model- ling DegTQ (days)	Mi Final model Jing Deg T50 (days)	$\gamma^2 \text{ er-}$	Kinet- ics
CA 7.1.2.2.1/04		/				105	, _e ęj		Too @w ob	<u>* 201</u>	<u></u> ð	<u>,                                     </u>		Ĵ,	
Loam	Laudun	Y	7.7	56.5	47.4	Q2.2	SFO.	L. C	Too Ow ob	servations	Offer		Too fee ob	servations	5
Silty clay loam	Filetto	Y	7.6	49.3	49.30	17.8		17.8	59.0	12.5	≫SFO	27.7	* 27.7	5.1	SFO
CA 7.1.2.2.1/05				20.7	\$ _2 _2		sfo		103	Q.7.7	~		171	( )	FOMO
Loam	Laudun	N	7.7			12.7	SFO	\$0.9	3 × 103	<u>g</u> @r/./	OŤØ	1,99	P31	6.3	FOMC
Sandy loam	Nogarole Rocca	Ν	7.7	2304	23.4	\$12.7 ×	SFO	28.80	95,60 ⁰ 66.2/ 89% \$	35011	SFQS	44.3 J	44.3	5.3	SFO
NA = not applicable ¹ Sites at the sar ² Geomean of re ³ expert judgme * Geomean for a	ne location are tree eplicate sites given nt ill plots and non-ci Lt TRA Lt TRA Lt AlexTRA Lt LAELTRA Lt LAELTRA LAELTRA LT LAELTRA LT LAELTRA LT LAELTRA LT LAELTRA		Geometric phi dependent plicates due t replicates due t replicates due coP1 coP1 coP1 coP1 coP1 coP1 coP1 coP1 coP1 coP1	to trials bei to to to trials bei to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to to t	42381 Tho Tho Ing the Came I Is Is The Came I Is The Came I Is Is The Came I Is Is The Came I Is Is Is The Came I Is Is Is Is Is Is Is Is Is I				95,60 1 66.2/ 898 9 1 16 1				93.8 No		



#### III. Conclusions

Persistence/trigger and modelling endpoints (DT₅₀ and DT₉₀) representing the degradation rate of spiroxamine in field soil dissipation studies were calculated in accordance with FOCUS (2014) and EFSA (2014) guidance.

The spiroxamine persistence/trigger DT₅₀ values ranged from 0.5 to 59.6 day and DT₉₀ values ranged from 43.5 to 433 days. The spiroxamine modelling DT₅₀ values (at 20°C and pF 2) ranged from \$6.1 to 133 days, with a geometric mean of 42.9 days. If not including cropped trials, modelling DT values (at 20°C and pF 2) ranged from 23.4 to 78 days, with a geometric mear of 43.8 days.

M01 persistence/trigger DT₅₀ values ranged from 17, \$ to 223 days and DT₉₀ values ranged from 59 742 days. Modelling DT₅₀ values ranged from 23.440 1,000 days (default), with a geometric mean of 66.2 days. Formation fraction was not determined as formation may have been affected by photolytic factors according to EFSA (2014). If not including cropped trials, modellingDT₅₀ values at 2020 and pF 2) ranged from 23.4 to 1,000 days, with a geometric mean of 82% days

M02 persistence/trigger DT₅₀ values ranged from 21 to 161 days and DT₉₀ values ranged from 696 to 533 days. Modelling DT₅₀ values ranged from 27.7 to 196 days, with a geometric mean of 69. K days. Formation fraction was not determined as formation may have been affected by photologic factors according to EFSA (2014). If not including cropped trials, modeling DF50 values (at 20°C and pF 2) ranged from 44.3 to 196 days, with a geometric mean of 93.8 days

#### Assessment and conclusion by applicant

Study meets the current guidance and the requirements in 283/201

The study was conducted to guideline(s) FOCUS 2006, 2014 (required guideline). The study is considered valid to assess best fit and model ing DD% values for spiroxamine and associated metabolites in field soil studies

M

### CA 7.1.2.22

Soil accumulation studies

Soil dissipation studies conducted under Point CAO.1.2.2 show that DisT90_{field} for spiroxamine and metabolites M01 and M02 can exceed me year, Additionally in the absence of further information DisT90field for spiroxamine metabolite M03 is also assumed to exceed one year. The potential for accumulation of spiroxamino and metabolites M01, M02, M03 and M06 in soil is addressed by consideration of worst-case wil accumulation PECs, see @P 9.19.

Soil accumulation studies are therefore pot considered necessary.

# dsorption and desorption in soil

#### 7.1.3.1 Adsorption and desorption

Use of plant protection products containing the active substance spiroxamine will result in contact with soil, therefore the soil sorption characteristics of the active substance and major metabolites (as defined under Point CA \$4.1) are investigated in laboratory studies according to the data requirements laid down in Compossion Regulation (EU) No 283/2013 under Points CA 7.1.3.1.1 and CA 7.1.3.1.2, respectively.

### **Overview**

The mobility in soil of spiroxamine and its degradation products relevant for assessment was studied by batch equilibrium tests on a variety of different soils. A summary of the resulting modelling soil sorption parameters are presented below:



 Table CA 7.1.3.1-1:
 Overview of soil sorption modelling parameters for spiroxamine and as ciated metabolites

•			
Compound	Kfoc A	1/n ^B	Sorption dependant of
	[mL/g]	[-]	Soil pH (Y/N)
spiroxamine	4111 (geomean, n=8)	0.892 (average, n=8) 🔔	
M01	3271 (geomean, n=4)	0.848 (average, n=4)	N N
M02	2695 (geomean, n=4)	0,8₽8 (average, n₽)	
M03	1677 (geomean, n=4)	0.900 (average, 1954)	
M06	Study on-going	Study on-going	Study op-going
A Geometric mean			
B Arithmetric mean			

The adsorption and desorption of metabolites of spirox amine have been investigated in three studies (KCA 7.1.3.1.2/01 to KCA 7.1.3.1.1/03) which were evaluated during the previous EU review. Sorption of M01, M02 and M03 was established in four son types and the outcome of the studies reviewed for reliability using the EFSA 106 checklist v2.0. It was concluded that despite some minor deviations the outcome of the adsorption/desorption studies were reliable and suitable for use in the assessment. Some differences between the calculated Ko values and those reported were noted, but this was attributed to the use of averages in the original calculations. Since differences were minor, for consistency the reported values from the report were used in the fak assessment.

Adsorption of M01 was investigated in 4 different soils with K for ranging from 1237 to 10511 L/kg ( $\blacksquare$ , 1996). Adsorption was shown to be generally correlated with organic carbon content, and M01 (spiroxamine-desethy) exhibits mean in the mobility in soil according to the McCall mobility classification. No significant correlation was observed between soil sorption parameter K_{foc} with soil pH for M01 (spiroxamine-desethyl) ( $B^2=0.102$ ), therefore no pH dependence was concluded. The geomean of the four soils was considered appropriate for use in the risk assessment as previously concluded (EFSA Journal (2010);8(10):1719)).

Adsorption of 402 was investigated in 4 different soils with Ktoc ranging from 916.7 to 8993.6 L/Kg (Fent, 1996b). Adsorption was shown to be generally correlated with organic carbon content, and M02 (spiroxamine-despropyl) whibits medium to immobil@mobil@mobil@y in soil according to the McCall mobility classification. No significant correlation between soil soption parameter  $K_{foc}$  with soil pH for M02 (spiroxamine-despropyl) was observed (R²=0.005), therefore no pH dependence was concluded. The geomean of the four soils was thus considered appropriate for use in the risk assessment as previously concluded (EFSA Journal (2010), 8(10), 1719)).

Adsorption of M03 was also determined in A different soils, with the  $K_{foc}$  ranging from 350.5 to 24892.5 L/Kg (Fent, 1997). Adsorption was shown to be generally correlated with organic carbon content and M03 (spiroxamine-N-oxide) exhibits ordination immobile mobility in soil according to the McCall mobility classification. No significant correlation between soil sorption parameter  $K_{foc}$  with soil pH for M03 (spiroxamine-N-oxide) was observed ( $R^{2}$  0.331), therefore no pH dependence was concluded. The geomean of the four soils was thus considered appropriate for use in the risk assessment as previous concluded (EFSA Journal (2000);8(40):1710)).

One further study is being conducted to provide soil sorption properties for metabolite M06 (spiroxamine-acidy and will be provided as soon as available. As such, in order to provide a basis for the risk assessment, an stimated  $K_{to}$  value of 3.2 L/Kg for M06 for use in the preliminary risk assessment was obtained from KocWIN. This will be updated upon completion of the M06 OECD106 study.

The high sorption displayed by spiroxamine and its metabolites is reflected in the outcome of column leaching dudies investigating the leaching behaviour of aged residue of spiroxamine in soil. These studies demonstrated that in soil column studies, aged residues of spiroxamine did not significantly leachate to the column percolate with only 0.2 %AR being found in the leachate. The major residue in the leachate



was found to be M03 (N-oxide) representing only 0.03% of the applied radioactivity in column leachates. Overall, leaching behaviour of spiroxamine (including individual isomers) or its major soil metabolites is not envisaged.

## CA 7.1.3.1.1 Adsorption and desorption of the active substance

The adsorption and desorption of spiroxamine has been investigated in two studies (KCA 7.1.3.1.4)/01 and KCA 7.1.3.1.1/02) which were evaluated during the previous EU review.

The applicant considers the adsorption endpoints from baren equilibrium studies are appropriate for use in risk assessment.

			"O *	s is	SY U
Substance	<b>Report reference</b>	Document no.		Comment	ê, û
Spiroxamine	KCA 7.1.3.1.1/01	<u>M-00618901-2</u>	~ Submitted	for first appoval of	f spirox
			omine, 1999.	Reviewed under U	P. Consid-
				valid and acceptabl	A
Spiroxamine	KCA 7.1.3.1.1/02	<u>M-006186-02-1</u>	Submitted	for first renewal of	spirox- 🖉
			amme, 2010.	Reviewed under U	P. Consid-
			Concered?	walid and acceptabl	le. S
					$\odot$

The resulting soil sorption parameters for the active substance spirox mine are sumpharised below:

	amine		<u> </u>	~		Â.	
Study	Soil mame		on properti	es 🔊 🕺	Spil so	option para	meters
	~ ~	<b>T</b> øxtureÖ	p B A		K _f	Kfoc	1/n
	O	ç v		<u>(%)</u>	O(L/kg)	(L/kg)	
KCA	Laacherhof	Loaspy sand	~ 6.4 °	¢28	12.78	710	0.785
7.1.3.1.1/01	Laacberhof Č AXSa (0- Socm)	sand			Z.		
<u>M-006189-010</u>	Standard Soil	Sand	5.3 5 7 7 7 7	× 65°	<i>Q</i> 4.61	659	0.768
	Hoetchen "un	Silotoam	5.8	2.4	44.98	1874	0.831
* ¥	Clay soll	Silty day	1.4 k	<u>Ø</u> 6	41.07	6417	0.885
	Laacherhod A&Xa (30-60 cm	boamy, sand		0.3	7.25	2415* ^B	0.833* ^B
KCA 7.1.3.1.102	Vero Beach	Stand	\$ 6.70 ~~	0.2	8.55	4276* ^C	1.06* ^C
<u>M-006186-02-1</u>	Grape Vine-	Sands loan	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	0.45	14.47	3216	1.05
	Howe C Wolf Roach Staney K	Sandy	D [×] 67	1.12	15.09	1347	1.02
Ő	Wolf Reprch	©″Loam [™]	7.8	0.97	381.65	39346	1.02
J.	🗶 Stanley 🔬	SiltyClay	5.1	1.05	892.59	85008	1.01
Ű Å	<u> </u>	<i>v</i>				4111	0.892
19 D						(geo-	(mean,
	A A A					mean,	n=8)
	10 27					n=8)	

## Table CA 7.1.3.1.1-1: Overall summary of Freundlich soil adsorption parameters for spirox-

* Value X cluded from calculations (i.e. geometric mean and arithmetic mean)

A pH (9.01M CaCl₂) unless otherwise stated

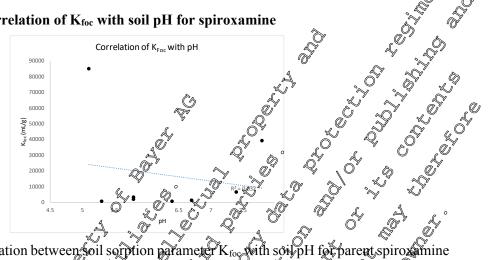
B Excluded for modelling endpoints due to being sub-soil

C Excluded for modelling endpoints as oc<0.3%



The correlation for the active substance spiroxamine of soil sorption parameter K_{foc} with soil pH is presented below:

#### Figure 7.1.3.1.1-1: Correlation of K_{foc} with soil pH for spiroxamine



There was no strong correlation between soil sorption parameter K_{fo}, with soil pH for parent spirovamine (R²=0.032), therefore no pH dependence was concluded (note the dissociation constant pKa, value for parent spirovamine is 6.9, see CA 2.8).

Data Point: KCA 7.1.3.1.101 5 6 6
Report Author:
Report Year: $0^{\circ}$ 1995 $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$
Report Title: Adsorption/Desorption of KNGG 4168 on soils
Report No: $\mathcal{O}$ $\mathcal{O}$ PF4038 $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$
Document No $\underline{N}$ <u>Mo00618001-2</u> $\underline{N}$ <u>No 20618001-2</u>
Guideline(s) followed in EPA Ref.: 163-1, Learbing and Adsorption/Desorption
study: 🔪 🗸 🗸 👘 Ö
Deviations from current Yes (refer below)
test guideline: Some minor deviation(s) not relevant for the reliability of the study (described in
Study symmatry
Previous evaluation: A yes, valuated and accepted
DAR (1995), RAR (2010), RAR (2017)
GLP/Officially recoge Ses, conducted under CLP/Officially recognised testing facilities
nised testing facilities: D A R R
Acceptability Yes 2

#### Executive Summary

The adsorption and desorption of [cyclohexy[-1-¹⁴C]-spiroxamine on four European soils and one European subsoil was studied using the batch equilibrium method with a tiered approach.



Parameter			Soil		
Soil Designation	Laacherhof AXXa (0- 30cm)	Standard Soil 2.1	Hoefchen "im Tal"	Clay soil LUFA Speyer	Laacherhof AXXa (30-60 cm)
Textural Classification (USDA)	Loamy sand	Sand	Silt loam	Siltoclay	Loandy sand
pH (CaCl ₂ )	6.4	5.3	5.8	7.4	63
Organic carbon (%)	1.8	0.7	م 2.4	Ç 0.64 🔬	× _013 _

Preliminary tests were performed to determine the appropriate soil:solution ratios and equilibrium time and to evaluate stability of the test substance in CaCl solution (without soil, potential for sorption of the stability of the test substance to test vessels and any effects of the melusion of a brocide in solution.

In the preliminary tests, soil:solution ratios of 1:10 and equilibrium time 24 hours was determined for all soils and the subsoil. After shaking the test substance in CaCle without soil recoveries of 94.3 - 97.1% AR were reported, indicating sorption to test sessels was per occurring. Stability of spiroxamine was also monitored in CaCl₂ solution without soil and results show 99% AR present as ancharged spiroxamine after 9 days.

Freundlich isotherm tests were performed with all soils using the indirect and paratlel methods. A soil:solution ratio of 1:10, and 24 hours equilibrium time for adsorption and desorption were used for all soils. For the adsorption step, appropriate solutions of the test substance were applied to the samples and the samples were shaken for 24 hours at  $20 \pm 16$ C in the darl Following the adsorption step, the samples were removed from the shaker, centrifuged, and the adsorption supernatants removed. Chromatographic analysis of supernatants of adsorption from Standard soil 2.1, Hoefchert? im Tal", Clay soil LUFA Speyer at 5.0 mg/L show >90% AR identified as spiroxamine. Chromatographic analysis of supernatants of adsorption and 0.5 mg/L also showed >90% AR identified as spiroxamine.

For the desorption step,  $\odot 20$  m/s volume of fixesh  $\odot 0$  M  $\bigcirc aCl_2$  solution was added and the samples were shaken for a further 24 hours at  $20 \pm 1$  C in the dark. Following the desorption step, the samples were removed from the shaker, centrifuged, and the desorption supernatants removed. The desorption supernatants were analysed by LSC. The soil samples were combusted in a sample oxidiser and analysed by LSC to determine the radioactivity present. Chromatographic analysis of supernatants of desorption in the subsoil Laacherhof A X a 30-60 cm at 5.0 and 0.5 mg/L also showed >90% AR identified as spiroxamine.

Mass balances ranged from 81.898.8% AR. The amount of Fadioactivity adsorbed on the soil at adsorption equilibrium ranged from 25.0-93.6% AR. After the adsorption phase, 50.67 - 82.44% AR was adsorbed to Taacherhof A Xa 0-30 cm soil, 24.93 - 60.70% AR adsorbed to Standard soil 2.1, 81.86 - 93.61% AR to Hoefchen im Ta 2 , 81.64 - 95.90% AR.

Freundlich adsorption coefficients (Kf) ranged from 4.61-44.98 L/kg. When normalised to organic carbon, Kreundlich adsorption coefficients (Kfoc) ranged from 658.8-6417.1 L/kg, indicating that spiroxamine exhibits low mobility in soft according to the McCall mobility classification (McCall et al 1981⁷). The 1/n values canged from 6768-0885, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range. The OECD 106 Checklist (v2) was used to evaluate the study however, all final parameters are taken from the study report. The evaluation confirmed acceptability for all soils according to the quality criteria and therefore acceptable for regulatory use.

⁷ McCall P.J., Laskowski D.A., Swann R.L. and Dishburger H.J. (1981). Measurement of sorption coefficients of organic chemicals and their use, in environmental fate analysis, in Test Protocols for Environmental Fate and Movement of Toxicants. Proceeding of AOAC Symposium, AOAC.



Soil	Laacherhof A XX a, 0-30 cm (Loamy sand)	Standard soil 2.1 (Sand)	Hofchen "im Tal" (Silt loam)	Clay soil LUFA Speyer (Silty clay)	Laacherhof A XX a, 30-60 cm (Loamy sand)
OC (%)	1.8	0.7	2.4	0.64 ≫	
pH (CaCl ₂ )	6.4	5.3	5.8	7.4C	AG.3
$K_{f}(L/kg)$	12.78	4.61	44.98	41.07	7.25
K _{foc} (L/kg)	709.9	658.8	1874.0	6417.1	0 [°] 2415
1/n	0.785	0.768	0,831	0.885	0.893
R ²	1.000	0.999	<b>A</b> .000	Ø 1.000 (	
A. Materials		I. Materials	and Methods *		
. Test Items		Ő,			
Test substance:	[cy	clohexy $fr^{-14}C$	piroxamine	A 6ª .	
Lot/Batch No.:	755				
Specific activity	y: 2.5	MB@mg			°∼y ×
Radiochemical j	purity: 🔊		O" ~ O"		°
Structure:		enotes position or	The second secon		
2. Test System (s	soil) 🔬 🖉		Ô,	ý,	

#### A. Materials

#### 1. Test Items

2. Test System (soil) Four Entrepean soil th contracting organic carbon, pH and clay content were used Four Exoppean soils and one of b soil Š Ô K. 0 Ô

## Table CA 7.1.3. 1.1-2: Physice-chemical properties of test soils

Parameter			Soil		
Soil Designation	Laacherhof QXXa (0-	Standard Soil	Hoefchen "im Tal"	Clay soil LUFA Speyer	Laacherhof AXXa (30-60
Geographic Location	30cmr)				cm)
City	Monheim	Germany	Burscheid	Südpfalz	Monheim
Country			Germany	Germany	Germany
Textural Classification	Loamy sand	Sand	Silt loam	Silty clay	Loamy sand
$\begin{array}{c} (\text{USDA}) & & & & \\ \text{Sand} & & & & \\ \text{Silt} & & & & \\ \text{Chas} & & & & \\ \text{Chas} & & & & \\ \end{array}$	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	89.4	3.6	15.0	68.4
Silt Silt Char (%)	S //	10.5	80.8	42.3	19.3
Chay (%)	5.0	0.1	15.6	42.7	12.3
рН С					
in H ₂ O	7.0	5.9	6.0	7.6	7.7
in CaCl ₂	6.4	5.3	5.8	7.4	6.3



Parameter			Soil		
Soil Designation	Laacherhof AXXa (0- 30cm)	Standard Soil 2.1	Hoefchen "im Tal"	Clay soil LUFA Speyer	Laacherhof [©] AXXa (30-60 cm)
Organic Matter (%) *	3.1	1.2	4.1	<u>j</u> ĝ	Ø.5 D
Organic carbon (%)	1.8	0.7	2.4	<b>W</b> .64	0.3
Cation Exchange Capacity (meq/100 g)	8.0	5.0	10.0	21.1	

Calculated by multiplying organic carbon content by 1.724 (not reported)

#### **B. Study Design**

#### 1. Experimental Conditions

The test system for adsorption and desorption of spiroxamine of four European softs and one European Š subsoil consisted of Teflon centrifuge tubes with screw caps

In preliminary tests, the adsorption of the test item to the test system surface, the optimal soil to solution ratio, the appropriate adsorption and desorption equilibration omes and the stability of the test item in CaCl₂ solution (without soil) were determined.

Freundlich isotherm tests were performed with all soils using the indirect and parallel methods. A soil:solution ratio of 1:10, and 24 yours equilibrium time for adsorption and desorption were used for all soils. Solutions of the radioabelled test substance in accounting were prepared and diluted with 0.01 M CaCl₂, such that test substance application achieved concentrations of 4.459-4867 (two application solutions made for highest concentration as initial solution volume was not sufficient for all soils), 0.441, 0.047 and 0.0097 mg/L. The volume of organic solvent added was not reported (but assumed to be within acceptable limits). Õ  $\bigcirc$ 

2 g dry weight of sod was transferred into centrifying tubes and 20 mLOf 0.01 M CaCl2 containing test substance were applied to the samples. The samples were then shaken for  $\mathbb{Z}4$  hours at  $20 \pm 1^{\circ}$ C in the dark. For the desorption step, 20 mL volume of fresh 0.01 MCaCl solution were added and the samples were shaken for a further 24 bours under the same conditions. After the adsorption step, a representative supernatant from each soil was subjected to chromatographic analysis by TLC.

Adsorption phase & &	
Parameter	Description
Soil condition	Soils were air-dried and sieved to 2 mm
Soil sample weight	2 g (dry weight)
Equilibration Flution	No pre-equilibration conducted
Control (preliminary experiment)	No soil test item in 0.01M CaCl2 only)
A sominant application fatters	0,01,0.05, 0.5 and 5 mg/L (4 concentrations)
Test item concentration	Measured concentrations (LSC) in test solution: 4.459- 4.867 (two application solutions made for highest concen- tration as initial solution volume was not sufficient for all soils), 0.441, 0.047 and 0.0097 mg/L
Identity and concentration of co-solvent	Not reported for dosing stock Study media – 0.01M calcium chloride
Soil: Solution atio	1:10



		Description
Number of repli-	Control	Duplicate
cates	Treatments	Duplicate
	Time	24 hrs
Equilibration condi-	Temperature	20±1°C
tions	Dark	In the dark
	Shaking method	Overhead shaker
Method of separation	of supernatant	Centrifugation
	Speed	Not reported for main test, preliminary test cemirifuged at >1700 g
Centrifugation	Duration	Not reported for main test or reliminary test centrifuged for 20 mins
	Method of separating supernatant	Supermatant was carefully decanted.
Desorption phase		
Parameter		Description y y y a g
Soil samples from ads	sorption phase used	Yas 2 2 2 2 4
state/adsorbed amoun		Orangeo from 49.76 to 5.90% (reported for definitive test). See OECD 106 Checklist below for furthe details for each solv.
Equilibrium solution a treatment for desorpti	and quanticy used oper (	The decanted solution was replaced by fresh aqueous 0.01 M CaCl ₂ solution
Soil: Solution ratio		
	Control &	Duplicate D
Number of reploates	Treatments O	Duplicate ^O
Number of reploates	Treatments &	Duplicate 2
	Jime 9 A	24 hrs 0 0 0
Number of reploates Desorption Equilibra- tion conditions	Time J	24 hrs 7 20+8C 7 7
Desorption Equilibra-	Time A Temperature A Dark & A	24 hrs 0 0 0
Desorption Equilibra-	Time Temperature Temperature Temperature	$24 \text{ hrs } 0$ $20 \pm \text{SC} \qquad 5$ $\text{In the dark} \qquad 5$
Desorption Equilibra- tion conditions	Time Temperature Temperature Temperature	20±1°C 2° In the dark 2° Overhead shaker
Desorption Equilibra- tion conditions	Time Temperature Dark Shaking@tethod ofQupernatant	24 hrs 2 20+5C Ir the dark Overhead shaker Centrifugation Not reported for main test, preliminary test centrifuged at

## 2. Analytical Proceedines

After each adsorption an desorption stop the aqueous supernatant was separated from the soil by centrifugation and the amount of piroxamine in the supernatants was analysed by liquid scintillation counting (LSC). Are liquet of supernatant from the highest concentration (and 0.5 mg/L nominal for Laacherhof XXa 90-60cm) for each soil was also analysed by normal-phase TLC using a mobile phase of acetonitrie/water/triethylamine (80:18:0.5, v/v/v) or chloroform/methanol/methylethylketone (6:2:1, v/v) and a Bio Imaging analyser, quantified with BioAnalyze Version 3.0.

The partition of the test item in the adsorption and desorption batch equilibrium experiment was determined based on the radioactivity content in the supernatant only (i.e. the indirect method). After the



desorption step, the soil was air-dried and the radioactivity content determined by combustion/LSC to establish the material balance.

Parental mass balance was determined >90% by TLC analysis of the supernatant.

Adsorption and desorption isotherms were calculated by linear regression analysis of the adsorption or desorption data according to the Freundlich equation.

Additional information on stability of spiroxamine in CaCl₂ solution (without soil) was determined in the preliminary tests, with >99% of radioactivity confirmed as spiroxamine using the same TLC conditions as described above after 9 days in solution.

The limit of detection (LOD) was not specified in the report; however, the concentrations of the tes substance used are sufficient to allow adequately accurate measurements of levels of the test substance

#### **Results and Discussion** II.

A. Results of preliminary tests Soil:solution ratios of 1:10 were also determined for both adsorption and desorption phases with an

O Shaking an aqueous solution of the test substance in the absence of soil gave recoverv of 94.3 to 97.1% AR indicating that adsorption to the sest vessel was not occurring

was monitored in a prefiminary test, giving Stability of spiroxamine in CaCl₂ solution (without sol) >99% as unchanged spiroxamine.

#### B. Transformation of test substance

Stability of spiroxamine during the isotherm determinations was monitored by TOČ analysis of the supernatant for all soils, showing >90% AR identified as spinoxamine.

Ò

C. Findings Mass balances ranged from 81.4.98.8% AR. The amount of radioadivity adsorbed on the soil at adsorption equilibrium ranged from 25.0-93.6% dR.



	(mean values) for spiroxamme									
Soil	Concentration	Concentration	Concentration	Adsorption	Mass	Â,				
	initial	supernatant	soil	percentage	balange	F				
	(mg/L)	(mg/L)	(mg/kg)	(%)						
Laacherhof A	0.010	0.002	0.080	82.44	87.68					
XXa, 0-30 cm	0.047	0.010	0.365	<u>7</u> 8.58	\$94.3 <b>4</b> \$	わ				
(Loamy sand)	0.441	0.145	2.960	\$67.11	× 98 2 ×	3				
	4.460	2.200	2.595	50.67	97.88	. O				
Standard soil	0.010	0.004	0.060	Q 60.70 . Ø	\$6.93	Ś				
2.1	0.047	0.021	∮ 0.260 L	55.29	Q 89.06	 √				
(Sand)	0.441	0.267	1.740 Q	°39.45	ر 97 <b>.8</b> 7 م	•				
	4.460	3.347	11.125	<u>39.45</u>	<b>98.75</b>					
Hofchen "im	0.010	0.001	∘ 0.09 <b>0</b> °	2 <b>9306</b> 1 2	× 87.27 ×					
Tal"	0.047	0.004	0, 435	92.69 © 88.38	90,82					
(Silt loam)	0.441	0.051	J 39895	© 88.38	∽ 9 <b>;</b> ,74 "€°					
	4.460	0,809 ~	\$6.505	<u>1</u> 81-86	<b>\$5.68</b>					
Clay soil LUFA	0.010	Ø.001.	0.020	99.38	<b>95.68</b> 81.82					
Speyer	0.047	0.006	× 0,4¥0 ×	88.22 V	\$ 84.98					
(Silty clay)	0.441	0.078	3:685	مَنْ 83. <b>56</b> ا	\$ \$3.59					
	4.460	0.820	36.395	81661 🔊	<u>م</u>					
Laacherhof A	0.010	\$ \$0.004	0.069	266.27	88.24					
XXa, 30-60 cm	0.047	°∼ 0.020	°° 0,0270 ÅS	57.53	94.11					
(Loamy sand)	0.441	(k) 0. <b>236</b> "(k)	2.045 <i>K</i>	× 46.43	98.45					
	4.868	) <u>2</u> 982 V	18.855	\$ 38774	94.51					

Table CA 7.1.3.1.1-3: Concentrations at adsorption equilibrium and recovery of radioac	tivity
(mean values) for spiroxamine	0

Bold values used to calculate the percept loss

Mass balance (determined as total radioactivity) Calues about are after the desorption step Α

For the four topsoil Laacherhot XXa 9-30cm, Standard soil 2.1, Hofcher "im Tal" and Clay soil LUFA Speyer), Freundlich adsorption coefficients (K) ranged from 4.61-4498 L/kg. When normalised to organic carbow, Freundlich adsorption coefficients (K_{foc}) ranged from 658.8-6417 L/kg, indicating that spiroxampe is likely to exhibit low mobility in soft The Feundlich exponent 1/n values ranged from 0.768-0.885, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.

For the subsoil (Laacherhof AXXa, 30-60 cm), a Freundlich resorption coefficient of (K_f) 7.25 L/kg was calculated, with Freundrich accorption coefficient  $(K_{foc})$  of 2415.3 L/kg when normalised to organic carbon. The Freundlich exponent 1/n values of 0.833 indicates that the concentration of the test item affects its adsorption behaviour in the examined concentration range. In comparison to the topsoil equivalent, while operall sorption is lower, it is greater than expected indicating sorption may not be solely related to organic carbon content

Soil C	Laacherhof & XX a, 0-30 cm (Loamy sand)	Standard Soil 2,0 (Sand)	Hofchen "im Tal" (Silt loam)	Clay soil LUFA Speyer (Silty clay)	Laacherhof A XX a, 30-60 cm (Loamy sand)
OC (%)		≈♥0.7	2.4	0.64	0.3
pH (Ca )	6.4	5.3	5.8	7.4	6.3
$K_{f}(L/kg)$	A12.78	4.61	44.98	41.07	7.25
K _{for} (L/kg) 1/k	709-9	658.8	1874.0	6417.1	2415.3
1/10	0.985	0.768	0.831	0.885	0.833
$R^2 \sim O^{\nu}$	1.000	0.999	1.000	1.000	1.000

Table CA 7.1.3.1.1.4. Freundlich adsorption coefficients for spiroxamine



#### D. Evaluation of the Data according to EFSA Evaluators Checklist

The results of the determination of the Freundlich Isotherm were analysed using the Excel-sheet provided by EFSA (summarised in Table CA 7.1.3.1.1-6). The concentrations in the supernatant and the soil as given in the report were used as input data. Individual replicate concentrations were used in the calculation. Individual replicate concentrations were not available, so mean values as given in the report have been used in the calculation and as the adsorption isotherms were conducted with only 4 concentrations the confidence intervals were calculated by added formulae.

Relevant quality checks were performed to evaluate the acceptability of the study. For all soils these checks confirmed that the mass balance was generally acceptable, as although the lowest concentration samples had mass balances <90% the magnitude of difference from 90% was small and not considered to affect the outcome of the study (full range of mass balance was 9.8-98, 8%). The percentage adsorption was acceptable for all soils (24.41 - 93.71%). The LOQ was not reported, however, the analytical method (LSC) ought to have been acceptable assuming reasonable volumes used for counting. The validity of using the indirect method, based on and d * scal/solution ratio > 0.3, was confirmed. The degree of sorption was sufficient, and the mass balance at the highest concentration was conjected for stability and used to calculate the 'f' value following EFSA (2017).

Soil	Mass balance at highest concentration (% AR)	checklist (%)
Laacherhof AXXa (0-30	2°° 9788 ~~	
cm)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Standard soil 2.1	6 0 ⁹ 8.755 0 [°]	90 0 11.12
Hoefchen "im Tal"	95.68 S	\$ \$ 90 \$ \$ 13.89
Clay soil LUFA Speyer	\$ 94511 O ?	
Laacherhof AXXa (30	\$94.51 \$	90 ° 4 14.94
60 cm)		
1 As reported from abramatage	phic analyzis of dearnting sun	armitant Q

#### Table CA 7.1.3.1.1-5: Calculation of f' values for checklist

As reported from chromatographic analysis of adsorption superpatant

The  $K_{fE} / K_f$  ratio ranges give maxima abay 1.2 for all soils and the subsoil. However, sorption is high for all tested soils/subsoils, with both  $\delta$  and  $K_d$  soil/solution ratio passing with good margins. Furthermore, the ratio of 1.2 is only an initial proposal, it is considered that this does not change the overall outcome of the study. The R of the standard linear regression ranged from 0.998 to 1.000 and the visual fit of both the standard regression and the residual plots were good.

Soil A Soil	Units	VQuar ity@ri- teria	Lascher- 7 Anof AXXa (0-30cm)	Standard soil 2.1	Hofchen "im Tal"	LUFA Speyer	Laacher- hof AXXa (30- 60cm)
Adsorption method (direct/indirect)	ð - Ö		Adirect	Indirect	Indirect	Indirect	Indirect
Soil : solution fatio 🔬 🔪	g.Grĺ			1:10	1:10	1:10	1:10
Mass balance of ¹⁴ CY (at all tested concentra- tions)		>90%	<mark>87.68-</mark> 98.12	<mark>86.93-</mark> 98.75	<mark>87.27-</mark> 95.68	<mark>81.82</mark> - 92.59	88.24- 98.45
f – due to loss pro-	Ľ,		11.91	11.12	13.89	18.0	14.94
Actsorbed percentage $(\delta) \sim 0^{10}$	%	>20%	50.17- 82.21	24.41- 60.02	81.03- 93.71	83.08- 90.45	38.54- 66.05
$K_d x$ (soil:solution ratio)		>0.3	1.01-4.62	0.32-1.50	4.27- 14.90	4.91-9.47	0.63-1.95

## Table CA 7.1.3. 11-6: Results of the EFSA 106 data evaluation

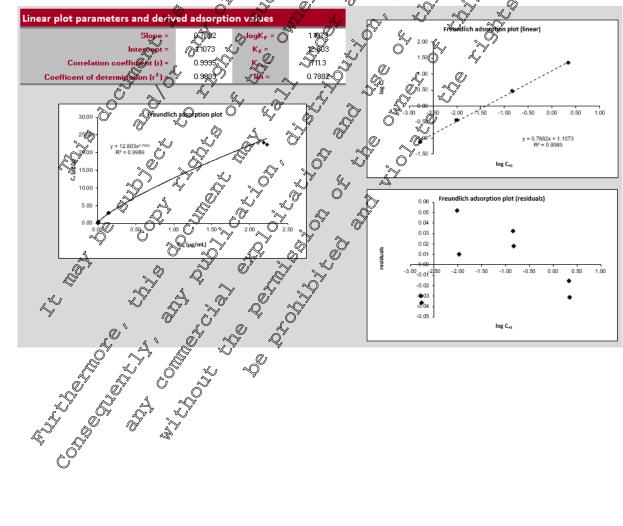


Soil	Units	Qual- ity cri- teria	Laacher- hof AXXa (0-30cm)	Standard soil 2.1	Hofchen "im Tal"	LUFA Speyer	Laacher- hof AXX (30- (30-	^d D
$K_{fE}$ / $K_{f}$	-	<1.2	1.165- 1.307	1.238- 1.804	1.172- 4 1.204	1.252- 1.276	1.628	
^{ads} K _F	L/kg	*	12.803	4.613	45.184	44.702	7,250	Ĉ,
(95% confidence inter- val)**			11.51- 14.23	402-5.17	39,66- 50.48	38.81-× 5108	∕6 <b>,</b> 63-7.9€	6
^{ads} 1/n	-	*	0.788	0.773	Ô [®] .834	,0 <b>,9</b> 03 ~	0.837	Ő
(95% confidence inter- val)**			0.76-0.8	0.740- 0.805	0.807- 0 <b>85</b> 60		0.862 4	
Ads R ²	-	>0.975	0.999	0.998	s. <b>6</b> .999	× 0.999	Q 0.99	
^{ads} K _{F,OC}	L/kg	*	Q11.3 Q	° 659	سير1882 کر	<b>\$9</b> 84.6 °~	2446.5	
Visual fit to Freundlich isotherm			Excellent	Excellent	Excellent	Excellent	Excellent °	
Residual plots randomly distributed		L'AND CAR	Good @	Good	Good	Good		

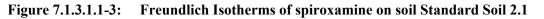
* As no extraction of soil was carried out dese values are based on the worst-case total recovered radioactivity recovered (see bold values in Table CA 7.1.9.1.1-3), or rected for stability, see Pable CA 7.1.3. Si-5

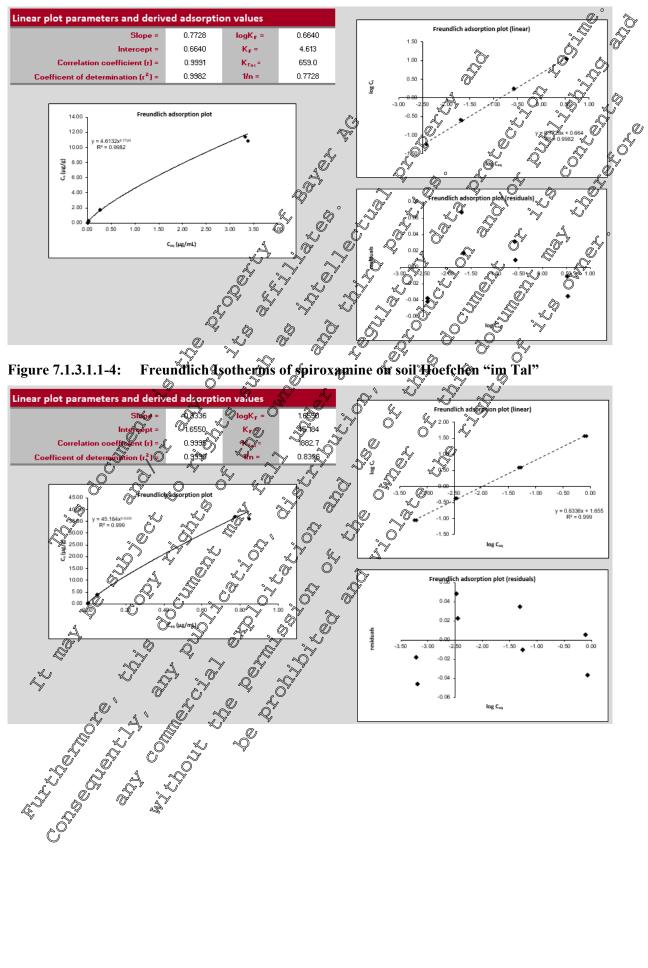
** Confidence intervals provided in the PFSA Excel spreadsheet were reconculated manually as available input data consisted of only 4 concentration levels

# Figure 7.1.3.1.1-2: Freundlich Isotherins of spiroxamine of soil Lacher Hof AXXa (0-30cm)

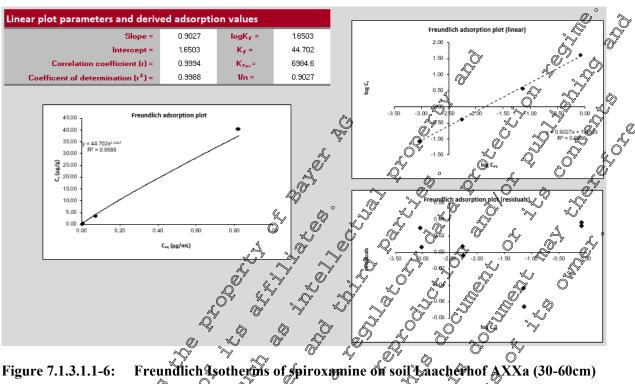






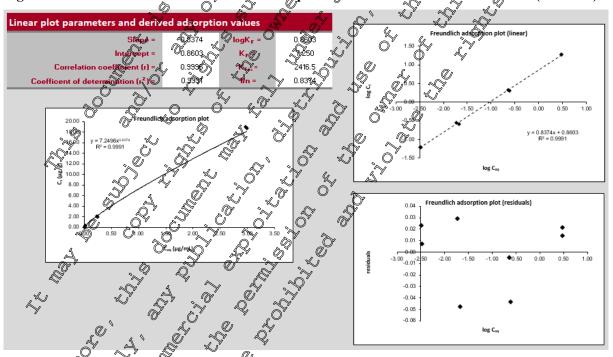






Freundlich Isotherms of spiroxamine on soil LUFA Speyer Figure 7.1.3.1.1-5:

AXXa (30-60cm) Figure 7.1.3.1.1-6:



Overall the study has been conducted to good standard, although certain criteria that might be expected in a modern study have not been reported this does not impact study reliability.

> III. Conclusions

L)

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and a second Freundlich adsorption coefficients (Kf) ranged from 4.61-44.98 L/kg (n=4). When normalised to organic carbon, Deundlich adsorption coefficients (Kfoc) ranged from 658.8-6417.1 L/kg, indicating that spiroxamine exhibits low mobility in soil according to the McCall mobility classification (McCall et al 1981⁷). The 1/n values ranged from 0.768-0.885, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.



Adsorption was shown to be generally correlated with organic carbon content, there was no clear correlation with the pH of the soils.

The OECD 106 Checklist (v2) was used to evaluate the study. The evaluation confirmed acceptability for all soils according to the quality criteria and therefore acceptable for regulatory use. A number of minor differences in the derived  $K_{FOC}$  values were noted but this was attributed to rounding errors and for consistency the endpoints determined in the study report are used and considered to have no invact on the risk assessment.

#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/201

The study was conducted to study guideline(s) OECD 106 (required guideline). Although the study has some deficiencies when compared to the EFSA OECD 106 checklist, the study is considered valid to assess the adsorption and desorption characteristics of the spiro amine in soil

Data Point:	KCA 7.1.3.1.1 92 K K K K K K K K K K K K K K K K K K
Report Author:	
Report Year:	
Report Title:	Adsorpton/desorption of KWG 4168 of five Americal soils
Report No:	PF4135 x x x x x x x x
Document No:	
Guideline(s) followed in	EPA, Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmetal
study:	Chate § 103-1 2 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
	Chate § 163-1 Yes (refer below) Some minor deviation(s) not relevant for the reliability of the study (described in
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in
	study summary) a study summary)
Previous evaluation	yes, evaluated and accepted and a company of the co
C n	RAR(2010), RAR(2017) N N N
GLP/Officially@ccog-	Yes, conducted under GLP Officially recognised testing facilities
nised testing facilities	
Acceptability/Reliability:	Yes 2 A BY O' C B

Executive Summary

The adsorption and desorption of [cyclohexyKJ-¹⁴C] and [1,3-dioxolan-4-¹⁴C]-spiroxamine on five North American soils was studied using the batch equilibrium method with a tiered approach. [cyclohexyl-1-¹⁴C]-spiroxample was used for determination of equilibrium time, whilst all other tests were performed with [1,3 dioxolan-4-¹⁴C]-spiroxamine

Parameter	(			Soil		
Soil Designation		(Sand)	Grape Vine- yard (Sandy Joam)	Howe (Sandy loam)	Wolf Ranch (Loam)	Stanley (Silty clay)
Textural Classifica (USDA)	A	Sand Sand	andy loam	Sandy loam	Loam	Silty clay
pH (CaCl ₂ )	× 0	×6.7 ~Q	5.8	6.7	7.8	5.1
Organic carbon (%	y C	0.2	0.45	1.12	0.97	1.05

Preliminary tests were performed to determine the appropriate soil:solution ratios and equilibrium time. In this study preliminary tests did not investigate adsorption of the test substance to the test vessels or stability of the test substance in calcium chloride solution, these aspects were addressed by reference to the study M-006189-01-2 (see CA 7.1.3.1.1/01).

Freundlich isotherm tests were performed with all soils using the indirect and parallel methods. A soil:solution ratio of 1:20, and 24 hours equilibrium time for adsorption and desorption were used for

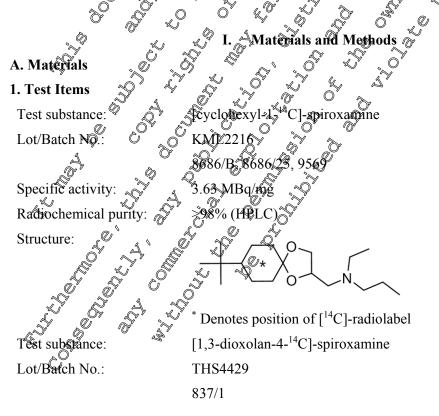


all soils. For the adsorption step, appropriate solutions of the test substance were applied to the samples and the samples were shaken for 24 hours at  $20 \pm 1^{\circ}$ C in the dark. Following the adsorption step, the samples were removed from the shaker, centrifuged, and the adsorption supernatants removed and malysed by normal phase TLC and LSC. For the desorption step, a 20 mL volume of fresh 0.01 M CaCl₂ solution was added and the samples were shaken for a further 24 hours at  $20 \pm 1^{\circ}$ C in the dark. Following the desorption step, the samples were removed from the shaker, centrifuged, and the desorption supernatants removed. The desorption supernatants were analysed by LSC and the highest concentration solutions of each test substance were also analysed by normal phase TLC. The soil samples were combusted in a sample oxidiser and analysed by LSC to determine the radioactivity present.

Mass balances ranged from 94.8-103.9% AR. The amount of radioactivity adsorbed on the soil at ad sorption equilibrium ranged from 23.2-97.8% AR.

Freundlich adsorption coefficients (Kf) ranged from 8.55-892 59 L/kg. When normalised to organic carbon, Freundlich adsorption coefficients (Kfoc) ranged from 347-83008 L/kg, indicating that spiroxamine exhibits low mobility in soil according to the McCall probility classification (McCall et al 1981⁷). The 1/n values ranged from 1.01-1.06, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range. The OECD 106 Crecklist (v2) was used to evaluate the study, however all final parameters used are taken from the study report. The evaluation confirmed acceptability for all soils according to the quality criteria and therefore acceptable for regulatory use.

Soil	Vero Beach (Sand)	ywrd (Sandy ( loada)	S Howe (Sandy loanty	Wolf Rapch	Stanley (Silty clay)
OC (%)	0.2	0°45 Q	1.12	¢ 0.97 %	1.05
pH (CaCl ₂ )	6.70	\$5.80	6.00	ي7.80 م	5.10
$K_{f}(L/kg)$	<b>\$</b> .55 <b>\$</b>		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>د 381.69</u>	892.59
K _{foc} (L/kg)	\$\$4276 ° *	3216	ي≪أ347 [∪]	[™] 39 <i>3</i> 46	85008
1/n	\$ 1.06 \$	ŷ "Ŷ.05	~~ 1.0 <b>2</b>	J. 02	1.01
IX (	2 ³⁷ 0.996 , 7	0.970	× 0,999 V	~Q1.000	1.000





Specific activity:	4.30 MBq/mg
Radiochemical purity:	>99% (HPLC)
Structure:	4.50 MBq/mg >99% (HPLC) + + + + + + + + + + + + + + + + + + +
	* Indicates position of radioabel
2. Test System (soil)	
Five North American soils	were used. The soils were collected from field sites in VerorBeach (Florida,
USA), Grape Vineyard (Ca	antonna, OST), now findiana, OST), web Ranch (Cantonna, OST) and
	d varied in organic carbon, pH and Play content, After collection, soils were
<b>c</b>	d passed through a mm seve. L
Table CA 7.1.3.1.1-7: Ph	ysico-chemical properties of test soils
Parameter	Soil & Soil & Soil
Soil Designation	Vero Beach gard and Rowe Well Ranch Stanley
Geographic Location	
City	Noro Beach, Source H Product October

Geographic Location		o S		ð _s o «	<i>"</i>
City	Vero Beach,	California	HoweUndiana	California	[∞] Stanley, Kansas
	Florida				Stanicy, Kansas
Country 🗞	USA	SSA &	USA V	J USA	USA
Textural Classification (USDA) Sand	Sand	Sandy Dam	∑ Sand⊗loam &	toram	Silty clay
Sand (%)	v . <b>98</b> 07 "S	64.0	©65.7 √ 26€	<i>Q</i> 29.7	17.0
Silt (%)	≪ 0.3 _©	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	N 26 V	29.7 45.1	41.0
Clay & (%).	0 1.00 [°] §	30.2 [×]		25.2	42.0
рН	, Q A	NY W			
in CaCl ₂	~~~ 6.7 J	5.8	~~~ 6.7×	7.8	5.1
Organic Matter (%) *		S 0.78	¥>93	1.67	8.79
Organic carbon (%)	¥ 49.2 ~	0.45	1.12	0.97	1.05
Cation Exchange Capacity (meq/100 g)	5 3.90°	5.6	5 10.0	19.0	27.0
* Calculated by multiplying orga	ble carbon content	by 1.724 (not repo	orted)		

### B. Study Design

### 1. Experimental Conditions

The test system for adsorption and desorption of spiroxamine on five North American soils consisted of Teflon centrifuge tubes with screw caps. All vessels used were cleaned with methanol and concentrated sulfuric acid and conditioned with non-radiolabelled test substance in order to minimize any adsorption to the vessels walls

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In preliminary cests, the optimal soil-to-solution ratio and the appropriate adsorption and desorption equilibration ones were determined.

Frequidich sotherm tests were performed with all soils using the indirect and parallel methods. A soil solution ratio of 1:20, and 24 hours equilibrium time for adsorption and desorption were used for all soils. Solutions of the radiolabelled test substance in acetonitrile were prepared and diluted with 0.01 M CaCl₂, such that test substance application achieved concentrations of 5.443, 0.526, 0.055 and 0.012 mg/L. The organic solvent added was  $\leq 1\%$  of the CaCl₂ solution (v:v).



1 g dry weight of soil was transferred into centrifuge tubes and 20 mL of 0.01 M CaCl₂ containing test substance were applied to the samples. The samples were then shaken for 24 hours at  $20 \pm 1^{\circ}$ C in the dark. For the desorption step, 20 mL volume of fresh 0.01 M CaCl₂ solution were added and the samples were shaken for a further 24 hours under the same conditions. Stability of the test substance was moni-tored during the isotherm determinations by TLC analysis of the supernatant after the adsorption step (each soil, top concentration only).

Adsorption phase		
Parameter		Description of the second seco
Soil condition		Soils were air-dried and areved to 2 mm
Soil sample weight		1 g (dry weight)
Equilibration solution		No pro-equilibration conducted
Control (preliminary experiment)		Nor conducted (reference made to <u>M-008189-01-2</u> , (CA 7.1@1.1/01) where adsorption of the test substance to the test vessels showing to be minimally a <u>A</u>
Test item concentra- tion	Nominal application rates Analytically (LSS) measured concentra- tions	0.01, 0.05, 0.5 and 5 mg/L (4 concentrations) Measured concentrations (LSC) in test solution: 5.443, 0.526, 0.055 and 0.012 mg/L
Identity and concentration of co-Wivent		Bosing stock made up in acetomitrile
Soil: Solution ratio		
Number of replicates	Control	Not Chductor ( ) Deplicated ( )
Equilibration condi- tions	Time Temperature Dark Dark Shaking method Shaking method Speed rpm) Duration Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant Supervisitant S	24 hrs. 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±100 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±1000 20±10000000000
Desorption phase Parameter		Description
Soil samples from ads		
Amount of test in the adsorbed state/adsorbed amount mg ai kg sail		The amounts of test item adsorbed to soil after adsorption ranged from 23.2 to 97.8% (reported for definitive test). See OECD 106 Checklist below for further details for each soil.
Number of description cycles		3 (5 mg/L nominal concentration only) 1 (all other concentrations)
Equilibrium solution and quantity used per treatment for desorption		The decanted solution was replaced by fresh aqueous 0.01 M CaCl ₂ solution
Soil: Solution ratio		1:20



Parameter		Description	
Number of replicates	Control	Not conducted, reference to M-006189-01-2 where stability is demonstrated	
	Treatments	Duplicate	D ^e
Desorption Equilibra- tion conditions	Time	24 hrs	
	Temperature	20±1°C	Ŷ,
	Dark	In the dark and a start of the dark of the	e C
	Shaking method	Overhead shaker	, ô ^y
Method of separation of supernatant		Centrifugation	,
Centrifugation	Speed (rpm)	Notherported Nother Rest	
	Duration	Not reported 2 2 2	
	Method of separating ( supernatant	Supernatant was carefully decanted.	

#### 2. Analytical Procedures

After each adsorption and desorption step the aqueous supernatant was separated from the soil by centrifugation and the amount of spiroxymine to the supernatants was analysed by fiquid seintillation counting (LSC). An aliquot of supernatant from the bighest concentration for each soil was also analysed by normal-phase TLC using a mobile phase of acetonitrile/water/andionium hydroxide (80:18:2, v/v/v) and a Bio Imaging analyser, quantified with Tina version 2.08a,

The partition of the test item in the adsorption and desorption batch equilibrium experiment was determined based on the radioactivity content in the supernatationaly (i.e. the indirect method). After the desorption step, the soft was an drived and the radioactivity content determined by combustion/LSC to establish the material balance.

Stability of parent test substance was determined as 97.0, 97.1, 96.6, 80.4 and 61.3% in Vero Beach, Grape Vineyard Howe Wolf Ranch and Stanley sorts, respectively, by TLC analysis of the supernatant after the adsorption step.

Adsorption and desorption isotherms were calculated by linear regression analysis of the adsorption or desorption data according to the Freundlich equation.

The limit of detection (LOD) was not specified in the report, however, the concentrations of the test substance used are sufficient to allow adequately accurate peasurements of levels of the test substance.

C C A Result and Discussion

#### A. Results of preliminary tests

Adsorption of the test substance to the test vessels was not assessed in this study, however, the report made reference to study M-0.06189-01-2 (see CAV 7.1.3.1.1/01), where adsorption of the test substance to the test vessels was shown to be minimal and stability of the test substance in calcium chloride solution (without soil) was shown to be suble over a period of 9 days.

Initially in proximitely tests a soil-to-solution ratio of 1:10 was selected for the Grape Vineyard, Howe, Wolf Ranch and Stanley Soils and a ratio of 1:2 for the Vero Beach soil by reference to the study M-006189-0-2 (see CA 7.1.3.1.601). This led to percentages adsorbed of 86.5-94.9, 71.3-94.6, 76.2-95.7, 98.3-99.0 and 99.3-99.6 for the Vero Beach, Grape Vineyard, Howe, Wolf Ranch and Stanley soils, respectively In light of this, a soil to solution ratio of 1:20 was chosen for all soils. The equilibration time was determined using a soil to solution ratio of 1:20 for all soils and monitoring adsorption over 72 hrs.  $\sqrt[6]{2}$ 

#### **B.** Transformation of test substance

Stability of the test substance was monitored during the isotherm determinations by TLC analysis of the



supernatant after the adsorption step (each soil, top concentration only). The stability was 97.0, 97.1, 96.6, 80.4 and 61.3% for the Vero beach, Grape Vineyard, Howe, Wolf Ranch and Stanley soils, respectively.

#### C. Findings

Mass balances ranged from 94.8-103.9% AR. The amount of radioactivity adsorbed on the soil at adsorption equilibrium ranged from 23.2-97.8% AR. For the controls without soil, no sorption to the test vessels was measured.

	(	cs) for spiroxam	<u>70</u> . A	, O	
Soil	Concentration		Concentration	Adsorption	🖌 Mass 😽
	initial	supernatant 🕅	soil	percentage ( <b>ð</b> )	balance (%)
	(mg/L)	(mg/L){{	(mg/kg) 🐇		$\sim \sim \sim \sim$
Vero Beach	0.012	0.009© ″	0.060	27.43°	<u>, 97453</u>
(Sand)	0.055	0.042	Ø.260 Q	23,94 (	) ^v <b>20</b> 7.96
	0.526	0.404	2.44	2021	103.41
	5.443	<b>3</b> .461 ~	<i>_©</i> 39.640	36.42 38.47	🖄 101 🔊
Grape Vinyard	0.012	Q 0.007		<u>ک</u> 38.4	96.05 ⁹
(Sandy loam)	0.055	L 0.06 ×	\$0.390		× 1,90.28
	0.526	Q <u>0</u> 335	> 3.820° (	ک <u>کې کې کې</u>	°∻j103.90
	5.443 🖉	ͺ≪Ž.897 @ [°]	\$ 50010	046.77	<b>%</b> , 101.64
Howe	0.012	[∞] 0.007	0.090	چ 40.56	O [™] 98.28
(Sandy loam)	0.055		@•0.460 [*]	× 42,29 6	99.27
	0.526	Ø.327 🔊	<u> </u>	× ~&7.89 ×	103.18
	5.443	2.928	@ <u>56</u> 310 🤬	46.22	101.08
Wolf Ranch	0.012	🔊 0.0007 ^A	× × 220 °	\$ 94,20	95.79
(Loam)	Ø ^v 0.055	\$ \$903 \$	S 1.049	94.50	97.27
	<u></u>	ר.032	° 9.870 v	<b>\$</b> 3.95	101.37
	گ چ5,443 ∿	« 0.26 ² » »	109.620	<b>95.19</b>	99.42
Stanley 🏷	0.0120	0' 0.0003 ^A	00.230	<i>9</i> 7.60	94.79
(Silty clay)	0.055	0.0013 ^A	1.070 ≼	97.66	98.54
×~	0,526 🖉	@0.013 °	10,260	97.66	101.42
	.443	© 0.122	¥ 106.430 O	97.77	102.08

Table CA 7.1.3.1.1-8: Concentrations at adsorption equili (mean values) for spiroxamine	brium and re	ecovery of	radioactivi	ŧ
(mean values) for spiroxamine	40 ×	ž	Q A	¥*

Bold values used to calculate the percent loss

A Due to rounding the potential of  $(\mu_{c})$  values from Appendix 16/17 of the study report were used to calculate these values

Freundlich adsorption overficients (K) ranged from 8.55-892.59 L/kg. When normalised to organic carbon, Freundlich adsorption coefficients (K_{foc}) ranged from 1347-85008 L/kg, indicating that spiroxamine is likely to exhibit low mobility in soil. The Freundlich exponent 1/n values ranged from 1.01-1.06, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range

# Table CA 7.1.3,191-9: Freundlich adsorption coefficients for spiroxamine

Soil	(Sand)	Grape Vine- yard (Sandy loam)	Howe (Sandy loam)	Wolf Ranch (Loam)	Stanley (Silty clay)
OC (%)	0.2	0.45	1.12	0.97	1.05
pH (CaCl ₂ )	£ [™] 6.760 [™]	5.80	6.70	7.80	5.10
Kr (D/kg)	O 855	14.47	15.09	381.65	892.59
K _{foc} (L/kg)	4276	3216	1347	39346	85008
1/n 💍	1.06	1.05	1.02	1.02	1.01
R ²	0.996	0.998	0.999	1.000	1.000



#### D. Evaluation of the Data according to EFSA Evaluators Checklist

The results of the determination of the Freundlich Isotherm were analysed using the Excel-sheet gro-vided by EFSA (summarised in Table CA 7.1.3.1.1-11). The concentrations in the supernatant as given gro-vided in the report were used as input data (note – concentration ( $\mu g/mL$ ) calculated from provided LSG data). Individual replicate concentrations were used in the calculation.

The degree of sorption was sufficient, and the mass balance at the highest concentration was corrected for stability andthen used to calculate the 'f' value, following EFSA (2012).

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	al a	_0*	
Soil	Mass balance at highest concentration (% AR)		'f Value for input into
Vero beach	101.57	971.0	1.489
Grape vineyard	101.64 🔬 🔊	°	
Howe	101.08	96.6	2.36 s
Wolf ranch	99.42	Ø 80Q	<u>0²0.070[*] y</u>
Stanley	102.08	× 361.3 A	37.42
A croported from abromatogra	phia analysis of advantion supernotes	t de N	

Table CA 7.1.3.1.1-10: Calculation of 'f' values for checklist
----------------------------------------------------------------

¹As reported from chromatographic analysis of advorption supermant.

The percentage adsorption was acceptable for all soils (29.31 - 97.77%). The FOQ was not reported, however, the analytical method (LSP) ought to have been acceptable assuming reasonable volumes used for counting. The validity of using the indirect method, based on a Kd * soil/solution ratio > 0.3, was confirmed. The degree of sorption was sufficient; however, the order to calculate a conservative "f" value, the worst-case total recovered radioactivity was used. The K_{fE} 4/K_f ratio ranges give ranges above 1.2 for the Wolf ranch and Standey softs. However, sorption is high for all tested soils/subsoils, with both  $\delta$  and K_d x soil/solution ratio passing with good margins. Furthermore, the ratio of 1.2 is only an initial proposal, it is considered that this does not change the overall outcome at the standard linear regressions ranged from 0.989 to 0.999 and the visual fit of both the standard regression and the residual plots were good.

Soil 2 C	Units	<i>x</i> teria 3	Vero Beaetr (Sand)	Grape Vipeyard (Sandy loam)	Howe (Sandy loam)	Wolf Ranch (Loam)	Stanley (Silty clay)
Adsorption method (direct/indirect)	- 42		, Undirect	Indirect	Indirect	Indirect	Indirect
Soil : solution atio	ganL		1:20	1:20	1:20	1:20	1:20
Mass balance of ¹⁴ C (at all tested concentra- tions)		>969%	\$7.53- 103.41	96.05- 103.90	98.28- 103.18	95.79- 101.37	94.79- 102.08
f - due to loss pro-			48	1.31	2.36	20.07	37.42
Adsorbed percentage		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	£ 22.42-	34.21-	37.03-	93.88-	97.41-
(δ) 🗸 🐧			<b>♀</b> 39.71	46.95	49.06	95.20	97.84
K _d x (soil:solution ratio)		>0.5	0.29-0.66	0.52-0.89	0.59-0.96	15.34- 19.84	37.66- 45.28
		<1.2	1.039-	1.029-	1.051-	1.267-	1.619-
K _{fE} / KfS	Q.	<u><u></u> <i>¬</i>1.2</u>	1.071	1.040	1.068	1.272	1.623
adsKay D	`≈£/kg	*	8.535	14.442	15.043	377.138	876.665
(95% contrelence inter-	la l		6.12-	11.61-	12.31-	318.84-	743.51-
val)***©			11.90	17.96	18.38	446.09	1033.67
^{ads} 1/n	-	*	1.047	1.043	1.014	1.020	1.008
(95% confidence inter-			0.935-	0.972-	0.950-	0.986-	0.979-
val)**			1.159	1.114	1.078	1.053	1.036

#### Table CA 7.1.3.1.1-10: Results of the EKSA 106 data @aluation

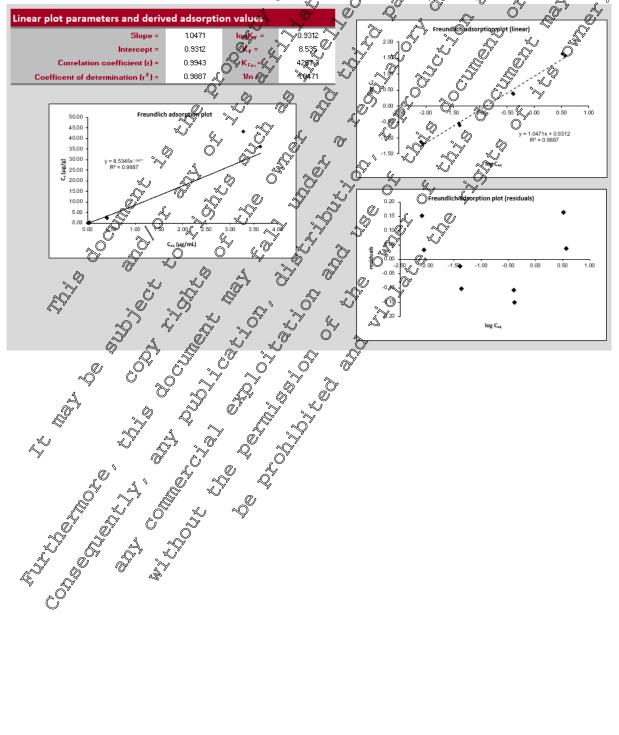


Soil	Units	Qual- ity cri- teria	Vero Beach (Sand)	Grape Vineyard (Sandy Ioam)	Howe (Sandy loam)	Wolf Ranch (Loam)	Stanley (Silty)° class	
Ads R ²	-	>0.975	0.989	0.995	0.996	% 0.999 🗞	<b>9</b> 999	0
^{ads} K _{F,OC}	L/kg	*	4267.3	3209.3	1343.2	38880.2	~\$3491 <i>A</i>	
Visual fit to Freundlich isotherm			Good	Good	Good	Good	Food	ĝ
Residual plots randomly distributed * As no extraction of soil			Good	Good	Good	Good	Good	, ,

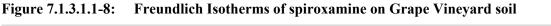
Confidence intervals provided in the EFSA Excel spreadsheet were re-calculated manually available input data con-sisted of only 4 concentration levels

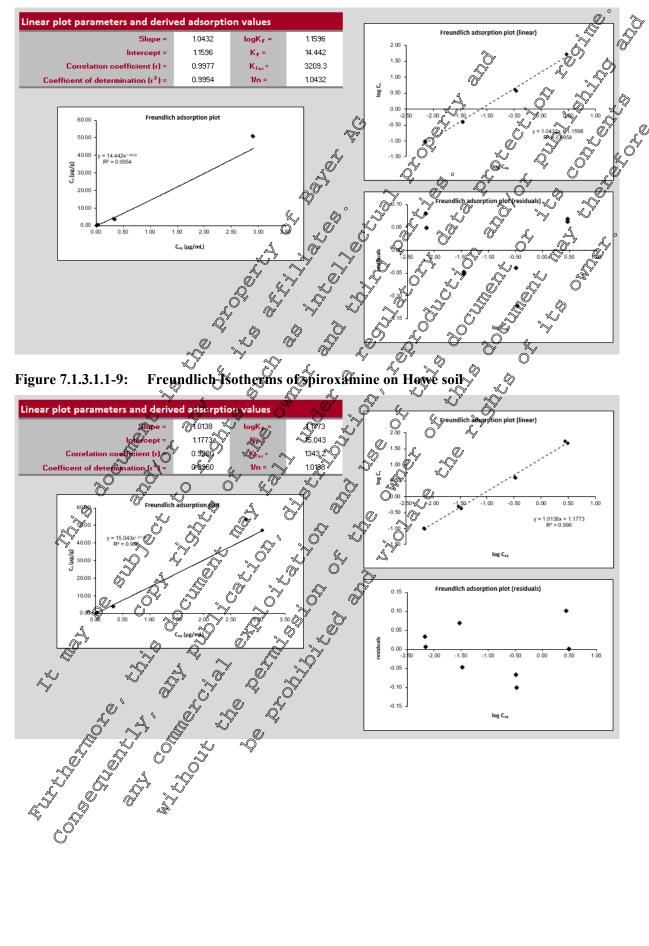
**

#### Freundlich Isotherms of spiroxamine on Vero Beach soft Figure 7.1.3.1.1-7:











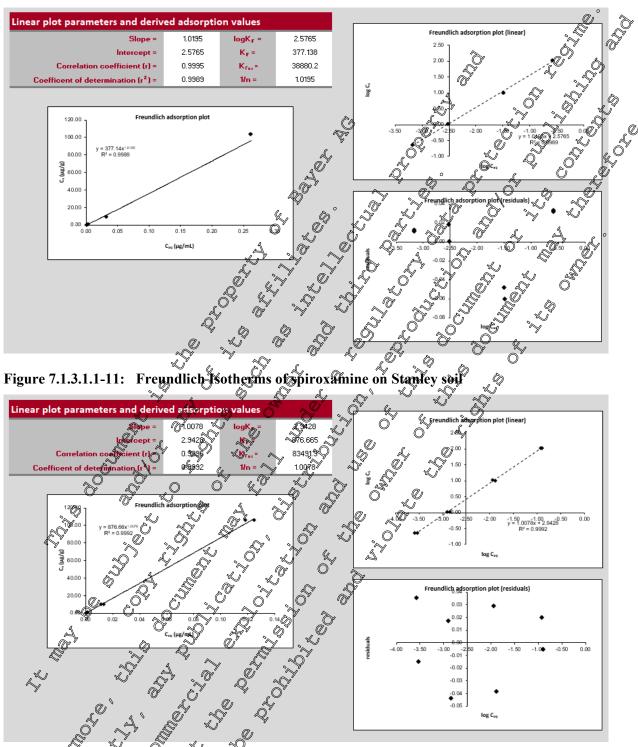


Figure 7.1.3.1.1-10: Freundlich Isotherms of spiroxamine on Wolf Ranch soil

Overall, the study was conducted to a reasonable standard and the study conclusions considered reliable.

🕅 III. Co



Frondlich adsorption coefficients (Kf) ranged from 8.55-892.59 L/kg. When normalised to organic carbon, beundlich adsorption coefficients (Kfoc) ranged from 1347-85008 L/kg, indicating that spirox-amine exhibits low mobility in soil according to the McCall mobility classification (McCall et al 1981⁷). The 1/n values ranged from 1.01-1.06, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.



Adsorption was shown to be generally correlated with organic carbon content, and there was a weak correlation observed between pH and sorption, where Kfoc was lower as pH increased ( $r^2=0.153$ ).

The OECD 106 Checklist (v2) was used to evaluate the study. The evaluation confirmed acceptability for all soils according to the quality criteria and therefore acceptable for regulatory use. A number of minor differences in the derived  $K_{FOC}$  values were noted but this was attributed to rounding errors and for consistency the endpoints determined in the study report are used and considered to have no impact on the risk assessment.

#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/202

The study was conducted to study guideline(s) OECD 106 (required guideline). The study is considered valid to assess the adsorption and desorption characteristics of the spiroxamic in soil. Although the study has a number of deviations from the current version of OBCD 106 (2002) it is, considered valid to assess the adsorption and desorption characteristics of the spiroxamine in soil.

Data Point:	KCA 7.1.3 Q1/03 K
Report Author:	
Report Year:	
Report Title:	2004 2 2 Partition conficients of soil metabolites of spiroxamine
Report No:	MEX 04/370
Document No:	MH&F 04(370
Guideline(s) followed in ⁵ /	A1-085664-01-15 0 7 7 7 9 None 5 6 7 6 7 7 7 7
study:	
Deviations from current	None None S S S S S S S None S S S S S S S S
test guideline:	
Previous evaluation.	ves, evaluated and accepted 3 2 and a compared with the second second second second second second second second
	RAR (2016), RAB (2017)
GLP/Officiall@recog	not applicable V V V V
nised testing facilities:	
Acceptability/Reliability	Supportive Stilly
Â ^Y , O	

#### Executive Summary

This study is submitted as supporting information only (it was previously included in the RAR (2010), RAR (2017) and is therefore included for completeness).

The study involved the estimation of the partition coefficients of the main soil metabolites of spiroxamine by QSAR calculations. However, the study is no longer required or has since been superseded (based or real values) and consequently a full summary is not provided.

# CA⁷7.1.3.1.2 Adsorption and desorption of metabolites, breakdown and reaction

m

The adsorption and desorption of metabolites of spiroxamine have been investigated in three studies (KCA 7.1.3, 1.2/0) to KCA 7.1.3, 1.1/03) which were evaluated during the previous EU review. In addition:

- One our the study providing supplemental information to the study KCA 7.1.3.1.2/03 (M-000089-01-1)
- One further study is being conducted to provide soil sorption properties for metabolite M06 (spiroxamine-acid) and will be provided as soon as possible.

The applicant considers the adsorption endpoints from batch equilibrium studies are appropriate for use



in risk assessment (in agreement with the previous EFSA conclusion: EFSA Journal (2010);8(10):1719).

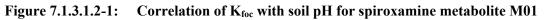
Substance	Report reference	Document no.	Comment 🖉 🥎
Metabolite M01	KCA 7.1.3.1.2/01	<u>M-006084-01-1</u>	Submitted for first renewal of spirov- amine, 2010. Reviewed under UP. Consid- ered valid and acceptable
Metabolite M02	KCA 7.1.3.1.2/02	<u>M-006086-01-1</u>	
Metabolite M03	KCA 7.1.3.1.2/03	<u>M-006089-01-1</u>	
Metabolite M03	KCA 7.1.3.1.2/04	<u>M-006087-01-1</u>	Previously submitted bornot evaluated In-
Metabolite M06	KCA 7.1.3.1.2/05	TBA	New data not yesteviewed under UP.

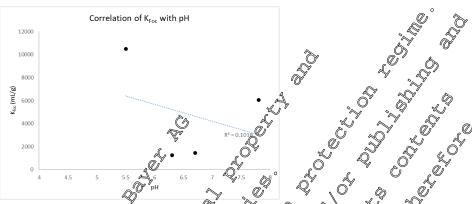
The resulting soil sorption parameters for metabolites of spiroxamine are spinmarised below: Table CA 7.1.3.1.2-1: Overall summary of Freemallich soil adsorption parameters for metabolites of spiroxamine

			× U			à à	
Study	Soil name	S S	oil properti	rç 👋	CSoil sa	ption@ara	meters
		Texture	ph A *	OC O	Kr A	L/kg) ~	🏸 1/n
	Å		6 8		0 (L/kg)	(E/kg) `>>	
Metabolite M01	Vero Beach	Sand	6.3 6.7	0.32	3.96	© 123⁄2	0.867
KCA	Howe	Sandy V loam	6.7	≫ 1.120♥	<b>\$</b> 6.27	1403	0.813
7.1.3.1.2/01		🎸 loamQ″	an a	~~~	× . 9	Ô	
<u>M-006084-01-1</u>	Wolf Ranch	Loam	~~ 7.8 s	_0\$97 🛒	58.81	≪6063	0.862
	Stanley	Silty clay	5.00	0 ⁹ 1.49	156.61	10511	0.852
	Stanley A	×°		× 0*		3271	0.848
	Û,	Ş "Q	N 5	) 	0 ~	(geo-	(mean,
	\$ . ° >		~ <u>`</u> ?			mean,	n=4)
Č	ř "N – <del>í</del> í	<u> </u>	1 2,	<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	S.	n=4)	
Metabolite M	Yero Beach	⊖ San¢	×6.3 °	0.32 → 0.32 1.92	Ž.93	917	0.876
KCA	O Howe	Sandy	5 6.7 S	1.92 🔬	12.79	1142	0.827
7.1.3.1.2/02			**************************************				
<u>M-006000-01-1</u>	Wolf Ranch	Æoam 🔬		° 0.976	54.39	5607	0.922
	0. 4. 10	Silty clay	°~5.5	1,49	134.0	8994	0.886
	\$° * \$	× ~		Â		2695	0.878
Č	F A &	× ×		ð		(geo-	(mean,
Ŵ				a a a a a a a a a a a a a a a a a a a		mean,	n=4)
~0~						n=4)	
Metabolite ₄ M03	Vero Beach	Sand	63	0.32	1.77	552	0.939
KCA 7.1.3.1.203	Howe ~	Sandy 🔌	6:40 0.50	1.12	3.93	351	0.871
7.1.3.1.203		loam	~0				
<u>M-026089-01-1</u>	Wolf Ranch	⊳″Loa@or″	₹7.8	0.97	15.9	1641	0.890
$\sim$	Stapley	Silty elay	6 ^y 5.5	1.49	371	24893	0.835
(I)			1			1677	0.900
L.		S Q				(geo-	(mean,
	N. Š.,	Ŭ, Ĉ				mean,	n=4)
		Ŷ				n=4)	
pH (Q 01M Ca	l2) unless other	stated					

The correlation for the spiroxamine metabolite M01 of soil sorption parameter K_{foc} with soil pH is presented boow:



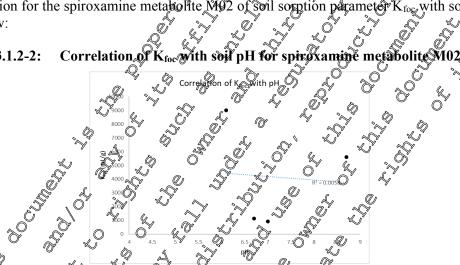




There was no strong correlation between soil softption parameter  $K_{fog}$  with soup H for M01 (spiroxamine-desethyl) ( $R^2=0.102$ ) therefore as all the source of the s Ô desethyl) (R²=0.102), therefore no pH dependence was concluded

with soft pH is pre-The correlation for the spiroxamine metabolite M92 soil sorption parameter k sented below:

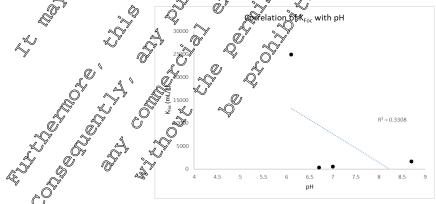




There was no strong correlation between soil sorption parameter Koc with soil pH for M02 (spiroxaminedespropyl) (R²=0.005), therefore no pH dependence was concluded.

spiroxanthe metabolite M03 of soil prption parameter K foc with soil pH is pre-The correlation for Ì sented below:

Correlation of the with soil per for spiroxamine metabolite M03 Figure 7.1 3.1.2-3:



There was no strong correlation between soil sorption parameter K_{foc} with soil pH for M03 (spiroxamine -N-oxide) ( $R^2$ =0.331), therefore no pH dependence was concluded.



#### Existing studies, previously evaluated

Data Point:	KCA 7.1.3.1.2/01
Report Author:	
Report Year:	1996
Report Title:	Adsorption/desorption of KWG 4557 on four different soils
Report No:	FM760
Document No:	<u>M-006084-01-1</u> & A A
Guideline(s) followed in	USEPA (=EPA): Section N, 163%; EU (=EEC): 95/36/EC of July(1995;
study:	USEPA (=EPA): Section N, 163%; EU (=EEC): 95/36/EC of July(1995;
	OECD Guideline for Testing of Chemicals No 106
Deviations from current	Yes (refer below)
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in
	Some minor deviation(s) not relevant for the reliability of the study (described in study summary)
Previous evaluation:	yes, evaluated and accepted a fraction of the second secon
	RAR (2010), RAR (2017) = 0 = 0 = 0 = 0 = 0 = 0 = 0 = 0 = 0 =
GLP/Officially recog-	Yes, conducted under CIP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q

#### **Executive Summary**

The adsorption and desorption  $\mathfrak{G}[cyc] \mathfrak{Shexy}[\mathcal{D}^{-14}C] \mathfrak{M}01$  ( $\mathfrak{G}$ ) iroxanine-desethyl on four North American soils was studied using the batch equilibrium method with a Gered approach.

Parameter				A L	
Soil Designation		Vero beach	Howe	Wolf Raneb	Stanley
Textural Classificat	tion (USDA)	Sand	$\bigcirc$ Sandy loam $\bigcirc$	Loam	Silty clay loam
pH (CaCl ₂ )		63° ^	~~~~6.7 ~ ©	C, 7,8	5.5
Organic carbon (%	<i>۲</i> کړ کړ	0.32	1.10	y <u>9</u> 0.97	1.49

Preliminary tests were performed to determine the appropriate soil:solution ratios and equilibrium time and to evaluate stability of the test substance in CaCl₂ solution with soil (under test conditions), potential for sorption of the test substance to test vessels and any effects of the inclusion of a biocide in solution.

In the preliminary tests, soil solution ratios of 6.20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), equilibrium time for adsorption (a hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were determined. As part of the equilibrium time determination, the stability of the test substance was monitored and shown to be 399% for Vero Beach, Howe and Wolf Ranch soils after 72 hrs and 65% for Stanley soil after 24 hrs. In control samples, shaking the test substance in CaCl₂ solution in the absence of soil gave a recovery of 39.1% AR after 72 hrs, indicating that adsorption to the test vessels was not occurring

Freundlich isotherm tests were performed with all soils using the indirect and parallel methods. For the adsorption step, appropriate solutions of the est substance were applied to the samples and the samples were shaken for 1 of 48 hours at  $22 \pm 1$ °C. Following the adsorption step, the samples were removed from the shaker, centrifueed, and the adsorption supernatants removed. Chromatographic analysis of supernatants showed >85% AR present as unchanged test substance in after the adsorption step (i.e. 1 hour for VeroBeach Wolf Ranch and Stanley soils and 48 hours for Howe soil).

For the desorption step, a 20 mL volume of fresh 0.01 M CaCl₂ solution was added and the samples were shaken for a further 1-48 hours at  $22 \pm 1^{\circ}$ C. Following the desorption step, the samples were removed from the shaker, centrifuged, and the desorption supernatants removed. The desorption supernatants were analysed by LSC and the highest concentration solutions of each test substance were also

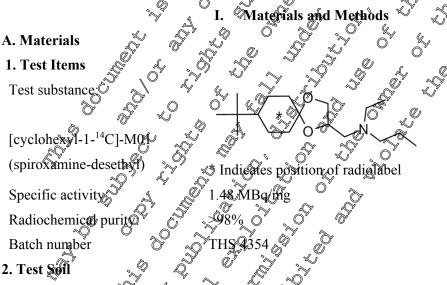


analysed by HPLC (with radiochemical detection). The soil samples were combusted in a sample oxidiser and analysed by LSC to determine the radioactivity present.

Mass balances ranged from 88.8-103.3% AR. The amount of radioactivity adsorbed on the soil a adsorption equilibrium ranged from 49.8-95.9% AR. After the adsorption phase, 49.76 - 70.81% are was adsorbed to Vero beach soil, 66.95 – 89.09% AR adsorbed to Howe soil, 74.66 – 88.17% AR to WM ranch and 88.94 - 95.90% AR.

Freundlich adsorption coefficients (Kf) ranged from 3.96-156 L/kg. When formalised to ganic Carbon, Freundlich adsorption coefficients (K_{foc}) ranged from 1227-10511 L/kg/indicating that MOV (spire)amine-desethyl) is likely to exhibit low mobility in soil. The 1/n values ranged from 0.813 0.867 Adsorption was shown to be correlated with organic carbon content, there was no clear correlation with the pH of the soils. The OECD 106 Checklist (v2) was used to evaluate the study, however all final paranteters used are taken from the study report. The evaluation confirmed acceptability for all soil according to the quality criteria and therefore acceptable for regulatory use. \$1

Soil	Vero Beach (Sand)	Howe C	Volf Runch (Loam)	
OC (%)	0.32	$\sim 1.12 \sim$	Ŏ [*] , (0.97 , O [*]	لا ي 1.49
pH (CaCl ₂ )	6.3	6.7 °	0 7.8	5.5
$K_{f}(L/kg)$	3.96	\$\$ 16Q27 ~~	58.81 S	<b>U</b> 156,61
K _{foc} (L/kg)	1237	0 1453	<b>6963</b>	\$ <b>1051</b> 1
1/n	0.867 🖌 🖉		9.8620	Ø Ø.852
R ²	1.000 .	0.999	Q 1.000 %	<b>%</b> 1.000



Four North American soils were used. The soils were collected from field sites in Vero Beach (Florida, USÅ), Howe (Indiana, USA), Wolf Ranch (Confornia, USA) and Stanley (Kansas, USA), and varied in USA), Howe (Indiana, USA), Worlt Ranch (Confornia, USA) and Stanley (Kansas, USA), and varied in organic carbon of H and clay content. After collection, soils were homogenized, air-dried, and passed through a 2 min size.



Pa	rameter		S	oil	Q°
Soil D	Designation	Vero beach	Howe	Wolf Ranch	Stanley
Geographic Lo	ocation			ð	
City		Vero beach, Flor-	Howe, Indiana	Fresno, Capitornia	Stanley, Kansas
		ida		4	
Country		USA	USA	<b>≪</b> UŠA	VSA V
Textural Class	sification (USDA)	Sand	Sandy loam	Loam	Silty Ray loater
Sand	(%)	98.7	65.7	0 ⁵ 29.7 V	×17.0 ×
Silt	(%)	0.3	26.4	45.1 °	410 0
Clay	(%)	1.0	T.9 🔊	25.2 ^Q	A2.0
pН		K.			
in H ₂ O		7.0 0	6.7 °	8.7	6.4
in CaCl ₂		6.3	r of Q	7.8	0° 30.5 A
Organic Matte	er (%) *	0.55	×1.93 ℃	J 1,0 ~	2.57
Organic carbo	n (%)	8.32 ×	× 1.12 ×	Q.97	S 1.49
Cation Exchan	nge Capacity	n.a.	S D S	J 19,5	Ç Qa.
(meq/100 g)	<u> </u>		<u>à</u>		°∼y ⊂
-	g Capacity (%)				×
maximum	de la companya de la comp	n.a.		م <u>م</u> 32.0	O n.a.
at 1/3 bar	Ô	2,8	Ŷ ¶4.8 [™]	16.8	34.0
n.a.: not analyse	ed 🦄	arbon content bol.72	Å S.		
* Calculated by	multiplying organic @	arbon content bOI.72	4 (mot reported) 🛛 🔍		

#### **B. Study Design**

#### 1. Experimental conditions

The test system for adsorption and desorption of \$101 (spiroxaphine-desethyl) on four North American soils consisted of borosilicate glass centrifuge tubes with Teflon seals and screw caps.

In preliminary tests, the adsorption of the test item to the test system surface, the optimal soil-to-solution ratio, the appropriate adsorption and desorption equilibration times, the stability of the test item and the effects on inclusion of biocide in the solution were determined.

Freundlich isotherm texts were performed with all soils using the indirect and parallel methods. Soil:solution ratios of 6:20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), and equilibrium time for adsorption (I hour for Vero Beach, Wert Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for VergeBeach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were used. Solutions of the radiolabelled test substance of acetonitrile were prepared and diluted with 0.01 M CaCle such that test substance application achieved concentrations of 4.78, 0.47, 0.05 and 0.01 mg/L. Biocide was not included in isotherm solutions as it was demonstrated that this gave no improvement for stability purposes. The volume of organic solvent added was not clearly reported (but assumed to be within acceptable limits).

6 (Vero beach), 2 (How or 1 (Wolf ranch and Stanley) dry weight of soil were transferred into centrifugeubes and 20 mL of 0.01 M CaCl₂ containing test substance were applied to the samples. The samples were then shaken to 1 (all soils except Howe) or 48 hours (Howe) at  $22 \pm 1^{\circ}$ C in the dark. For the desorption step 20 mb volume of fresh 0.01 M CaCl₂ solution were added and the samples were shaken for a further 1 or 48 hours under the same conditions. After the adsorption step, the supernatant was subjected to chromatographic analysis by HPLC (top concentration only).



#### Adsorption phase

Parameter		<b>Description</b>
Soil condition		Soils were air-dried and sieved to 2 mm
Soil sample weight		1 g (dry weight) per replicate for Wolf Ranch and Stabley soils 3 g (dry weight) per replicate for Bowe soil 6 g (dry weight) per replicate for Vero Beach for
Equilibration solution		No pre-equilibration conducted
Control (preliminary	experiment)	No soil (test item in 0.01) CaCl ₂ only)
Test item concentra- tion	Nominal application rates Analytically (LSC) measured concentra- tions	Nominal concentrations were not specified (assumed 601 to 5 mg/L) Measured concentrations (LSC) in test solution; 4.78, 047, 0.05 and 0.01 mg/L (4 concentrations)
Identity and concentra		Dosing stock made p in acelonitrile Study media - calcium chloride and HgCl ₂ added as bio
Soil: Solution ratio		1:20 (Wolf Rench and Stanley) 3:20 (Howe soil) 6:20 (Vero Beach)
Number of repli- cates	Control Q . L.	Not stated 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Equilibration condi- tions	Triane Pemperature 2 Dark 5 Shaking method	14/rs (Vero Beach, Wolf Ranch & Stanley soils)       48 hrs (Howe Soil)       22± C       10 the dails       Overhead shaker
Method of separation	Speed (rpm) Duration Method of separating Supernatant	Centrifugation 5000 rptp 15 minutes 5 Simpernatant was carefully decanted.
Desorption phase // // // // // // // // // // // // //	O ^Y A ^Y , O ^Y A ^Y	Description
Soil samples from ads	esent in the adsorbed	The amounts of test item adsorbed to soil after adsorption ranged from 49.76 to 95.90% (reported for definitive test). See OECD 106 Checklist below for further details for each soil.
Number of description Equilibrium Solution treatment for description	and quantity used per	1         The decanted solution was replaced by fresh aqueous         0.01 M CaCl ₂ + HgCl ₂ solution. Approximately 43-48 mL         was used as equilibration solution.
Soil Solution ratio	A CÍ	1:20 (Wolf Ranch and Stanley) 3:20 (Howe soil) 6:20 (Vero Beach)



Parameter		Description	
	Control	Not stated	$\gg$
Number of replicates	Treatments	Duplicate	
	Time	1 hrs (Vero Beach, Wolf Ranch & Stanley soils) 48 hrs (Howe soil)	
Desorption Equilibra- tion conditions	Temperature	22±1°C	)
	Dark	In the dark	
	Shaking method	Overhead maker	Å
Method of separation of	f supernatant	Centrifegation	)`
	Speed (rpm)	60004pm Q & A A	
Centrifugation	Duration	1 Agninutes 2	
	Method of separating supernatant	Supermatant was carefully decanted.	

#### 2. Analytical Procedures

After each adsorption and desorption step the aqueous superviatant was separated from the soil by centrifugation and the amount of M01 (priroxamine-desethy) in the upermatants was quantified by liquid scintillation counting (LSC).

The partition of the test item in the adsorption and desorption batch equilibrium experiment was determined based on the radioactivity content in the supernatant only (i.e. the indirect method). After the desorption step, the soil was air-drived and the radioactivity content determined by combustion/LSC to establish the material balance.

Parental mass balance was determined >85% by HPCC/radio-detection analysis of the supernatant only.

Adsorption and desorption isotheories were calculated by linear regression analysis of the adsorption or desorption data according to the Freundlich equation  $\sqrt{2}$ 

Additional information on stability of M01 (spiroxamine desets)) was determined in the preliminary tests. HPLC analysis of the supernatant over duration of 24, 48 and 72 hrs showed for the Vero beach, Wolf ranch and Howe soils >99% AR present as M01 (spiroxamine-desethyl) after 72 hrs and for the Stanley soil *ca*. 65% AR present as M01 (spiroxamine-desethyl) after 24 hrs. The reverse phase High Performance Liquid Chromatography (HPCC) system used a Lichrospher 100 RP-18 column and gradient elution of accontinuity 4 - 0.5% triethylamine and water  $\pm 0.5\%$  triethylamine and radio-detector.

The limit of detection (LOD) was not specified in the report, however, the concentrations of the test substance used are likely sufficient to allow adequately accurate measurements of levels of the test substance.

Results and Discussion

#### A. Results of Preliminary Pests

Soil:solution ratios of 6:20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), equilibrium time for adsorption (Khour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were determined. Receivery from control samples without soil were >99.1% AR showing any sorption of the metabolite M01 (spiroxamine desethyl) to the test vessels was minimal.

As part of the equilibrium time determination, stability of the test substance was monitored and shown to be >99% for Vero Beach, Howe and Wolf Ranch soils after 72 hrs and *ca*. 65% for Stanley soil after 24 hrs.  $0^{\circ}$ 

#### **B.** Transformation of test substance

Stability of M01 (spiroxamine-desethyl) was monitored during the isotherm determinations by HPLC



analysis of the supernatant after the adsorption step. The majority of the radioactivity in the supernatant was unchanged metabolite M01 (spiroxamine-desethyl) (only minimal details are provided in the report but a recovery of >85% over all soils was quoted).

#### C. Findings

Mass balances ranged from 88.8-103.3% AR. The amount of radioactivity adsorbed on the soil sorption equilibrium ranged from 49.8-95.9% AR.

		(° <b>F</b> -	al a	0 * <u>«ĭ</u>	
Soil	Concentration	Concentration	<b>Concentration</b>	Adsorption	🧉 Mass
	initial	supernatant	🖓 soil 👋	percentage	🛠 balance 🞸
	(mg/L) ^A	(mg/L) A 📎	(mg/kg)		(% AR) B
Vero Beach	0.011	0.003 🔬	⊘°0.025 ≉	J 709.81 D	°∼√103.255
(Sand)	0.047	0.015© [*]	0 195	<b>@6</b> 7.83	10102
	0.474	0.139	Ø 983 Q	62.31	D 100.50 /
	4.783	2%403 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	7.933	A 49076 v	99.76
Howe	0.011	Ø.001 ×	0.067	89.09	😒 101 ي 🕉
(Sandy loam)	0.047	Q_0.0007∨	Q. 267 🖑	085.77	93.84
	0.474	در ⁰ 0.0 <b>%</b> 4 کې	×2.600~	82,35	<b>99</b> .16
	4.783	Q 1.581 g	≫ 21.35 [™]	ଁ <u>,</u> 66.95 ଚ	≈>99.63
Wolf Ranch	0.011 🖉	<u>,</u> ≪0.002 ⊘ [*]	\$ 0.190	Ø8.17	<b>%</b> 96.91
(Loam)	0.047	[≫] 0.007	°° 0,790 °	© 85.48 [©]	⊙ [∞] 98.10
	0.474		©7.520 🏷	× 79.97	96.01
	4.783	ð.212 ₍	71.41 ×	× ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	97.85
Stanley	0.011	0.001	0210	\$ <b>9</b> 5.90	96.30
(Silty clay	9.047	× 0.003	0×880 0×	§ 95.09	98.08
loam)	0.474	S 2,930 S	8.860	93.64	88.82
	<u>5</u> 4.583 ~	° ≪Ø.529	<u></u>	<b>88</b> .94	90.29

	K, Y	~~~	S.Q.
Table CA 7.1.3.1.2-3:         Concentrations at adsorption equilibrium	and recovery	ofradio	activity,
(mean values) for M01 (spiroxamine-deseth			?' v~

Bold values used to calculate the percent loss. A Note: these Ques have been calculated from the reported values of  $\mu g/2\mu$  mL

Mass balance (determined as total radioactivity) values quoted are aften desuption step В

Freundlich adsorption coefficients (K_{for}) ranged from 3.96-156L/kg. When normalised to organic carbon, Freundlich adsorption coefficients (K_{for}) ranged from 1237-10510 L/kg, indicating that spiroxamine is likely to exhibit low mobility in soil. The Freundlich exponent 1/n values ranged from 0.813-0.867, indicating that the Doncentration of the test item affects its adsorption behaviour in the examined concentration range.

	Table CA 7.1.3.1.2-4:	Freundlich ads	orption coefficients	for M01 (spiroxamine-deset	nyl)
--	-----------------------	----------------	----------------------	----------------------------	------

Soil	Vero Beach	Howe	Wolf Ranch	Stanley
Soil 🔊	Sand)	(Sandy loam)	(Loam)	(Silty clay loam)
OC (%) 3	0.32 0	0 <u>1.12</u>	0.97	1.49
pH (CaCl ₂ )	· 6.≵, ~ ~	o ^v 6.7	7.8	5.5
$K_{f}(L/kg)$	3.96	16.27	58.81	156.61
K _{foc} (L/kg)	A 237 V	1453	6063	10511
1/n 🖉 🖌	\$ 0.867, ~	0.813	0.862	0.852
$R^2$	0 1.000 ×	0.999	1.000	1.000

#### D. Evaluation of the lata according to EFSA Evaluators Checklist

The results of the determination of the Freundlich Isotherm were analysed using the Excel-sheet provided by EFSA (summarised in Table CA 7.1.3.1.2-6). The concentrations in the supernatant and the soil as given in the report were used as input data. Individual replicate concentrations were not available, so mean values as given in the report have been used in the calculation and as the adsorption isotherms were conducted with only 4 concentrations the confidence intervals were calculated by added formulae.



The degree of sorption was sufficient, and the mass balance at the highest concentration, corrected for stability, was used to calculate the 'f' value, following EFSA (2017). For Vero beach, Howe and Wolf ranch soils, ">99%" stability is used as reported from the preliminary test after 72 hrs (which covers the equilibration time used in the isotherm determination). For Stanley soil, the >85% stability as reported from the isotherm determination was used as the best available data.

Table CA 7.1.3.1.2-5:	Calculation of 'f	values for checklist

Soil	Mass balance at highest concentration (% AR)	Spability (%)	'f' value for input into checklist (%)
Vero beach	99.76	>99	
Howe	99.63	>99 &	0 197 0 X
Wolf ranch	97.85	>99% @°	× × 3.13
Stanley	90.29	\$ <b>8</b> 5	

From preliminary testing for Vero beach, Howe and Wolf ranch soils, and from chromatography analysis of adaption А supernatant for Stanley soil. L. Ľ

Relevant quality checks were performed to evaluate the acceptability of the study. Fofthe Vero Beach, Howe and Wolf Ranch soils, these checks confirmed that the mass batance (93.9-103.3%) was acceptable and that the percentage adsorption was generally acceptable for all soils (49.76, 95.45%). The LOQ was not reported, however, the analytical method (CSC) sught to have been acceptable assuming reasonable volumes used for counting The validity of using the indirect method, based on a Kd * soil/so-lution ratio > 0.3, was confirmed. The degree of sorphon was sufficient, however there were signs of degradation in Stanley soil, the effect of which could not be fully assessed with the limited data available in the report. The R² of the standard linear regressions ranged from 0.998 to 0.999 and the visual fit of both the standard regression and the residual plots were good. The K F K ratio ranges give ranges above 1.2 for Stanley soil. Sorption is high for all tested soils subsoils, with both and Ka x soil/solution ratio passing with good margins. For thermore, the ratio of 1.2 is only an initial proposal, it is considered that this does not change the overall outcome of the study. Consequently, all soils should be considered as reliable and included in the regulatory dataset Õ ~

Soil	Units	Quality crite-	Vero Beach	Howe	Wolf Ranch	Stanley
Adsorption method	a/mD		Indirect	Andirect	Indirect	Indirect
Soil solution ratio				3:20	1:20	1:20
Mass balance of ¹⁴ C	% &	¥90%	\$9.8-10 <del>3</del> 3	93.8-101.2	96.9-98.1	<mark>88.8</mark> -98.1
f – due teoloss processes *			× 024	1.37	3.13	23.25
Adsorbed per- centage $(\delta)$	% ®	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	049.8-72.7	67.0-90.9	74.7-86.4	89.0-95.5
K _d x soil:solu- tion ratio			0.99-2.67	2.03-10.00	2.95-6.33	8.05-21.00
K _{fE} / K _f	- C	ي <1.2 €	1.017-1.026	1.015-1.021	1.038-1.044	1.322-1.354
ads $K_{f}$	🛇 LAkg 🔨	-	3.933	15.94	60.26	160.50
95% confi- denice inter- val**		*	3.10-4.99	9.85-25.79	44.97-80.75	95.70-269.19
ads 1/n	-		0.857	0.794	0.877	0.867

Table CA	7.1.3.1.2-	6. Rest	lts of the H	E <b>RSA</b> 106 data	<b>O</b> aluation
	0			· * (0)	

a.

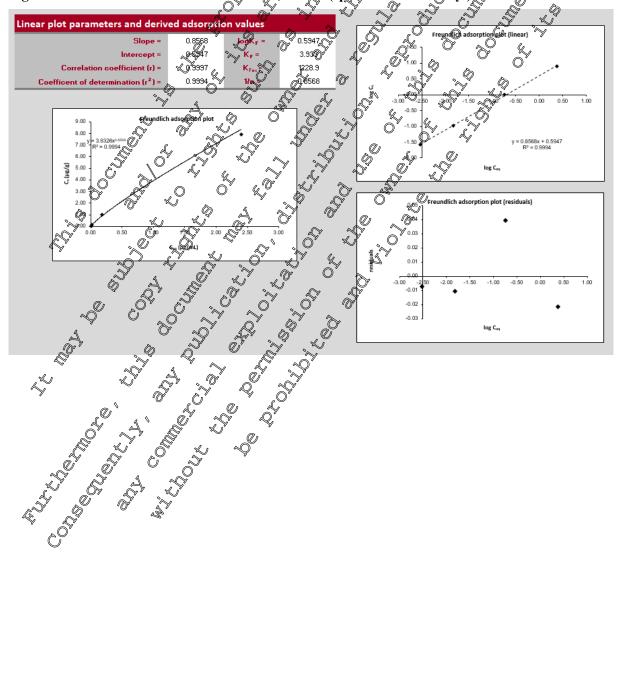


Soil	Units	Quality crite- ria	Vero Beach	Howe	Wolf Ranch	Stanley
95% confi- dence inter- val**	-	*	0.793-0.921	0.686-0.902	0.808-0.945	0.767 0.967
ads R ²	-	>0.975	0.999	0.998	<b>8</b> .999	0.999
ads K _{foc}	L/kg		1229	1423	6206	0 ⁹ 10766
Visual fit to Freundlich iso- therm	-	-	Good 💎	Good	Good &	Good Of
Residual plots randomly dis- tributed	-	-	Good	Good	Cod of	Good of

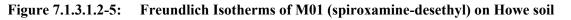
* As no extraction of soil was carried out, these values are based on the worst-case total recovered radioactivity recovered (see bold values in Table CA 7.1.3.1.2-3) confected for stability, see Table CA 01.3.1.2-3

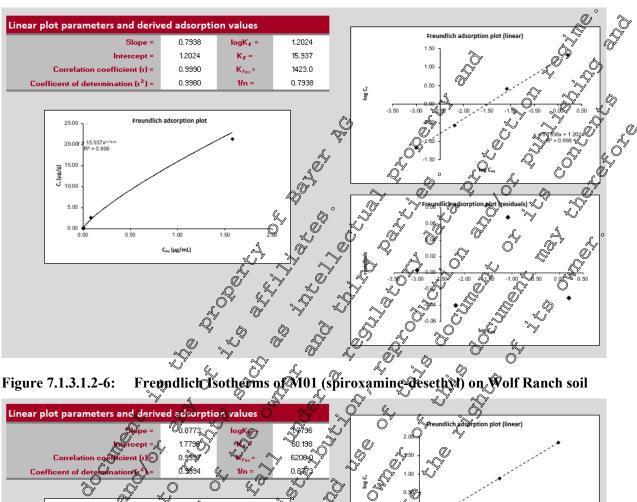
** Confidence intervals provided in the EFSA Excel spreadsheet were re-calculated manually as available inproduta consisted of only 4 concentration levels

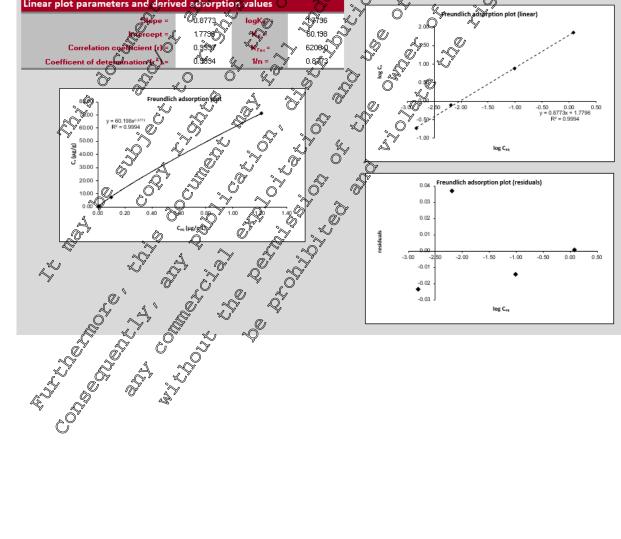
## Figure 7.1.3.1.2-4: Freundlich Isotherms of Mov (spiroxamine-desethyl) of Vero Beach soil





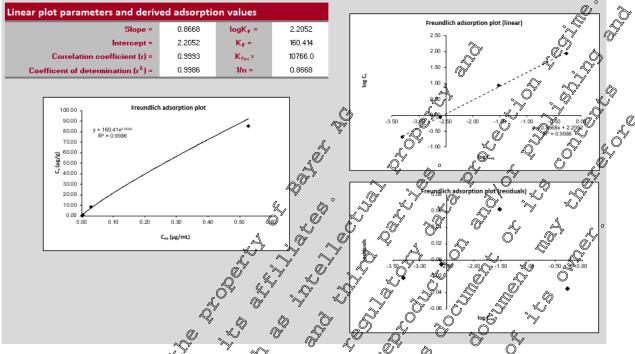












Overall, the study was conducted the a reasonable standard and all soils should be considered as reliable and included in the regulatory dataset.

#### a gill. O Conclusions &

Freundlich adsorption coefficients ( $K_f$ ) ranged from 3.96-156 L/kg (n=4). When normalised to organic carbon, Freundlich adsorption coefficients ( $K_{foc}$ ), ranged from 4237-10511 L/kg, indicating that M01 (spiroxamike-deschyl) exhibits medium to immobile mobility in set according to the McCall mobility classification (McCall et al 1981⁷). The 1/5 value tranget from 0.813-0.867, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.

Adsorption was shown to be generally correlated with organic carbon content, there was no clear correlation with the pH of the soils.

The OECD 106 Checklist (v2) was used to evaluate the study. The evaluation generally confirmed acceptability according to the quality cateria and therefore acceptable for regulatory use. A number of minor differences in the derived  $K_{rec}$  values were noted but this was attributed to the original calculation being performed on averages rather than single timponts. Since the differences were very minor, for consistency the endpoints determined in the study report are used and considered to have no impact on the risk assessment.

#### Assessment and conclusion by applicant:

Study meets the current guidence and the requirements in 283/2013.

The study was conducted to study guidefine(s) OECD 106 (required guideline). The study is considered valide to assess the adsorption and desorption characteristics of the spiroxamine metabolite M01 (spiroxamine-desethyl) in soil.



Data Point:	KCA 7.1.3.1.2/02
Report Author:	0
Report Year:	1996
Report Title:	Adsorption/Desorption of KWG 4669 on four different soils
Report No:	FM761
Document No:	<u>M-006086-01-1</u>
Guideline(s) followed in study:	EPA, Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate § 163-1; Leaching and Adsorption/Desorption Studies of October 18, 1982 PC, Com-mis- sion Directive 95/36/EC amending Council Directive 91/414/EKC (Annexes I and II, Fate and Behaviour in the Environment, July 14, 1995 OECD – Guideline for Testing of Chemicals No.: 106 Adsorption/Desorption, May 12, 1981
Deviations from current test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the rehabilit of the study (described in study summary)
Previous evaluation:	yes, evaluated and accepted RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under CLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes of y y y y y y y y y y

#### **Executive Summary**

The adsorption and desorption of [cyclohexyl-1-¹⁰C]-M92 (sphoxamine-despropyl) on four North American soils was studied using the batchequilibrium method with a piered approach.

Parameter			So So		
Soil Designation		Vero beach	Howe y	Wolf Ranch	Stanley
Textural Classification	(USDA)	Sand a	Sandy loam	Loam	Silty clay loam
pH (CaCl ₂ )		6.3	6.7	y .8	5.5
Organic carbon (%)		₩0.32 m	<u>مَحْ جَانِ جَانَ جَا</u>	[©] 0.97	1.49

Preliminary tests were performed to determine the appropriate soil: solution ratios and equilibrium time and to evaluate stability of the test substance in CaCl solution with soil (under test conditions), potential for sorption of the test substance to test vessels and any effects of the inclusion of a biocide in solution.

In the preliminary tests, Soft:solution ratios of 6/20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), equilibrium time for adsorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were determined. As part of the equilibrium time determination, the stability of the test substance was monitored and shown to be 99% for Vero Beach, Howe and Wolf Ranch soils after 72 hrs and ca. 81% for Stanleo soil after 24 hrs. Incontrol samples, shaking the test substance in CaCl₂ solution the absence of soil for 72 hours gave a mean recovery of 97.0% AR indicating that adsorption to the test vessel was not occurring.

Freundlich isotherm tests were performed with all soils using the indirect and parallel methods. For the adsorption step, appropriate solutions of the test substance were applied to the samples and the samples were shaker for 1 of 48 hours at  $22 \pm 5$  C. Following the adsorption step, the samples were removed from the staker centrifuged, and the adsorption supernatants removed. Chromatographic analysis of supernatants were reported to show >90% AR present as unchanged test substance in all soils after 1hr (Verobeach, Wolf ranch and Stanley soils) or 48hr (Howe soil).

For the desorption step, a 20 mL volume of fresh 0.01 M CaCl₂ solution was added and the samples were shaken for a further 1-48 hours at  $22 \pm 1^{\circ}$ C. Following the desorption step, the samples were removed from the shaker, centrifuged, and the desorption supernatants removed. The desorption supernatants were analysed by LSC and the highest concentration solutions of each test substance were also

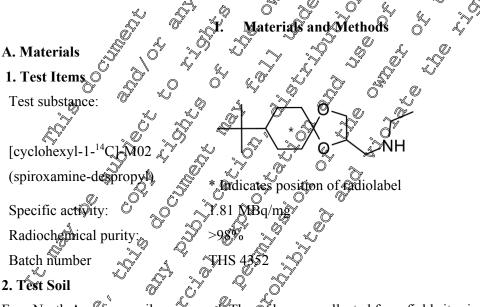


analysed by HPLC (with radiochemical detection). The soil samples were combusted in a sample oxidiser and analysed by LSC to determine the radioactivity present.

Mass balances ranged from 90.33-100.25% AR. The amount of radioactivity adsorbed on the soil at adsorption equilibrium ranged from 41.58-93.49% AR. After the adsorption phase, 41.58 - 60.6% AR was adsorbed to Vero beach soil, 61.58 - 82.67% AR adsorbed to Howe soil, 72.99 - 81.4% AR to Wolf ranch and 86.90 - 93.49% AR to Stanley soil.

Freundlich adsorption coefficients (K_f) ranged from 2.93-134.0 L/kg. When normalised to organic carbon, Freundlich adsorption coefficients (K_{foc}) ranged from 916.7-8993.6 L/kg, indicating that M01 (spiroxamine-desethyl) exhibits medium to immobile mobility in soil according to the McCarl mobility classification (McCall et al 1981⁷). The 1/n values ranged from 0.827-0.922, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range. Adsorption was shown to be generally correlated with organic carbon content and there was no clear correlation with the pH of the soils. The OECD 106 Checklist (v2) was used to evaluate the study, however all final parameters used are taken from the study report. The evaluation confirmed acceptability for all soils according to the quality criteria and therefore acceptable for regulatory use.

Soil	Vero Beach J Howey D Wolf Ranch & Stanley
	(Sand) (Sandy Joam) (Sandy Joam) (Sitty clay (Dam)
OC (%)	
pH (CaCl ₂ )	7.0 % 6.7 % 3.7 % 5.7 %
$K_{f}(L/kg)$	2.93 2 212.79 5 34.39 734.0
K _{foc} (L/kg)	9167 2 11406 2 5606.8 2 8993.6
1/n	0.886
R ²	0.999



Four North American soils were used. The soils were collected from field sites in Vero Beach (Florida, USA), Howe Ondiana, USA), Wolf Ranch (California, USA) and Stanley (Kansas, USA), and varied in organic carbon, pH and day content. After collection, soils were homogenized, air-dried, and passed through 2 mm reve.



Par	ameter		S	oil	<u> </u>
Soil D	esignation	Vero Beach	Howe	Wolf Ranch	Stanley
Geographic Lo	cation			ð	
City		Vero beach, Flor-	Howe, Indiana	Fresno, Capitornia	Stanley, Kansas
		ida		4	5 5 B
Country		USA	USA	<b>≪</b> UŠA	S USA S
Textural Classi	ification (USDA)	Sand	Sandy loam	Loam	Silty Ray loator
Sand	(%)	98.7	65.7	0 ⁵ 29.7 V	217.0 C
Silt	(%)	0.3	ي [®] 26.4	45.1 ^O	410 0
Clay	(%)	1.0	T.9 🔊	25.2 ^Q	A2.0 0 4
pН		<b>W</b>			
in H ₂ O		7.0 0	6.7 ⁽¹⁾	8.7	6.4
in CaCl ₂		6.3	r of Q	7.8	O DE A
Organic Matter	r (%) *	0.55	×1.92 ô	J 1.0 2	2.56
Organic carbor	n (%)	8.32 ×	× 1.12 ×	Q 20.97 Q	\$ 1.4 <b>9</b>
Cation Exchange	ge Capacity	n.a.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>مِ</u> كَّ 19 مَ	for the a.
(meq/100 g)			· ~ ~		
Water Holding	Capacity (%)				Ky .
maximum		n.a.		ي 32.0	O″ n.a.
at 1/3 bar	Ô		Ŷ Ŷ4.8 ^Ŷ	~~ ¹⁶ .8 ¢	34.0
n.a.: not analysed	d 🏷	arbon content bol.72	á Sì		
* Calculated by r	multiplying organic@	arbon content bOI.72	4 (mot reported) 🛛 🖏		

#### **B. Study Design**

#### 1. Experimental conditions

The test system for adsorption and desorption of 102 (spiroxantine-despropyl) on four North American soils consisted of borosilicate glass centrifuge tubes with Teflon seals and screw caps.

In preliminary tests, the adsorption of the test item to the test system surface, the optimal soil-to-solution ratio, the appropriate adsorption and desorption equilibration, times, the stability of the test item and effects of the inclusion of a biocide in solution were determined.

Freundlich isotherm texts were performed with all soils using the indirect and parallel methods. Soil:solution ratios of 6:20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), and equilibrium time for adsorption (I how for Vero Beach, Werf Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for VergeBeach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were used. Solutions of the radiolabelled test substance of acetonitrile were prepared and diluted with 0.01 M CaCl_k such that test substance application achieved concentrations of 5.27, 0.54, 0.06 and 0.01 mg/L. Biocide was not included in isotherm solutions as it was demonstrated that this gave no improvement for stability purposes. The volume of organic solvent added was not clearly reported (but assumed to be within acceptable limits).

6 (Vero Brach), 2 (How or 1/g (Wolf Ranch and Stanley) dry weight of soil were transferred into centrifugeubes and 20 mL of 0.01 M CaCl₂ containing test substance were applied to the samples. The samples were then shaken to 1 (all soils except Howe) or 48 hours (Howe) at  $22 \pm 1^{\circ}$ C in the dark. For the desorption step 20 mb volume of fresh 0.01 M CaCl₂ solution were added and the samples were shaken for a further 1 or 48 hours under the same conditions. After the adsorption step, the supernatant was subjected to chromatographic analysis by HPLC (top concentration only).



#### Adsorption phase

Parameter		Description
Soil condition		Soils were air-dried and sieved to 2 mm
Soil sample weight		1 g (dry weight) per replicate for Walf Ranch and Stapley soils 3 g (dry weight) per replicate for Prowe soil 6 g (dry weight) per replicate for Vero Beach for
Equilibration solution		No pre-equilibration conducted
Control (preliminary e		No soil (test item in 0.01) CaCl ₂ only)
Test item concentra-	Nominal application rates	Nominal concentrations were not specified (assumed $601$ to 5 mg/L)
tion	Analytically (LSC) measured concentra- tions	Measured concentrations (LSC) in test solution, 327, 054, 0.06 and 0.01 mg/L (4 concentrations)
Identity and concentra	ation of co-solvent	Dosing store, madeop in acetonitrile
Soil: Solution ratio		3:20 (Wolf Ranch and Stanley) 6:20 (New Sealt) 6:20 (VeroBeach)
Number of repli-	Control Q	Quplicate 6 0 0 0
cates	Treatments	Dupligate 2 2
Equilibration condi- tions	Time y y Temperature	1 kfrs (Vero Beach, Wolf Ranch & Stanley soils)         4 hrs (Howe soil)         22±1         7         1 n the dark
Ś	Shaking method	Overhead shake
Method of separation		Centrifugation Q S
ð á	Speed@rpm) O &	6000 rpm & W
Centrifugation	Duration 🔅 🔬	No minantes
Ê,	Method of separating	Supernatant was carefully decanted.
Desorption phase		
Parameter		Description
Soil samples from ade	orntion whase insed	Yes
Son sumplex from ue		The anounts of test item adsorbed to soil after adsorption
Amount of test item p	resent in the adsorbed	ranged from 41.58 to 93.49% (reported for definitive test).
state/adsorbed amoun	t (mg a.i./kg soil)	Seo OECD 106 Checklist below for further details for each
L L		<u>5</u> 01.
Number of desorption	cyclies O'	
Equilibrium solution a treatment for desorption		The decanted solution was replaced by fresh aqueous 0.01 M CaCl ₂ solution. Approximately 20 mL was used as equilibration solution.
		1:20 (Wolf Ranch and Stanley)
Soil: Solution atio	A A	3:20 (Howe soil)
Lý ví ô		6:20 (Vero Beach)
	L.	
õ		



Parameter		Description	
	Control	Not stated $Q_{\ell}^{\circ}$	~
Number of replicates	Treatments	Duplicate	F.
	Time	1 hrs (Vero Beach, Wolf Ranch & Stanley soils) 48 hrs (Howe soil)	-
Desorption Equilibra- tion conditions	Temperature	22±1°C	Ď
tion conditions	Dark	In the dark	n`
	Shaking method	Overhead Maker	Ś
Method of separation o	f supernatant	Centrifegation	, O` V
	Speed (rpm)	60004pm Q' & A A	•
Centrifugation	Duration	1 minutes 2	
	Method of separating supernatant	Supermatant was carefully decanted.	

#### 2. Analytical Procedures

After each adsorption and desorption step the aqueous superplatant was separated from the soil by centrifugation and the amount of M02 (priroxamine-despropy) in the superplatant was adalysed by liquid scintillation counting (LSC).

The partition of the test item in the adsorption and desorption batch equilibrium operiment was determined based on the radioactivity content in the supernatant only (i.e. the indirect method). After the desorption step, the soil was air-drived and the radioactivity content determined by combustion/LSC to establish the material balance.

Parental mass balance was determined >90% by HPC/radio-detection analysis of the supernatant only. Adsorption and desorption isother is were calculated by linear regression analysis of the adsorption or desorption data according to the Freundich equation

Additional information on stability of M02 (spiroxamine despress)) was determined in the preliminary tests. HPLC analysis of the supernatant over duration of 24, 48 and 72 hrs showed for the Vero beach, Wolf ranch and Howe sous >99% AR present as M02 (spiroxamine desprops)) after 72 hrs and for the Stanley soil *ca.* 81% AR present as M02 (spiroxamine desprops) after 24 hrs. The reverse phase High Performance Liquid Chromatography (HPEC) system used a Kichrospher 100 RP-18 column and gradient elution of actionitrile + 0.5% tricthylamine and water + 0.5% triethylamine (starting gradient 55:45, v/v) and radio-defector.

The limit of detection (LOF) was not specified in the report, however, the concentrations of the test substance used are likely sufficient to allow adequately accurate measurements of levels of the test substance.

Results and Discussion

#### A. Results of Preliminary Test

Soil:solution ratios of 6:20 (Vero Beach) 3:20 (Howe) and 1:20 (Wolf Ranch and Stanley), equilibrium time for adsorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) and desorption (1 hour for Vero Beach, Wolf Ranch and Stanley soils and 48 hours for Howe soil) were determined. Recovery from control samples shaking an aqueous solution of the test substance in the absence of sourfor 72 hours gave a mean recovery of 97.0% AR indicating that adsorption to the test vessel was not occurring.

As part of the equilibrium time determination, the stability of the test substance was monitored and shown to be >99% for Vero Beach, Howe and Wolf Ranch soils after 72 hrs and *ca.* 81% for Stanley soil after 24 hrs.



#### **B.** Transformation of test substance

Stability of M02 (spiroxamine-despropyl) was monitored during the isotherm determinations by HDL°C analysis of the supernatant after the adsorption step. The majority of radioactivity in the supernatant was  $\mathcal{A}$ unchanged metabolite M02 (spiroxamine-despropyl) (only minimal details are provided in the report^{$\mathcal{O}$} but a recovery of >90% over all soils was quoted).

#### C. Findings

Mass balances ranged from 90.33-100.25% AR (based on total radioactivity). The amount of radioactivity adsorbed on the soil at adsorption equilibrium ranged from 41.5893.49% AR.

	(incan valu		poxamme-despre	hha of (	
Soil	Concentration	Concentration	<b>Concentration</b>	Adsorption	Mass
	initial	supernatant	(mg/kg) ^A	percentage	balance
	(mg/L) A	(mg/L) ^A	$\bigvee$ (mg/kg) A	(%) ^{*0*}	✓ (% AR) ^B ( °
Vero Beach	0.013	0,005 ~	0.025 ~♥	<u>1</u> 60,69	<b>8</b> 8.54 <b></b>
(Sand)	0.056	<b>\$</b> 22.	20.1	§ 60.28 ×	_≪ 95.92
	0.538	0.25	× 0,957 ×	\$3.38 C	S 96. S
	5.268	0 [°] 3.078	× 7.300 0	چې 41.5%	100.25
Howe	0.013	o [™] 0.002 [™]	0.06 <u>7</u>	° 81039 N	<b>9</b> 4.32
(Sandy loam)	0.054	9.009	0.299	2.67	98.62
	0.513	°~~0.136	or 2510 S	73.430	99.34
	5.363	2.000	_22.013	· 61.58	97.94
Wolf Ranch	0.013	5 <u>60003</u>	0.210	¢ <u>81</u> 743 , ?	95.77
(Loam)	0.086	0.012	_^y 0.8 <b>©</b> 90° [™]	£79.52	95.08
	Q.538 ~	0.13 [©]	× \$910 ×	<u>د</u> 75.42	92.94
	\$5.275°	A 1¢23	<b>₹</b> 76.890 U	0 [*] 72.99	97.49
Stanley	0.043 C	<b>\$</b> .001	0.24 <b>0</b>	83.49	93.78
(Silty clay	P Q.956 L	0.004	× 1.030 Ø	<b>\$\$92.83</b>	94.21
loam)	0.538	× 0,048 🔬	× ~9.800	[®] 91.11	90.33
<u> </u>	5.268	0.690	91.550	@ 86.90	94.62

Table CA 7.1.3.1.2-8:	Concentrations	at adsorption	equilibrium	and re	cover	of radi	oactivi
(	mean values) for	· M02 (spinoxa	amine-despro	₽¥₽°	Q.	Å	Ø Åa

Bold values used to calculate the percent loss A Note: these values have been catculated from the reported values of µg/20 mL

В Mass balance (determined as oral radioactivity) values offored and after the desorption step

Freundlich adsorption coefficients (K_f) ranged from 2,93-1134.0 L/kg. When normalised to organic carbon, Freundlich ansorption coefficients (K_{foc}) ranged from 206.7-8993.6 L/kg, indicating that M02 (spiroxamine-despropyl) Sukely of exhibit low nobility in soft. The Freundlich exponent 1/n values ranged from 0.827-4000, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range

7.1.3.1.2.9. Freundlich adsorption coefficients for M02 (spiroxamine-despropyl)

Soil Sero Beac (Sand)		Wolf Ranch (Loam)	Stanley (Silty clay loam)
$OC(\%)$ $\swarrow$ $(\%)$ $(\%)$	S 1.12	0.97	1.49
$pH(CaCl_2)$ $7.0$	6.7	8.7	6.1
K _f (L/kg) 2.93	12.79	54.39	134.0
K _{foc} (L/kg) 0 906.7	1141.6	5606.8	8993.6
1/n 5 5.876	0.827	0.922	0.886
$\mathbb{R}^2$ $\mathcal{I}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$	0.998	1.0000	0.999

#### D. Evaluation of the data according to EFSA Evaluators Checklist

The results of the determination of the Freundlich Isotherm were analysed using the Excel-sheet provided by EFSA (summarised in Table CA 7.1.3.1.2-11). The concentrations in the supernatant and the soil as given in the report were used as input data. Individual replicate concentrations were not available,



so mean values as given in the report have been used in the calculation and as the adsorption isotherms were conducted with only 4 concentrations the confidence intervals were calculated by added formulae.

The degree of sorption was sufficient, and the mass balance at the highest concentration, corrected for stability, was used to calculate the 'f' value, following EFSA (2017). Chromatographic analysis of supernatant during the isotherm test showed a reported ">99%" stability for Verce Beach, Howg and Wolf ranch soils, and ">90%" for Stanley soil. Therefore, 99% and 90% have been used below as appropriate.

Soil	Mass balance at highest concentration (% AR)	Stability (%)	'f' value for mput into
Vero beach	100.25	99.Q × °	L. 0.75 C Q
Howe	97.94	× <u>29</u>	
Wolf ranch	97.49	· · · · · · · · · · · · · · · · · · ·	3.48
Stanley	94.62		14:84
¹ From chromatographic analy	sis of adsorption supernatant dur	tog isothêrm test 🖉 🔗	O L A C

Table CA 7.1.3.1.2-10: Calculation of 'f' values for checklist
----------------------------------------------------------------

Relevant quality checks were performed to evaluate the acceptability of the study. For the vero Beach, Howe and Wolf Ranch soils, these checks confirmed that the mass balance (90.39-100.25%) was acceptable and that the % adsorption was generally acceptable for all soils (49.76-95,45%). The LOQ was not reported, however, the analytical method (1SC) was considered acceptable assiming reasonable volumes used for counting. The validity of using the indirect pethod, based on a Kdr soil solution ratio > 0.3, was confirmed. The R² of the standard linear regressions ranged from \$998 to 0.999 and the visual fit of both the standard gression and the residual plots were good. The  $K_{\rm fE}$  /  $K_{\rm fP}$  atio ranges give maxima very slightly above 1.2 for Stanley soil only. However, sorption is high for all tested soils/subsoils, with both  $\delta$  and  $K_{d}$  soil/solution ratio gassing with good margins. Furthermore, the ratio of 1.2 is only an initial proposal, it is considered that this does not change the overall outcome of the study.

# Table CA 7.1.3.1.2.11: Results of the FFSA 106 data evaluation

Soil	Units	Quality crite-	Veræ Beach	Howe	<b>Wolf Ranch</b>	Stanley
Adsorption of method	- 43	DC. Not	Indirect	/ Indiræt	Indirect	Indirect
Soil solution ratio	ġ'nıL		\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	3:20	1:20	1:20
Mass balance of ¹⁴ C			\$5.92-00.25	93.8-101.2	92.94-97.49	90.33-94.62
f - due to loss	% <b>%</b>		\$0.75 ¢	0.04	3.48	14.84
Adsorbed per- centage (8)	9/0/ 		41.58 61.54	61.59-84.62	73.02-80.77	86.90-92.86
K _d x soil:solu- tion ratio		~~>0.3 ~~	0.71-1.60	1.60-5.50	2.71-4.20	6.63-13.00
$K_{fE}/K_f$		v <u>z</u> v.2 ~	1.012-1.018	1.000-1.001	1.045-1.050	1.190-1.206
ads K _f	Ľ/kg	· · ~	2.937	12.594	54.785	138.350
95% conf dence in of- val**			2.11-4.08	9.22-17.20	49.589-60.525	79.15-241.84
ads Pn	- 2		0.871	0.815	0.928	0.903
95% con dence inter- val**	-	*	0.774-0.968	0.737-0.891	0.902-0.953	0.784-1.203
ads R ²	-	>0.975	0.999	0.999	1.000	0.998



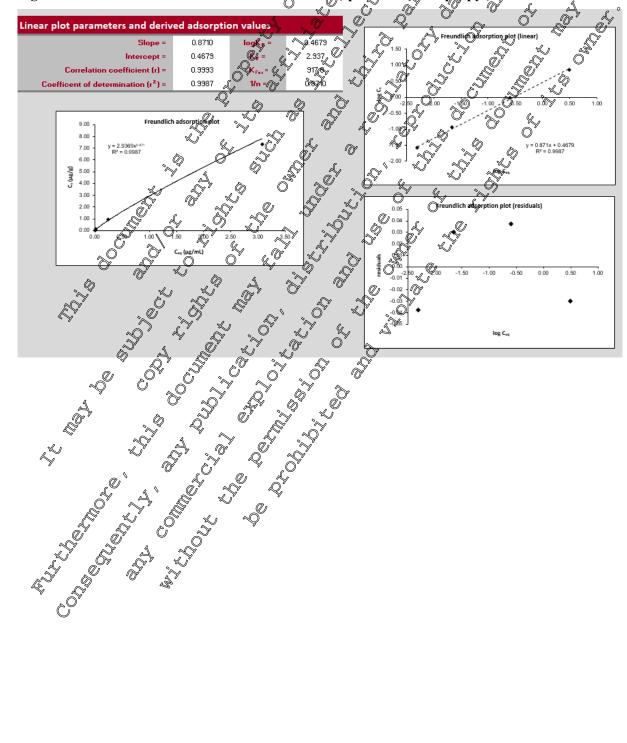
**

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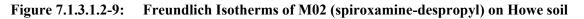
Soil	Units	Quality crite- ria	Vero Beach	Howe	Wolf Ranch	Stanley
ads K _{foc}	L/kg		917.8	1124.4	5648	9285
Visual fit to Freundlich iso- therm	-	-	Good	Good	Geod	Good of
Residual plots randomly dis- tributed	-	-	Good	Good	Good	Good S

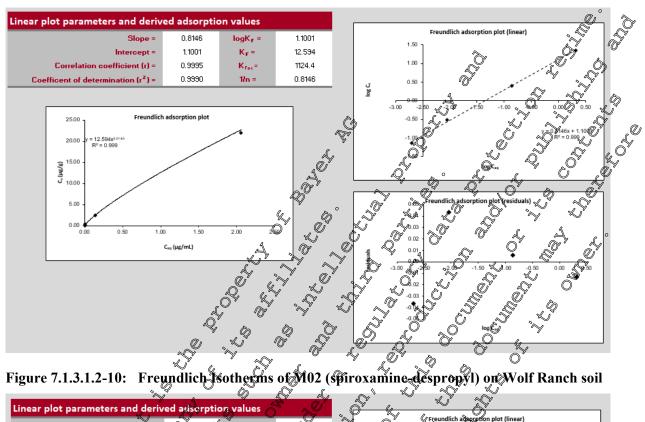
creu (see poid values in Table CA 7.1.3.1.2-8) corrected for stability, see Table CA 7.1.3.1.2-b Q Q Confidence intervals provided in the EFSA Excel spreadsheet were re-calcolated manually as available input data con sisted of only 4 concentration levels sisted of only 4 concentration levels

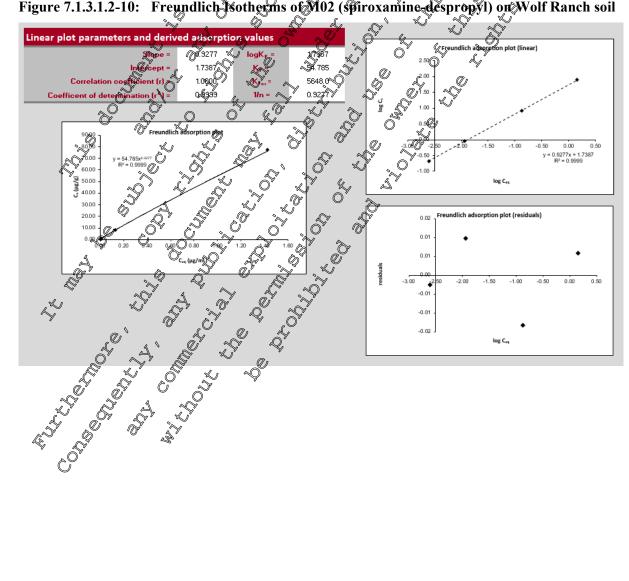
Į. Freundlich Isotherms of M02 (spirosamine despropyl) on Vero Beach soil Figure 7.1.3.1.2-8:





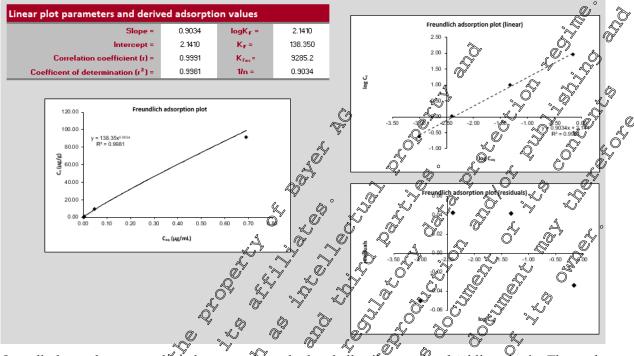












Overall, the study was conducted to a good standard and all soils pass the checklist criteria. The study conclusions can thus be considered reliable.

#### A GIII. O Corclusions

Freundlich adsorption coefficients  $(K_f)$  ranged from 2.93-134.0 L/kg (n=4). When normalised to organic carbon, Freundlich adsorption coefficients  $(K_{foc})$  ranged from 916.7-8993.6 L/kg, indicating that M02 (spiroxamine-despropyl) exhibits medium to infimobile mobility in soil according to the McCall mobility classification (McCall et al 981%). The 14 values ranged from 0.827-0.922, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.

Adsorption was shown to be generally correlated with organic carbon content and there was no clear correlation with the pt of the soils.

The OECD 106 Checklist (v2) was used to evaluate the study. The evaluation confirmed acceptability according to the quality criteria and therefore acceptable for regulatory use. A number of minor differences in the derived  $Q_{FOC}$  values were noted but this was attributed to the original calculation being performed on averages rather than single timpoints. Since the differences were very minor, for consistency the endpoints determined in the study report are used and considered to have no impact on the risk assessment.

#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) OECD 106 (required guideline). The study is considered valid to assess the adsorption and desorption characteristics of the spiroxamine metabolite M02 (spiroxamine-desproyel) in soil.



Data Point:	KCA 7.1.3.1.2/03
Report Author:	
Report Year:	1997
Report Title:	Adsorption/desorption of [cyclohexyl-1-14C] WAK 6301 on four different fils
Report No:	FM763
Document No:	<u>M-006089-01-1</u>
Guideline(s) followed in	OECD – Guideline for Testing of Chemicals No.: 106 Adsorption/Desorption
study:	May 12, 1981
Deviations from current	Yes (refer below) Some minor deviation(s) not relevant for the refubility of the midy (described in study summary)
test guideline:	Some minor deviation(s) not relevant for the reliability of the gody (described in
	study summary)
Previous evaluation:	yes, evaluated and accepted Q ^y Q ^o L ^y C ^y Q ^y
	$ $ KAR (2010), KAR (2014) $Q^{\prime}$ $\sim$ $Q^{\prime}$ $\sim$ $Q^{\prime}$ $\sim$ $Q^{\prime}$
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes to or

#### **Executive Summary**

The adsorption and desorption of [cyclohexy].  $1^{-14}$ C] M03 (spiroxanine-N-oxide) on four NortDAmerican soils was studied using the batcloequilibrium method with a diered approach.

Parameter			Ś	à s	Soj		×,
Soil Designation	~0	Vero bea	ch	W Howe	Ş W	olf Ranch	🖉 Stanley
Textural Classification	ı (USDA) [∭] ″	🔬 Sand	× (	, Sandy loam	\$``\	Loan	Silty clay loam
pH (CaCl ₂ )		0 63 °		6.7	Č,		5.5
Organic carbon (%)	× Å	0.32			& u	0.97	1.49

Preliminary tests were performed to determine the appropriate soil:solution ratios and equilibrium time and to evaluate stability of the test substance in CaCl solution with soil (under test conditions), potential for sorption of the test substance to test vessels and any effects of the inclusion of a biocide in solution.

Soil:solution ratios of 6:20.0 ero Beach and Howe) 3:26 (Wold Ranche and 1:20 (Stanley), and equilibrium time for adsorption (48 hours for Vero Beach, Wolf Ranch and Howe soils and 1 hours for Stanley soil) and desorption (48 hours for Vero Beach, Wolf Ranch and Howe soils and 1 hour for Stanley soil) were determined. As part of the equilibrium time determination, the stability of the test substance was monitored and shown to be 99% for all soils in control samples, shaking the test substance in CaCl₂ solution in the absence of soil gave a recovery of 97.8% All after 72 hrs, indicating that adsorption to the test vessels was not occurring.

Freundlich isotherm tests pere performed with all soil cusing the indirect and parallel methods. For the adsorption step, appropriate solutions of the test substance were applied to the samples and the samples were shaken for 1 or 48 hours at  $22 \pm 1^{\circ}$ C. Following the adsorption supernatants removed. For the desorption step, a 20 mL volume of fresh 0.01 M CaCl₂ solution was added and the samples were shaken for a further 1-48 hours at  $22 \pm 1^{\circ}$ C. Following the desorption step, the samples were removed from the shaker, centrifuged, and the adsorption was added and the samples were shaken for a further 1-48 hours at  $22 \pm 1^{\circ}$ C. Following the desorption supernatants removed from the shaker, centrifuged, and the desorption supernatants were quantified by LSC. Supernatants of the highest concentration solutions of each soil were also analysed by Thin Layer Chromatography (TLC) with radiochemical detection. The soil samples were combusted in a sample oxidiser and quantified by LSC to determine the radioactivity present.

Mass balances ranged from 91.45-101.70% AR. The amount of radioactivity adsorbed on the soil at adsorption equilibrium ranged from 30.10-98.64% AR. After the adsorption phase, 30.10 - 41.72% AR was adsorbed to Vero Beach soil, 48.78 - 98.32% AR adsorbed to Howe soil, 68.89 - 81.49% AR to Wolf ranch and 95.59 - 98.64% AR to Stanley soil.

Freundlich adsorption coefficients (K_f) ranged from 1.767-370.899 L/kg. When normalised to organic



carbon, Freundlich adsorption coefficients (K_{foc}) ranged from 552.3-24892.5 L/kg, indicating that M03 (spiroxamine-N-oxide) exhibits medium to immobile mobility in soil according to the McCall mobility classification (McCall et al 1981⁷). The 1/n values ranged from 0.835-0.939, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range. Adsorption was shown to be generally correlated with organic carbon content and there was no dear correlation with the pH of the soils. The OECD 106 Checklist (v2) was used to evaluate the study, however all final parameters used are taken from the study report. The evaluation confirmed acceptability according to the quality criteria and therefore acceptable for regulatory use 1

		i Ca	- 4	
Soil	Vero Beach	Howe 💎	WolfRanch	C Stanley C (Silty Clay logm)
	(Sand)	(Sandy loam)	(Døam)	(Silty elay loam)
OC (%)	0.32	1.12	87	1.49.0°
pH (CaCl ₂ )	7.0	67		→ 0.1 ×
$K_{f}(L/kg)$	1.7674	<b>3292</b> 60	> 15.9163	370,8988
K _{foc} (L/kg)	552.3	د 350.5¢°	×1640.9	Q* 244892.5√
1/n	0.9388			° U.8.548
$\mathbb{R}^2$	0.9981	A 0.9990 C	Q 0.9996	0,9091 4 4 4 4 4 4 4 4 4 5 4 5 4 5 7 6 7 1 4 7 1 4 7 1 4 7 1 7 1 7 1 7 1 7 1 7
A. Materials	Ŷ,	Materials and Meth	0.9996	
1. Test Items				
Test substance:				
[cyclohexyl-1- ¹⁴ C				

#### A. Materials

#### of radiolaber [cyclohexyl-1 Indicates position (spiroxamine O MBq/mg Specific activity: Radiochemical pur Batch number

#### 2. Test Soil

Four North American Rils were used The Fils were collected from field sites in Vero Beach (Florida, USA), Howe Ondiana, USA, Wolf Ranch, California, USA) and Stanley (Kansas, USA), and varied in organic carbon, pH and chay coment. After confection soils were homogenized, air-dried, and passed through a mm sieve. a

#### Table CA 7.1.3.1.2.12: Physico-chemical properties of test soil

Para	ameter 🗸		S		
Soil Dé	signation	Wero Beach	Howe	Wolf Ranch	Stanley
Geographic	vignation cation	\$ \$			
City Of	())	Vero beach, Flor-	Howe, Indiana	Fresno, California	Stanley, Kansas
L E	X A X	ida			
Country O	Î Î Î	USA	USA	USA	USA
Textural Quissi	fication (USDA)	Sand	Sandy loam	Loam	Silty clay loam
Sand 🖒	(%)	98.7	65.7	29.7	17.0
Silt	(%)	0.3	26.4	45.1	41.0
Clay	(%)	1.0	7.9	25.2	42.0



Parameter	Soil					
Soil Designation	Vero Beach	Howe	Wolf Ranch	Stanley _{@1} °		
pН				Stanicy (		
in H ₂ O	7.0	6.7	8.7 嶡	6		
in CaCl ₂	6.3	6.7	7.8	\$.5		
Organic Matter (%) *	0.55	1.92	1,67	\$2.56		
Organic carbon (%)	0.32	1.12	×0.97	× 1.49 ×		
Cation Exchange Capacity (meq/100 g)	n.a.		2 19 2 19	7%a. 0		
Water Holding Capacity (%)		L.O. J.	<u>к</u> , о			
maximum	n.a.	25.5	32.0Q			
at 1/3 bar	2.8	14.8	× 168 ~	<u>34.0</u> ,∽		

* Calculated by multiplying organic carbon content by I

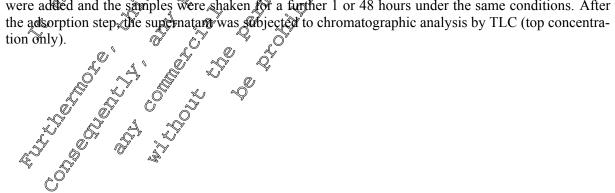
#### **B. Study Design**

**1. Experimental conditions** The test system for adsorption and desorption of M03 (spiroxamine-Novide) on four North American soils consisted of borosilicate glass centrifuge tobes with Tethyn seals and screw caps.

In preliminary tests, the adsorption of the test item to the test system surface, the optimal soil-to-solution ratio, the appropriate adsorption and desorption equilibration times, the stability of the test item and the effects of inclusion of a biceide in the solution were determined.

Freundlich isotherm tests were performed with all soils using the modirect and parallel methods. Soil:solution ratios of 6:20 Vero Beach and Howe) 3:29 (Welf Ranch) and 1:20 (Stanley), and equilibrium time for adsorption 48 hours for Oero Beach, Wolf Ranch and Howe soils and 1 hours for Stanley soil) and desorption (48 hours for Vero Beach, Wolf Ranch and Howe soils and i hour for Stanley soil) were used. Solutions of the adiolabelled test substance in acetonitrile were prepared and diluted with 0.01 M CaCl₂, such that test substance application achieved concentrations of 4.94, 0.49, 0.05 and 0.01 mg/L for solutions applied to Vero Beach and Hower For Wolf Ranch, concentrations of 4.94, 0.50, 0.05 and 0.01 mg/f were achieved and for stanley, concentrations of 5, 1, 0.50, 0.05 and 0.01 mg/L were achieved. Biocide was not included in isotherm solutions as it was demonstrated that this was not needed for stability purposes. The volume of organic solvent added was not clearly reported (but assumed to be within acceptable limits

6, 3 or 1 g dry weight of soil as appropriate were transferred into centrifuge tubes and 20 mL of 0.01 M CaCl₂ containing test substance were applied to the samples. The samples were then shaken for 1 or 48 hours at  $22 \pm 1^{\circ}$ C in the dark. For the desorption step, 20 mL volume of fresh 0.01 M CaCl₂ solution were added and the samples were shaken for a further 1 or 48 hours under the same conditions. After





#### Adsorption phase

Parameter		<b>Description</b>
Soil condition		Soils were air-dried and sieved to 2 mm
Soil sample weight		1 g (dry weight) per replicate for and Stanley soil 3 g (dry weight) per replicate for Wolf Ranch soil 6 g (dry weight) per replicate for Wero Beach and Howe soils
Equilibration solution		No pre-equilibration conducted
Control (preliminary	experiment)	No soil (test item in 0.01) (CaCl ₂ only)
Test item concentra-	Nominal application rates	Nomingly concentrations were not specified (assumed 601 to 5 mg/L)
tion	Analytically (LSC) measured concentra- tions	4.94, 0.49, 0.05, and 0.01 mg/L for Vero Beach and Howe. 4.94, 0.50, 0.05 and 0.01 mg/L for Wolf Ranch. 5.11 0.50, 0.05 and 0.01 mg/L for Stanley (4. Oncentrations)
Identity and concentra	ation of co-solvent	Dosing tock made up dv acetôrstrile
Soil: Solution ratio		1:20 (Stanfey) 3:20 (Wolf Ranch) 6:20 (Vero Beach and Howe)
Number of repli- cates	Control Treatments	Duplicate Deplicate Deplicate
Equilibration condi-	Time Temperature Dok Shaking method	In the dark       In the dark         Overwead shaker       In
Method of separation		Centrifugation O
Centrifugation	Speed (rpfo)	6000 rpm         0         0           15 minutes         0
رین Desorption phase	supernatant 27	Supernation was carefully decanted.
Parameter V		Description
Soil samples from ads	sorption phase used 7 %	Yes &
Å.	Yesent in the adsorbed	The amounts of test item adsorbed to soil after adsorption ranged from 30.10 to 98.64% (reported for definitive test). See OECD 106 Checklist below for further details for each soil.
Number of desorption	Acycles V	1
Equilibrium solution a treatment for desorpti	and quantity used per	The decanted solution was replaced by fresh aqueous 0.01 M CaCl ₂ solution. Approximately 20 mL was used as equilibration solution.
Soil: Solution ratio		1:20 (Stanley) 3:20 (Wolf Ranch) 6:20 (Vero Beach and Howe)



Parameter		Description	
	Control	Not stated	$\gg$
Number of replicates	Treatments	Duplicate	
	Time	1 hrs (Stanley soil) 48 hrs (Vero Beach, Wolf Ranch Howe soils)	
Desorption Equilibra- tion conditions	Temperature	22±1°C	)
tion conditions	Dark	In the dark	
	Shaking method	Overhead Maker	Å
Method of separation of	f supernatant	Centrifigation	Э` ,
	Speed (rpm)	6000 pm Q' & L' L' L'	
Centrifugation	Duration	1 Agninutes ~	
Centinugation	Method of separating supernatant	Supermatant was carefully decanted.	

#### 2. Analytical Procedures

After each adsorption and desorption step the aqueous superinatant was separated from the soil by centrifugation and the amount of M03 (prirox annue-Noxide) in the supermatants was quantified by liquid scintillation counting (LSC).

The partition of the test item in the adsorption and desorption batch equilibrium operiment was determined based on the radioactivity content in the supernatant only (i.e. the indirect method). After the desorption step, the soil was air-drived and the radioactivity content determined by combustion/LSC to establish the material balance.

Parental mass balance was defermined >99% in all soils by reverse phase Thin Payer Chromatography (TLC) analysis of the supernatationally using a mobile phase of acetonitrile/water/25% ammonia (80:18:2, v/v/v).

Adsorption and resorption isotherms were calculated by linear regression analysis of the adsorption or desorption data according to the Freundlich equation.

Additional information on stability of 103 (spiroxamine-Noxide) was determined in the preliminary tests. Chromatographic analysis of the supernatant after k or 48 fors showed >99% AR present as M03 (spiroxamine-N-oxide) for all soils

The limit of detection (LOD) was not specified in the report, however, the concentrations of the test substance used are likely sufficient to allow adequately accurate measurements of levels of the test substance.

### . Results and Discussion

#### A. Results of Preliminary Tests

Soil solution ratios of 6:20 (Vero Beach and Howe) 3:20 (Wolf Ranch) and 1:20 (Stanley), and equilibrium time for adsorption (48 hours for Vero Beach, Wolf Ranch and Howe soils and 1 hours for Stanley soil) and desorption (48 hours for Vero Beach, Wolf Ranch and Howe soils and 1 hour for Stanley soil) were determined. Shaking an aqueous solution of the test substance in the absence of soil for 72 hours gave a mean recovery of 97.8% AR indicating that adsorption of the test substance to the test vessels was not occurring.

As part of the equilibrium time determination, stability of M03 (spiroxamine-N-oxide) was monitored in the supernatant only and shown to be >99% for all soils after 72 hrs.

#### B. Transformation of test substance

Stability of M03 (spiroxamine-N-oxide) was monitored during the isotherm determinations by TLC



analysis of the supernatant after the adsorption step. >99% of the radioactivity was unchanged M03 (spiroxamine-N-oxide).

#### C. Findings

Mass balances ranged from 91.45-101.70% AR. The amount of radioactivity adsorbed on the adsorption equilibrium ranged from 30.10-98.64% AR.

		(° <b>F</b> -			
Soil	Concentration	Concentration	Concentration	Adsorption	A Mass A
	initial	supernatant	🖉 soil 🔬	percentage	🛛 🖓 balanee
	(mg/L) ^A	(mg/L) ^A	🖒 (mg/kg) ^A 🖓	`(%) ¢	≪ (% AR) ^B √
Vero Beach	0.011	0.007	0.013	38.65	<b>10</b> 1.70
(Sand)	0.048	0.028 🌾	⊘° 0.0€5 ×	J 419.72 O	∞92.0⊀€
	0.494	0.292	0 0,672	A0.80	91.58
	4.944	3.456	, <b>4</b> ,960 Q	^{0*} 30.10	<b>96:9</b> 9
Howe	0.011	0.004 ~~~	0.025	A 68.93 v	900.14
(Sandy loam)	0.048	Ø.015 ×		98.32	≪ 93.28°°
	0.494	Q 0.185V	₩ <u>1</u> ,027 ×	0 62.46	91.96
	4.944	2.5633 °∽	×8.038	~~~ 48, <b>7</b> 8	<b>98.</b> 17
Wolf Ranch	0.011	Q Q.002	≫ 0.052°	o 84.49 ô	≫98.62
(Loam)	0.051 🕡	<u>, 40.010</u>	S 0.207	° (\$1.44 O	¢ 95.12
	0.501	[™] 0.125	2.510	© 75.19 [℃]	o [™] 98.59
	4.944	ky 1. <b>63</b> 8 /y	<i>@</i> 22.707 [™]	<u>مَنْ 68</u> .89	91.45
Stanley	0.0 19		0.200	× 48.64 ×	94.54
(Silty clay	0.051	0.0008	0° 1300 c	×98.48	95.00
loam)	<b>9</b> .501	🗶 0.011 🔿	7%,000 (( ))	& 97. <b>7</b> 9	95.66
	<b>2 4</b> .944	<u>\$</u> _0 <b>2</b> 26	97.640	© 95.39	93.42

# Table CA 7.1.3.1.2-13: Concentrations at adsorption equilibrium and recovery of radioactivity

Bold values used to catchlate the percent loss A Note: these values have been calculated from the reported values opig/20 for B Mass balance determined as total radioactivity ovalues opid/are after the desorption step

Freundlich adsorption coefficients (Kr) ranged from 1. 567-370.899 Kg. When normalised to organic carbon, Froundlich adsorption coefficients (R_{foc}) ranged from 916.7-8993.6 L/kg, indicating that M03 (spiroxamine-N-oxide) is ikely to exhibit lov mobility in sol. The Freundlich exponent 1/n values ranged from 0.8348-09388, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range. To A

~Q		Y NY N	× •	,
Soil A	Vero Beach	Howe	Wolf Ranch	Stanley
0	🔊 (Sand) 🖉	Sandy Hoam)	(Loam)	(Silty clay loam)
OC (%)	0.32	~012	0.97	1.49
pH (CaCl ₂ )	7.0 0	Ø <u>6</u> .7	8.7	6.1
$K_{f}(\ell/kg)$	1.767Å	3.9260	15.9163	370.8988
K _{foc} (L/kg)	559.3	350.5	1640.9	24892.5
1/n	A` _€9388√	0.8714	0.8898	0.8348
R ²	.f _S\$U.9981 .∂	0.9990	0.9996	0.9991

Table CA 7.1.3.1.2	2-14: Freandli	ch adsorptio	n coefficients fo	r M03 (spiroxamine-N-ox	ide)
				· · · · · · · · · · · · · · · · · · ·	,

## D. Evaluation of the data according to EFSA Evaluators Checklist

The results of the determination of the Freundlich Isotherm were analysed using the Excel-sheet provided by ECSA (summarised in Table CA 7.1.3.1.2-16). The concentrations in the supernatant and the soil as given in the report were used as input data. Individual replicate concentrations were not available, so mean values as given in the report have been used in the calculation and as the adsorption isotherms were conducted with only 4 concentrations the confidence intervals were calculated by added formulae.

The degree of sorption was sufficient, and the mass balance at the highest concentration, corrected for



ð

stability, was used to calculate the 'f' value, following EFSA (2017). Chromatographic analysis of supernatant during the isotherm test showed a reported ">99%" stability for all soils, therefore, 99% has been used below.

Table CA	7131	2-15 Cal	culation	of 'f' <b>x</b>	values for	checklist
I abit Ch	1.1.0.1	2-13. Ca	iculation.	UI I V	anucsion	uncumpt

Soil	Mass balance at highest concentration (% AR)	Stability (%) ^A	Ö'f' value for input info checkist (%)
Vero beach	96.99	e 99 💭	3.98
Howe	95.17	A 99 O	5.78 0
Wolf ranch	91.45	<u>ه</u> 99 و	9.46
Stanley	93.42	<u>6</u> 99 K	<u> </u>

From chromatographic analysis of adsorption supernatant during isotherm test А

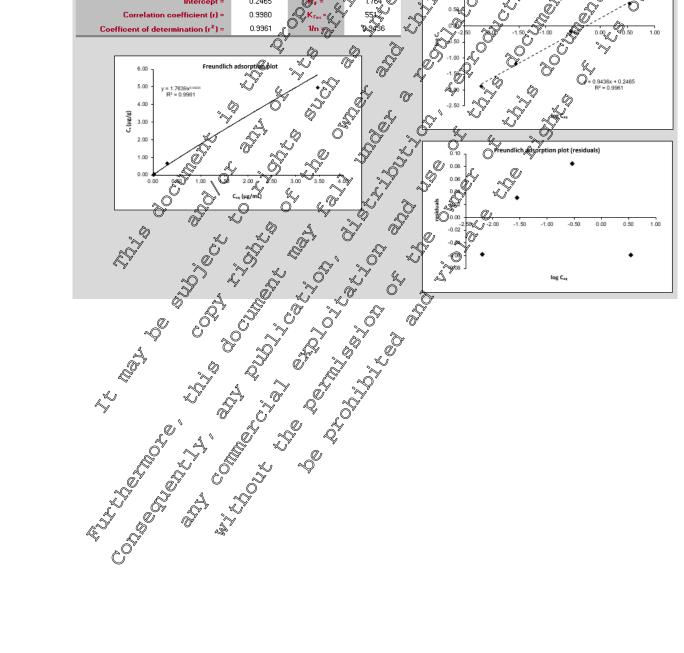
Relevant quality checks were performed to evaluate the acceptability of the study. These checks confirmed that the mass balance (91.45-101.70%) and the adsorption 30.1098.64% was acceptable for all soils. The LOQ was not reported, however, the analytical method (LSC) oughoto have been acceptable assuming reasonable volumes used for counting. The validity of using the ordirect method, based on a Kd * soil/solution ratio > 0.3, was confirmed. The  $K_{fr}/K_{f}$  ratio ranges are all below 1.2 for all soils. Table CA 7.1.3.1.2-16: Results of the EFSA 196 data evaluation of the standard solution of the s

						1
Soil	Onits	Quality crite	Vero Beach	Howe ~	Welf Ranch	Stanley
Adsorption method		1 - Q	Indirect	6 Indirect	Indipect	Indirect
Soil solution ratio	gmL (		×6:20 ×	6:20	3:20	1:20
Mass balance of ¹⁴ C		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	91.58-101.70	91.96 100.14	91.45-98.62	93.42-95.66
f – due to loss processes *		2 2 2 2	3.98 ³	5.78	9.46	7.51
Adsorbed per- centage $(\delta)$		<u>₹</u> 20%	30:10-41.05	48-78-68.42	68.89-81.37	95.58-98.61
K _d x soil:solu- tion ratio			×0.43-0.70	0.95-2.17	2.21-4.37	21.65-71.04
$K_{fE}/K_f$		×1.2 ~	1.107-1.152	1.092-1.134	1.132-1.159	1.082-1.085
ads K _f	L/kg O	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	§ 1.764	3.952	15.965	373.935
95% conf dence inter- val*			0,99-3.15	2.25-6.94	11.34-22.49	181.39-770.87
ads 1/n	~ - [®]		0.944 °C	0.882	0.894	0.837
95% confi- dence inter- val**			0.763-1.124	0.728-1.037	0.809-0.979	0.720-0.954
ads R ²		© ≥0.975	0.996	0.997	0.999	0.998
		7	·	·		

	No Pr	. Pa	"Nor	$\sim$
Table CA 7.1.3.1.2-16: Results	of the 🎼	FSA 196	data ev	alution
Table CIT /.1.9.1.2 TO: Results			unite cre	



Soil	Units	Quality crite- ria	Vero Beach	Howe	Wolf Ranch	Stanley
ads K _{foc}	L/kg		551.2	352.9	1645.9	25096
Visual fit to Freundlich iso- therm	-	-	Good	Good	ççod	Good O
Residual plots randomly dis- tributed	-	- carried out, these va	Good	Good	Good	Good C
** Confidence sisted of onl	intervals provide y 4 concentration	e CA 7.1.3.1.2-13) d in the EFSA Exce levels	el spreadsheet wer	re re-calc@ated m	anually as availabl	e input data cop
Figure 7.1.3.1	.2-12: Freun	dlich Isotherm	ıs ‰f M03¢spiı	roxamine-N-o	xide) on Vero	Beach soil
-		dlich Isotherm	as & M03 (spin		xřele) on vero	





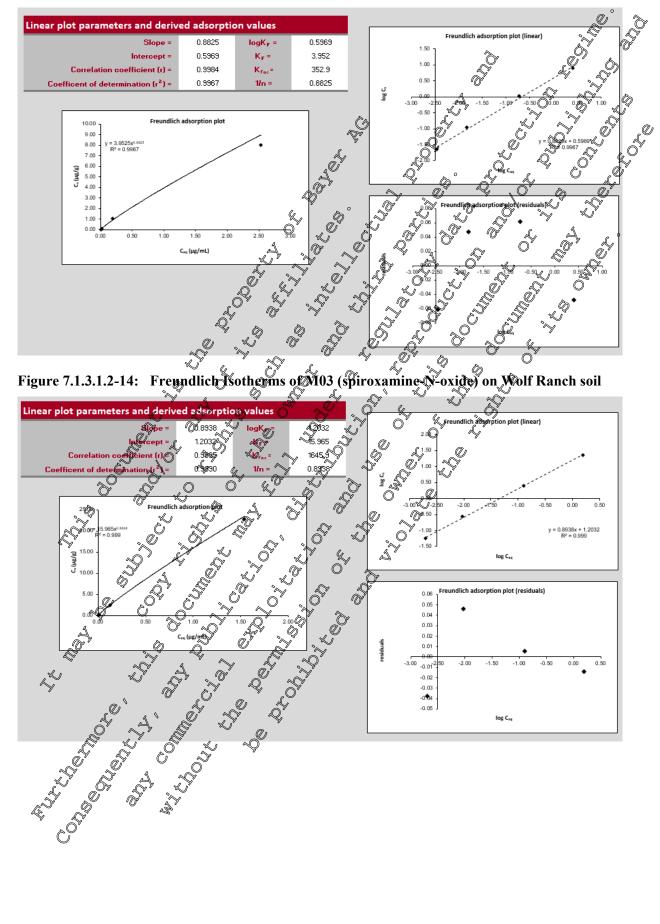


Figure 7.1.3.1.2-13: Freundlich Isotherms of M03 (spiroxamine-N-oxide) on Howe soil



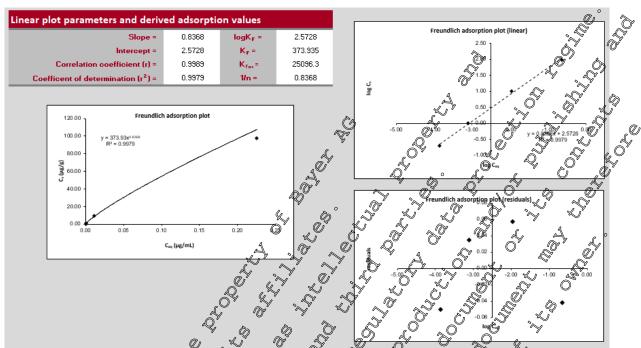


Figure 7.1.3.1.2-15: Freundlich Isotherms of M03 (spiroxamine-N-oxide) on Stanley soil

Overall, the study was conducted to a good standard, and all soils pass the checklist criteria. Overall, the study conclusions can be considered reliable.

# III. de Conclusions

Freundlich adsorption coefficients  $(K_1)$  ranged from 1.767-370.899 Dkg (n-4). When normalised to organic carbon, Freundlich adsorption coefficients  $(K_{0c})$  ranged from 552/3-24892.5 L/kg, indicating that M03 (spiroxamine-N-oxide) exhibits medium to immobile mobility in soil according to the McCall mobility classification (McCall et al 981). The 1/n values ranged from 0.835-0.939, indicating that the concentration of the test item affects its adsorption behaviour in the examined concentration range.

Adsorption was shown to be generally correlated with organic carbon content and there was no clear correlation with the put of the soils,

The OECD 106 Checklist (v2) was used to evaluate the study. The evaluation confirmed acceptability according to the quality criteric and therefore acceptable for regulatory use. A number of minor differences in the derived  $\hat{D}_{FOC}$  values were noted but this was attributed to the original calculation being performed on averages rather than single timpents. Since the differences were very minor, for consistency the endpoints determined in the study report are used and considered to have no impact on the risk assessment.

# Assessment and conclusion by applicant:

Study meets the current guarance and the requirements in 283/2013.

The study was conducted to study guideline(s) OECD 106 (required guideline). The study is considered value to assess the adsorption and desorption characteristics of the spiroxamine metabolite M03 (spiroxamine N-oxide) in coll.

Å

K 1



Data Point:	KCA 7.1.3.1.2/04
Report Author:	0
Report Year:	1998
Report Title:	Adsorption of [cyclohexyl-1-14C]WAK 6301 on Stanley soil before and affer de-
	struction of organic matter
Report No:	MR-598/98
Document No:	<u>M-006087-01-1</u>
Guideline(s) followed in	USEPA (=EPA): Section N, 163-1
study:	
Deviations from current	Yes Only two concentration were investigated in the study and no stability checks
test guideline:	Only two concentration were investigated in the study and no stability checks
	were conducted. Therefore, the OECD 106 checklist could on the complete Pon
	this study.
Previous evaluation:	No, submitted, not evaluated
GLP/Officially recog-	Yes, conducted und GLP/Officially recognised terming facultities
nised testing facilities:	
Acceptability/Reliability:	Supportive only by
Example Summary	

#### **Executive Summary**

The adsorption of [cyclohexyl-1-¹⁴C]-M03 (spiroxamine N-oxide) was investigated in this supplementary study on one North American soil, Stanley (silty day loan, pH S5, 1.49 % OC) using the indirect method. Two separate tests were conducted in Starley sold. One test to determine the adsorption of [cyclohexyl-1-¹⁴C]-M03 and a second using hydrogen peroxide to determine the effect of the organic matter of the soil sample. For each system two different concentrations (4.8.4 and 0.048 mg/L) were investigated. A soil/water ratio of 1:20 was used in both studies, which was determined from a previous study (Fent, 1997, CA, 7.1.3.1, 2003). For each study one gram (dry weight) of foil was combined with 20 mL of CaCl₂ solution. The soil solutions were agritated for 1 hoar in both the adsorption and hydrogen peroxide test in the dark at  $20\pm1^{\circ}$ 

For the adsorption study no desorption measurements were determined. After the adsorption step the aqueous supernatant was separated from the soil by centrifugation and the amount of M03 (spiroxamine-N-oxide) in the supernatants was determined and quantified by liquid scintillation counting (LSC) and thin layer shromatography (TLS).

The chromatographic analyses of the centrifuged supernatants (without hydrogen peroxide treatment) for the high-test concentration showed that 96% of the measured radioactivity could be assigned to parent. In the case of the  $H_2O_2$ -treated soil, the values were lower (*ca.* 85% AR).

Based on a carbon organic content of 1.49% the Ko value of Stanley was calculated to be 13,441 mL/g. The  $H_2O_2$ -treatment of soil was designed to have destroyed the organic carbon of the soil and lower the Kd value. However, the Kd value showed an increased value, resulting in an extremely high K_{oc} value. It was proposed by the study author that the treatment of the soil enhanced the sorption capacity and sorption locations. If this case, it is assumed to be due to the clay minerals (montmorillonit etc.).

Based on the classification system of McCallet *al.* (1980), M03 (spiroxamine-N-oxide) must be considered to be infinobile in soils like that tested in this study.

The OECD 106 checklist Sould not be used on the data presented in this summary as insufficient concentrations were provestigated. Therefore, this summary is supportive information only.

La Carta Car



#### I. Materials and Methods



#### 1. Test Items

Test substance:

[cyclohexyl-1-¹⁴C]-M0 (spiroxamine-N-oxide)

Radiochemical purity:

Specific activity:

	$+ \underbrace{*}_{N_{0}} _{N_{0}} \underbrace$
)3 )	* Indicates position of radiolabet 3.44  MBq/mg >99% (HPKC) KML 2352
	3.44 MBq/mg >99% (HPKC) KML 2352
	KML 2352 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2

#### 2. Test Soil

Batch number

The soil used in this study were collected from Starley (Kansas, USA). After collection, soils were homogenized, air-dried, and passed through a 2 mail sieve. For the adsorption study, a soil moisture of 3.11% (drying at 105°C) was determined for the sieved soil. For the hydrogen peroxide study, a soil moisture of 7.69% (drying at 105°C) was determined.

# Table CA 7.1.3.1.2-17: Physico-chemical properties oftest sol

Parameter 🌱	Soil Si Soil Si Soil Si
Parameter Soil Designation	Soil Soil Sitanley Soil Sitanley Soil Sitanley S
Geographic Location	Sanley Kansas
City	A Stanley Kansas
Country O	Stanley Kansas Stanley Kansas Sifty clay Cam
Geographic Location	Sifty clay dam
Sand S (%) d.	C A C LTO
$C_{14}$	2 A 2 Siny clay feam 2 A 2 A 2 A 2 A 2 A 2 A 2 A 2 A 2 A 2 A
Sand (%) & Sand Silt (%) & Sand Clay (%) & Sand pH in H ₂ O in CaCl ₂ (%) *	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
pH in H ₂ O in CaCl ₂	
in H ₂ O	[*] [*] [*] [*] [*] [*] 6.1
in H ₂ O in CaCl ₂	× × × × 5.5
Organic Matter (%) *	6.1 5.5 5.5 5.5 5.5 5.5 5.5 5.5 5
	1.49
Cation Exchange Capacity	0 0 x n.a.
(meq100 g)	
Water Holding Capacity (%)	n.a.
maximum 🖉 🔿 🖉	$\swarrow^{\vee}$ $\swarrow$ n.a.
Organic Carbon (%) Cation Exchange Capacity (med/100 g) Water Holding Capacity (%) maximum at 1/3 bar n.a.: not analysed	5.5 5.5 5.5 5.5 5.5 5.5 5.5 5.5
n.a.: not analysed O	
Water Holding Capacity (%) maximum at 1/3 bar n.a.: not analysed B. Study Design	

# 1. Experimental conditions

Two separate tests were conducted on Stanley soil. One test to determine the adsorption of [cyclohexyl- $1^{-14}$ C]-M03 and a second using hydrogen peroxide to determine the effect of the organic matter of the



soil sample.

For the hydrogen peroxide study 10 grams of soil was treated with 30 mL of a 30%  $H_2O_2$  solution for five hours. The soil was then boiled for a few minutes before being cooled and filtered. The remaining soil was air-dried.

For application [cyclohexyl-1-¹⁴C]-M03 was dissolved in 3 mL of acetonitrile resulting in a stock solution containing 9.537 MBq or 2.773 mg of test substance per 3 mL. From the stock solution two different concentrations (4.854 and 0.048 mg/L) were prepared following dilution with CaCl₂ solution.

A soil/water ratio of 1:20 was used in both studies, which was determined from a previous study (Fent, 1997, CA. 7.1.3.1.2/03). For each study, one gram (dry weight) of 601 was combined with 20 for of 0 CaCl₂ solution. The soil solutions were agitated for 1 four in both the adsorption and hydrogen peroxide test.

A decomption phase		
Adsorption phase Parameter		Description 2 2 2 2 2
Soil condition	4	Description 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Soli condition	<del>\</del>	
Soil sample weight		Sorter were fur-dried and sieved to 2, mm
Equilibration solution		No pre-equilibration conducted S
Control (preliminary e	$\sim \sim $	No soil stest substance in 0.01 M CaCl2 only
Concentration	Analytically (LSC) measured concentra-	Measured concentrations (LSC) in test solution: 4.854 and 0.048 mg/L
Identity and concentra	ntion of co-solvent	Dosing stock made up in acetopitrile
Soil: Solution ratio		
Number of repli-	Control &	Not stated 2 2 2
cates	Treatments O &	Duplicate 2
	Time 2 A	Thirs of the second sec
Equilibration condi- tions	Temperature	$20 \pm \Omega^{2} C$
	Dark	for the dark
le l	Darts Struking method	Overhead shaker
Method of separation,		Centrifugation
.4	Spæd (rpm)	\$2000 rujen
Centrifugation	Duration 0	v 15 minutes
	Method of separating supernating	Supernatant was decanted.
<i>v</i>		$(\bigcirc)^{\circ}$

### 2. Analytical Procedures

For the adsorption study no desorption measurements were determined. After the adsorption step the aqueous supernatable was oparated from the soil by centrifugation and the amount of M03 (spiroxamine-N-oxide) in the opernatants was quantified by LSC.

TLC analysis was used to determine the purity of the test substance and the proportion of any degradation products. Aliquots of 4 to 100  $\mu$ L were spotted on a SI-60 TLC plate. The components were separated by TLC in a saturated glass tank using the solvent system acetonitrile/H₂O/NH₄OH (80:18:2 v:v:v).

The partition of the test substance in the adsorption equilibrium experiment was determined based on the radioactivity content in the supernatant only (i.e. the indirect method). Adsorption and desorption isotherms were calculated by linear regression analysis of the adsorption or desorption data according



to the Freundlich equation.

The limit of detection (LOD) was not specified in the report, however, the concentrations of the dest substance used are likely sufficient to allow adequately accurate measurements of levels of the test substance.

#### II. **Results and Discussion**

The equilibrium concentrations of [cyclohexyl-1-¹⁴C]-MO2 (spiroxaming-N-oxide) is shown in Table CA 7.1.3.1.2-18. The proportion of [cyclohexyl-1-14C]-M03 (spiroxaroine-N-oxide) adsorbed onto soil Stanley ranged from 92.4-99.4% AR. The chromatographic analyses of the centerfuged supermitants after establishment of the equilibrium (without hydrogen peroxide reatment) for the high-test concertration, showed that 96% of the measured radioactivity could be assigned to parent. In the case of the  $H_2O_2$ -treated soil the values were lower (ca. 85% ÅR)

Table CA 7.1.3.1.2-18: Concentrations at	adsorption	ı eguilibrin	m for Cv	clohexyl-A	¹⁴ Cl- <b>M</b> 03 &
(spiroxamine-N-oxid	Ĩe) [°] ∼		A	Ŝ.	E N

Starting concentra- tion (mg/L)	Repli- cate	Concentrati	ðn in aqueous solution (μg/20 mL) Åt equilibrium	Adsorbed on sol at equilib-
4.854	А	<b>`9</b> 7.07©	@.41 ± @05 6	89.60 0.05 ∽
4.034	В	97.07	0.01 Q	95. H ± 0.05
0.048	A 🔊	0.96 🔊	0.03*	<u>0</u> ,0,93* ○
0.048	B	<b>)</b> ?96	@01±0.00 «	0.94 20.00
<ul> <li>* No duplicate meas</li> </ul>				

The constants of the proof isotherms according to Freundlich were calculated by linear regression. Freundlich constants and the Kd-values describing the adsorption are given in Table CA 7.1.3.1.2-19. ٦

Table CA 7.1.301.2-19 Adsorption sotherms from [cvclohexy-1-14C]-M03 (spiroxamine-N-ox-[®]ide)[©]

<i>`</i> ```````````````````````````````	- /				
Soil				Ka	КОС
Stapley (native		0.8096	, d ^r w	200	13,441
Stanley (H ₂ O ₂ trea	uted)	×0.9060		Å17	$\rightarrow \infty$
	Y .		n O s		

Based on a carbon organic content of 1.499, the Koc value of Stanley was calculated to be 13,441 mL/g. The H₂O₂-treatment of soft was designed to have destroyed the organic carbon of the soil and lower the Kd value, However, the Kd value showed an increased value, resulting in an extremely high  $K_{oc}$  value. It was proposed by the study author that the treatment of the soil enhanced the sorption capacity and sorption locations. In this case, it is assured to be due to the clay minerals (montmorillonit etc.).

Based on the classification system of McCall et al. (1980) M03 (spiroxamine-N-oxide) must be considered to be immobile in soils like that rested on this study

**_H**₩.

#### Conclusions

The adsorption  $\mathcal{O}$  [cyclonexy] $\mathcal{O}^{-14}$ C]-M03 (spiroxamine-N-oxide) was investigated in a supplementary study on one North American soil, Stanley (silty clay loam, pH 5.5, 1.49 % OC) using the indirect method. Two separate tests were conducted on Stanley soil. One test to determine the adsorption of [cvclohexy-1-¹⁴C]-M03 and a second using hydrogen peroxide to determine the effect of the organic matter Phe soil sample. For each system two different concentrations (4.854 and 0.048 mg/L) were investigated.



Based on the classification system of McCall *et al.* (1980) M03 (spiroxamine-N-oxide) must be considered to be immobile in soils. The OECD 106 checklist could not be used on the data presented in this summary as insufficient concentrations were investigated. Therefore, this summary is supportive information only.

#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013

The study was conducted to USEPA (=EPA): Section N, 163-1 study guidelines, which were incorce, at the time of study completion. However, the study does differ significantly to current OECD 106 guidelines and as a result should only be considered as supporting information only.

Data Point:	
Report Author:	
Report Year:	
Report Title:	TRA A A A A A A A A A A A A A A A A A A
Report No:	TBA Q. AN
Document No:	$TBA \overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{{\bullet}}{\overset{O}{\overset{O}{{}}}{\overset{O}{\overset{O}{\overset{O}{\overset{O}{{}}{\overset{O}{{}}}{\overset{O}{\overset{O}{{}}{\overset{O}{{}}}{\overset{O}{{}}}{\overset{O}{{}}{{\bullet{O}}{{}}}{{}}{{}}{\overset{O}{{}}{{}}}{\overset{{O}}{{}}{{}}}{{}$
Guideline(s) followed in	
study:	Commission Regulation (EC) No 283/2013 in accordance with Regulation (EC)
	140/1107/2809 0 ~ ~ Q/4 0 0 ·
Deviations from current	None & C & C & C & C & C & C & C & C & C &
test guideline:	
Previous evaluation:	No not previously albmitted S S
Remarks previous evalua-	Not applicable (New study, not previously submitted)
tion:	
GLP/Officially recognised	Yes, conducted under GLP officially recognised testing facilities
testing identities.	
Acceptability/Reliability.	Yes v v v v v
O**	

- **2
  - A study investigating the soil sorption properties of metabolite (106 is currenly on-going and will be supplied as part of a top up submission (estimate September 2021).

# CA 7.1.3.2 Aged sorption

A study investigating the aged Sorption properties of the active substance spiroxamine has not been performed (higher tier option)

# CAZ1.4 Mobility in soil

CA 7.1.4.1 Column deaching studies

# CA 7.1.4 A. 1 Column leaching of the active substance

Adequate soil sorption parameters for the active substance spiroxamine are provided under Point A 7.1 3.1.1 consequently column leaching studies with the active substance are not required. However, the existing study investigating the leaching behaviour of spiroxamine applied as a formulation (KCO 7.1.4.1.1/03 ( $\underline{M-006196-01-2}$ )) and two existing studies investigating the leaching behaviour of aged residue of spiroxamine in soil are available (KCA KCA 7.1.4.1.1/01 ( $\underline{M-006198-01-1}$ ) and KCA 7.1.4.1.1/02 ( $\underline{M-006194-01-1}$ )). These studies have therefore been included for completeness and as supplemental information.



Substance	<b>Report reference</b>	Document no.	Comment
Spiroxamine	KCA 7.1.4.1.1/01	<u>M-006189-01-2</u>	Submitted for first approval of spirox amine, 1999. Reviewed under UP. Consid-
Spiroxamine	KCA 7.1.4.1.1/02	<u>M-006194-01-1</u>	ered valid and acceptable.
Spiroxamine	KCA 7.1.4.1.1/03	<u>M-006196-01-2</u>	Submitted but no evaluated previously of Included for completeness only

The mobility of [cvclohexvl-1-14C]-spiroxamine and its degradation products were investigated by @ umn leaching experiments in three soils: BBA 2.1 (#SP149, loamy sand; pH 5.4, 0, 4% QC), BBA 2.1 (#SP149, sand; pH 5.7, 0.57% OC) and Laacherhof wilty loam; pH 6.4, 1.08% OC) following ageing for 1 and 3 months under aerobic conditions at 20% and 40% maximum water folding capacity in the dark.

[Cvclohexyl-1-14C]-spiroxamine was applied to the softs at two nominal application rates of 375 g a.s./ha and 750 g a.s./ha and aged for one and two months. Under the given conditions, the parent compound degraded in the three soil systems relatively quickly. The majority of radioactivity was identified as parent accounting for 54.7% AR, 39.0% AR and 25.7% AR by study termination in BBA 2.1 (Stell49), BBA 2.1 (SP 1121) and Laacherhof sons respectively. MOL desetbyl) was identified as a major metabolite in all three systems reading a maximum of 73% AR 8.5% AR and 8.1% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 1121) and Leacherhof soils respectively. Other metabolites such as M02 (despropyl), M03 (N-oxide), M66 (acid), M11 (desetbyl acid), M10 (despropyl acid) and M15 (ketone) were identified, however, no metabolite was detected at@reater.that 5% AR @ two consistent time points.

The high sorption displayed by spiroxamine and its metabolites is reflected in the outcome of column leaching studies, with only 0,2% AR being found in the leachate of the aged soils? The major residue in the leachate was found to be M03 (pirox@mine_S-oxide) representing only 6.03% of the applied radioactivity in column leachates. Qverall, leaching behaviour of spiroxamine (including individual iso-mers) or its major soil metabolites is not envisaged

Data Point: $\sqrt{2}$ 4.1.1/9 $\sqrt{2}$
Report Author:
Report Year: $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$
Report Title. Ceaching behaviour of KWG \$168 aged in soils
Report No.1 PF400 A O O
Docume@No: @ <u>M-@06198-@-1</u> @ %
Guideline(s) followed in BBA Ref Leaching behaviour of Plant Protection Products (4-2)
studie w state sta
Deviations from current V Non
test guideline: $Q^{*}$
Previous evaluation: A ges, evaluated and accepted
DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recognised testing facilities
nised testing facilities:
Acceptability Reliability & Vés

# Executive Summary

The mobility of [cyclohexyl-1-¹⁴C]-spiroxamine and its degradation products have been investigated by column leaching experiments in three soils: BBA 2.1 (#SP149, loamy sand; pH 5.4, 0.54% OC), BBA 2.1 (#SP149, sand; pH 5.7, 0.57% OC) and Laacherhof (silty loam; pH 6.4, 1.08% OC) following ageing



for 1 and 3 months under aerobic conditions at 20°C and 40% maximum water holding capacity in the dark.

[Cyclohexyl-1-¹⁴C]-spiroxamine was applied to the soils at two nominal application rates of 375 g.s./ha and 750 g a.s./ha and aged for one and two months.

Tests were performed in flow through systems consisting of glass flasks each containing 100°g soil (ary weight) attached to a quartz wool trap to collect organic volatiles followed by two calcium hydroxide traps to collect carbon dioxide. Application of [cyclohexyl-1-¹⁴C]-spiroxamine in a solvent (acetonic trile:trimethylamine, 100+0.5 v/v) were made to a sub-sample of soil before being thoroughly mixed. Soil samples were lightly agitated after application to aid distribution throughout the soil and to show solvent evaporation. Samples were aged for 1 or 2 months under aerobic incubation conditions (dark 20°C and 40% moisture capacity). Soil columns were leached using a peristaltic pump and 393 mL of water over 2 days, which corresponded to 200 mb of rainfall.

Extractable radioactivity from the soil declined in all three soils over the soils, 88.5% AR at DAT 0 to 70.5% AR by DAT 62 in BBA 2.1 (SP 149) soil. Similarly in BBA 2.1 (SP 1121) soil samples extractable radioactivity declined from 88.3% AR at DAT 0 to 59.5% AR by DAT 60. Similarly in Laacher of soil samples extractable radioactivity declined from 72.4% AR at DAT 0 to 94.0% AR by DAT 62.

Non-extractable residues (NER) increased from 10 5% AR at DAT 0 to 18.3% AR by DAT 62 in BBA 2.1 (SP 149) soil. Similarly in BBA 2.1 (SP 1121) soil samples con-extractable radioactivity increased from 10.4% AR at DAT 0 to 20.8% AR by DAT 60. Similarly in Laacherhor soil samples non-extractable radioactivity increased from 20.0% AR at DAT (po 25.4% AR by DAT 62.

Under the given conditions, the patent compound degraded in the three soil systems relatively quickly. The majority of radioactivity was identified as parent accounting for 54.7% AR, 39.0% AR and 25.7% AR by study termination in BBA 2.1 (SP 149); BBA 2.1 (SP 1121) and Laacherhof soils, respectively.

M01 (spiroxamine-desethyl) was dentified as a major metabolite in all three systems reading a maximum of 7.3% AR 8.5% AR and 8.1% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 1121) and Laacherhot coils respectively. Other metabolites such as M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide), M06 (acid), M11 (desethyl acid) M120despropyl acid) and M15 (ketone) were identified, however, no metabolite was detected at greater that 5% AR at two consistent time points.

With respect to the learnate, based on the applied radioactivity, the amount of radioactivity measured in the total water was  $0^{2} - 0.5^{6}$ . The different application rates and soil types did not influence the percentage of radioactivity in the learnate, and on the base of these findings, spiroxamine can be classified as immobile in soil after prior being  $0^{2} - 0.5^{6}$ .

A. Materials	Materials and Methods
	* Denotes position of [ ¹⁴ C]-radiolabel
Specific Activity:	2.59 MBq/mg
Radiochemical Purity:	>99%
Isomer A:B	55%: 45%



ñ

#### 2. Test System (soil)

The biologically active soil was dried in air to an extent that it could be sieved to a particle size of 100 mm. The study was performed using one test soil as characterised in Table CA 21.4.1-1.

	rnysico-chemical propert		
Parameter		💍 Soil 🔏	
Soil Designation:	BBA 2.1	🕅 BBA 2.1	Leachethof L
Batch	SP 149	SP 1121	
Textural Classification (USDA)	Loamy sand	SP 1121 Sand Sand Sand Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution Solution	Q ⁺ Shty loam y Q ⁺ 36?5 y Q ⁺ 52.5 Q ⁺ y Q ⁺ y
Sand [50 - 2000 (%) µm]	85.9	2 39.4 2 3 4 2 0 10 50 50 50 50 50 50 50 50 50 50 50 50 50	52.5 $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$ $52.5$
Silt $[2 - 50 \ \mu m]$ (%)	8.8	0 10.5Q	[™] [™] [™] [™]
Clay [< 2 $\mu$ m] (%)	5.3		$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array}{}\\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\$
pН		1 2 6 1 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	5 7.0 g
in H ₂ O (1:1)	6.0° × s	S 2 610 5	5 5 7.0 0
in 0.01M CaCl ₂ (1:1)	Q.4 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		64
Organic Matter (%)*		2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	1,00
Organic Carbon (%)	Q.54 S	0.57	©1.08
Cation Exchange Ca- pacity (meq/100 g)			
Moisture 40% of the maximum water hold ing capacity (g H ₂ Q			
100 g dry soil)			
Soil Microbial Pio-			
soil) 🚀		ST DAT 4	
contract	$P \implies 0 \text{ DA} = 81$		0 DAT: 310
		60 DXY: 64 0 DAT: -	62 DAT: 230
With a stine substant	0, <b>D</b> AT: 11, A	0 0 DÃT: -	0 DAT: 418
Q	DAT 65 . 4		62 DAT: 299

* Calculated by multipering organic carbon content by 1024 (not reported)

** The soil scople originally poposed to determine the pricrobial biomass at the end of the study was instead used for a leaching experiment.

# B. Study Design

# 1. Experimental Conditions

[Cyclohexyl-1, C]-spiroxanane was dissolved in acetronitrile:triethylamine (100+0.5 v/v) to make the two nominal opplication rates of 375 g ag./ha and 750 g a.s./ha. The parent compound was added to a soil subsample. This soil subsample was air-dried in a porcelain dish and ground. The parent compound was pipeted on the soil subsample. This sample was thoroughly mixed with a spatula and after evaporation of the solvent this subsample was added to the total amount of soil. The rest radioactivity in the porcelain dish was determined and deducted from the theoretically applied radioactivity.

Tests were performed in flow through systems consisting of glass flasks each containing 100 g soil (dry weight) and attached to an oil-coated quartz wool plug to collect organic volatiles followed by two calcium hydroxide traps to collect carbon dioxide.

Samples were aged for 1 or 2 months under aerobic incubation conditions (dark, 20°C and 40% moisture



capacity). Each column (450 mm length, 50 mm diameter) was packed with aged soil (280 mm) and flooded with water until the surface was reached. The soil columns were leached using a peristaltic pump and 393 mL of water over 2 days, reach corresponded to 200 mL of rainfall.

#### 2. Sampling

Duplicate samples for each soil were removed for analysis after 0, 30 (32) and 50 (62) days after ment (DAT) ment (DAT).

#### **3. Analytical Procedures**

The amount of radioactivity in the leachate fractions was determined by means of fiquid Scintillation counting (LSC). Soil samples were extracted three times at room temperature with acetopitrile by adk dition of solvent, vigorous mechanical shaking and centrifugation After each spaking process the supernatant was decanted through a folded filter paper. Radioactivity in extracts was determined by LOC. Degradation products were identified by comparison of the refention times of reference standards by means of two different TLC methods. Configuratory@analysis using/an alternative technique was conducted by TLC with co-chromatography against reference, items on selected samples. The limit of detection (LOD) in the extract was for a single peak≥0.2% AR and in the leachates ≥0,01% AR.

Volatile radioactivity in oil-coated quartz wool plug was extracted with 50 mb of ethyl acedite and quantified by LSC. Carbon dioxide the calcium hydroxide trans was released by acid precipitation and quantified by LSC. Non-extractable residues (NER) in extracted soils were determined by combustion.

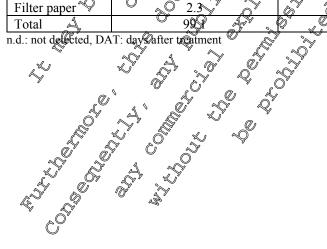
# Besults and Discussion

#### A. Data

The distribution and characterisation of radioactivity for the test soils incubated to 20°C following application of [cyclohesyl-1-10]-spirexamine are summarized in Table CA. 7.1.4.1-2 to Table CA 7.1.4.1-7.

# Table CA 7.1.41- 2: Mass balance of [cyclohexy]+1-14C]-spiroxamine at 20°C in BBA 2.1 (SP S149) soil under aerobic conditions [% TR] @

/Co		
\$~} [*]	🗴 💭 🖓 Incubation (Ime (DAT)	
Compound		
* *		62
Volatile	$n_{\rm s}$	11.9
Soil extracted	\$ 5 \$ 5 6 6 × 1 6 7 5 2	70.5
Soil bound	$0^{\circ}$ $0^{\circ}$ $0^{\circ}$ $0^{\circ}$ $0^{\circ}$ $0^{\circ}$	18.3
Filter paper 🔊		2.0
Total 🕰	999 99 101.0	100.7
1 1 1 1 1 1 1 1 1		





#### Table CA 7.1.4.1- 3: Mass balance of [cyclohexyl-1-14C]-spiroxamine at 20°C in BBA 2.1 (SP 1121) soil under aerobic conditions [% AR]

		Incubation time (DAT)	1	
Compound		DAT	~	6 W
	0	32	60	
Volatile	n.d.	12.3	0 17.8	3. 8
Soil extracted	88.3	69.1	A. 58	
Non-extractable resi- dues (NER)	10.5	<u>ک</u> 15.7	يدي 18.2	
Filter paper	2.6	s 2.1 5	<u>ک</u> ړ ک	Y N OY
Total	98.7	99.0	. 98	

n.d.: not detected, DAT: days after treatment

#### Table CA 7.1.4.1- 4: Mass balance of [cyclonexyl Jack C] spirox mine at 20 in Laacherhof soil Ô under aerobic conditions [% AR]

	Incubation time (DAT) a way in the
Compound	
Volatile	6d. 7 16,8 5 6 29.8
Soil extracted	⁹ 9.4 @ @ <u>6</u> 9.2 0 0 44.0
Non-extractable resi-	20.0V
dues (NER)	
Filter paper	
Total	99.4 Q S 29.0 C 29 8.9
n.d.: not detected, DAT: day	safter treatment of the second s

# Degradation of feyclonexyl-1-9 C]-spiroxafine at 20°C in BBA 2.1 (SP 149) soil under aerobic conditions [% AR] Table CA 7.1.4.1

Incubation time (DA1)	
Compound Definition of the compound Com	
	60
Spiroxamine $3$ $3$ $82.5$ $3$ $66.5$	54.7
M01 (desethyl) $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$	7.3
M02 (despropyl)	4.7
M03 (N-oxide), $3^{\circ}$ $3^{\circ}$ $1.9^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$	1.7
$M06$ (noid) $\approx 0$ $C = 2$ $n^{2}$ $n^{2}$ $\sim 0.7$	0.9
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	0.2
M12 (desptopyl acid) $n.d.$ $n.d.$ $n.d.$ $n.d.$ $n.d.$	0.2
M15 (ketone) $n = \frac{1}{2} \int n d d d d d d d d d d d d d d d d d d$	0.4
Unknown w nd. n.d.	0.4

n.d.: not detected, DAT: days after treatment

n.d.: not detected, DAT: days after treatment



# Table CA 7.1.4.1- 6: Degradation of [cyclohexyl-1-14C]-spiroxamine at 20°C in BBA 2.1 (SP 1121) soil under aerobic conditions [% AR]

		Incubation time (DAT)	
Compound		DAT	
	0	32	
Spiroxamine	81.7	50.1	Ø 39.0 ×
M01 (desethyl)	2.7	7.4	A 86 Y 29 0
M02 (despropyl)	2.3	A.7	5.5 5
M03 (N-oxide)	1.2	₹72.0 Ø	
M06 (acid)	n.d.	4.1	
M11 (desethyl acid)	n.d.	0.5	0.6%
M12 (despropyl	n.d.		Q 00.4 0 0 ⁴
acid)			
M15 (ketone)	0.4	k o n.d v	O n.t. V
Unknown	n.d.	ં ં મુન્યું છે.	
n.d.: not detected, DAT: da	ays after treatment		

All values expressed as percentage of applied radiotectivity (0.4)

All values expressed as percentage of applied radioartivity (% AR)

# Table CA 7.1.4.1- 7: Degradation of cyclobexyl 4⁴⁴Cl spiroxamine at 20°Cin Lascherhof soil under aerobic conditions (% ARI) 20°Cin Lascherhof soil

· ()	🖉 Incubation time (DAT)	
	" A BAT Q'	
		<u>62</u>
\$ 75 <b>6</b> 5	42.2 A	25.7
م» بي 1.3		× ~~ 8.1
2 Q1.1 Q C	· () • • 9.2 · V ()	5.8
		J 1.9
in an		1.0
jn.d.		× 0.2
n.d.		0.2
		0.2
nid. A	nd n	0.7
ري		0.4
		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

n.d.: not detected, DAT: days after treatment

All values expressed as percentage of applied radi@ctivity (% ARK

# B. Material Balance

Mass balances ranged from 99.1-191.0 % AR for BBAO2.1 (SP 149) soil, 98.1-99.0 % AR for BBA 2.1 (SP 1121) soil and 98.9-99.4 % AR for Laacherhof soil.

# C. Extractable and Non-Extractable Residues

Extractable radioactivity from the soil occlined in all three soils over the soils, 88.6% AR at DAT 0 to 70.5% AR by DAT 62 in BBA 2.1 (SP 149) soil. Similarly in BBA 2.1 (SP 1121) soil samples extractable radioactivity declined from 88.3% AR at DAT 0 to 59.5% AR by DAT 60. Similarly in Laacherhof soil samples extractable radioactivity declined from 79.4% AR at DAT 0 to 44.0% AR by DAT 62.

Non-extractable esidues (NER) increased from 10.5% AR at DAT 0 to 18.3% AR by DAT 62 in BBA 2.1 (SP 149) soil. Similarly & BBA 2.1 (SP 1121) soil samples non-extractable radioactivity increased from 10.4% AR at DAT 0 to 20.8% AR by DAT 60. Similarly in Laacherhof soil samples non-extractable radioactivity increased from 20.0% AR at DAT 0 to 25.4% AR by DAT 62.

### D. Volatile Radioactivity

Significant levels of volatile degradates evolved throughout the study period in all soils sampled. ¹⁴CO₂, reached a maximum levels of 11.9% AR, 17.8% AR and 29.5% AR by study termination in BBA 2.1



(SP 149), BBA 2.1 (SP 1121) and Laacherhof soils respectively.

#### E. Degradation of Parent Compound

Under the given conditions, the parent compound degraded in the three soil systems relatively dorckly The majority of radioactivity was identified as parent accounting for 54.7% AR, 39.0% AR and 25.7% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 1121) and Eaacherhof soils respectively.

M01 (desethyl) was identified as a major metabolite in all three systems reading a maximum of 7.3% AR, 8.5% AR and 8.1% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 121) and Laacherhof soils respectively. Other metabolites such as M02 (desproyel), M03 (N-oxide) M06 (acid), O M11 (desethyl acid), M12 (desproyel acid) and M15 (ketone) were identified, however, no metabolite was detected at greater that 5% AR at two consistent time points.

#### F. Leachate

With respect to the leachate, based on the applied radioactivity, the amount of radioactivity measured in the total water was 0.2 - 0.5 %. The different application fates and soil types did not influence the percentage of radioactivity in the leachate, and on the basis of these findings, sproxamme can be classified as immobile in soil after prior ageing.

Conclusions

The mobility of [cyclohexyl-1-¹⁴C]-spir@amin@and is degradation products were investigated by column leaching experiments in three soils: BBA 2.1 (#SP149, loams sand: pH 5.4, 0.54% OC), BBA 2.1 (#SP149, sand; pH 5.7, 0.57% OC) and Leacherkof (silty loams ph 6.4, 1.08% OC) following ageing for 1 and 3 months under aerobic conditions at 20°C and 40% maximum water holding capacity in the dark.

[Cyclohexyl-1-¹⁴C]-sorroxamine was applied to the soils at two nominal application rates of 375 g a.s./ha and 750 g a.s./ha and agedcfor one and two months.

Under the given conditions, the parent compound degraded in the three soil systems relatively quickly. The majority of radioactively was identified as parent accounting for 54.7% AR, 39.0% AR and 25.7% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 121) and Laacherhof soils respectively.

M01 (desethyl) was dentified as a major metabolite in all three systems reading a maximum of 7.3% AR, 8.5% AR and 8.1% AR by study termination in BBA 2.1 (SP 149), BBA 2.1 (SP 1121) and Laacherhof soils respectively. Other metabolites such as M02 (despropyl), M03 (N-oxide), M06 (acid), M11 (desethyl acid), XF2 (despropyl acid) and MF3 (ketone) were identified, however, no metabolite was detected a greater that 5% AR at two consistent time points.

Assessment and conclusion by applicant

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to BBA guidelines. The study is considered valid to assess the leaching behaviour of cyclobexyl-1. AC - spiroxamine in soil.

AT CI-



Data Point:	KCA 7.1.4.1.1/02
Report Author:	
Report Year:	1998
Report Title:	Leaching behaviour of KWG 4168 after aging in soil (aged leaching) in accord-
Report No:	PF4349
Document No:	<u>M-006194-01-1</u>
Guideline(s) followed in	EPA, Pesticide Assessment Guidelines, Subdivision, Chemistry, Environmen-
study:	tal Fate § 163-1, Leaching and Adsorption/Desorption Studies of October 18, 1952
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and acceptor RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under & LP/Q Picially recognised testing factories
nised testing facilities:	
Acceptability/Reliability:	Yes A Q A Q Q Q

#### **Executive Summary**

The mobility of [cyclohexyl-1-¹⁴C]-spiroxamine and its degradation products have been investigated by a column leaching experiment in one soil: Wolf Ranch (loam; pH 7.8 0.97% CC) following ageing for 30 days under aerobic conditions at 20° and 3% water content (143 bar) in the dark. [Cyclohexyl-1-¹⁴C]-spiroxamine was applied to the soil at a nominal application rate of 500 g a.9/ha (equivalent to 1.0 mg/kg).

Soil containing the aged residues were applied in a layer to the top of two 30 cm soil columns of the same soil type. The columns were insigated for 5 days with 0.03 M CaCl₂ solution correspond to an amount of rainfall of \$0.8 cm? The feachate was collected in 10 fractions of 100 ml each. Volatile compounds formed in the headspace of the columns were particed with air into the attached calcium hydroxide traps.

After draining the columns were puDin a freezer and the frozen soil was pushed out of the glass tubes. The frozen soil column was cut into a top section of aged soil and 5 segments of about even size constituting the untreated soil All samples were extracted three times at from temperature using acetonitrile and their a harsher extraction using methanol at 190°C. Characterication of soils extracts was determined using thin layer chromatography (FLC).

The total recovery of radioactively ranged from 94.4% to 963% AR for the two columns. A total of 26 -69% AR was attributed to spiroxaphine, which was found in the soil samples at day 0 until the end of the ageing period of 30 days. The corresponding mineralisation rate to carbon dioxide was 1.4% of the AR after the ageing and leaching procedure.

The parent compound and its metabolites showed a wery low potential of leaching. Nearly all the radioactivity applied to the soil columns via the aged soil remained in the upper soil segment (aged soil segment) after leaching. Only 4 d to 7.5% of the applied radioactivity was translocated into the segments 1 to 5 (0-30 cm)

Based on the opplied radioactivity, the amount of radioactivity measured in the total leachate was 0.17% for both columns. The anount of unchanged parent compound was determined to be <0.01% in column 1 and 0.02% of the applied radioactivity in column 2. More than eight metabolites were detected in the leachate extracts. The major residue was found to be M03 (N-oxide) representing 0.03% of the applied radioactivity in column 1 (cyclohexyl-1-¹⁴C)-spiroxamine was classified as being immobile in soil after aging.

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#### I. **Materials and Methods**

	N N
* Denotes position of	[ ¹⁴ C] oadiolabel
3.63 MBcong	
>98% 53% 46% 2	
53% 46% 0	A A

	I.	Materials a	and Methods			
A. Materials						° r
. Test Items						
[cyclohexyl-1- ¹⁴ C]-sr	biroxamine					
				, O ^x	к'' Д	
A. Materials . Test Items [cyclohexyl-1- ¹⁴ C]-sp Specific Activity: Radiochemical Purity Isomer A:B 2. Test System (soil) The biologically active nm. The study was pe		*				
		* Denotes pos	ftion of [ ¹⁴ C]	padiolabel		
Specific Activity:		3.63 MBang	ġ 🍣			
Radiochemical Purity	•	>98%				. KJ [¥]
Isomer A:B		53% 46%			r ór í	
. Test System (soil)			N D			. S
(soll)						
·· · · · · · · · · · ·	·1 1·1	o~ . K/			V SI	.0
The biologically active	e soil was dried	In air to an ex	tent that it co	ald be gieved	o a porticle s	ize of $\leq 2$
The biologically active nm. The study was per	e soil was drieg rformed using o	In air to an exone test soil as	tent that it co	in Table CA 7	o a particle s .1.45- 8.	$\bigcup_{ize of \leq 2}^{\mathbb{O}}$
The biologically active nm. The study was per Table CA 7.1.4.1- 8:	e soil was dried rformed using o Physico@hemi	à à	O' Á	in Table CA7	o a particle s .1.45- 8.	$\sum_{i=1}^{\infty} of \le 2$
	~~~	à à	O' Á			jze of ≤2
Table CA 7.1.4.1- 8:	~~~	à à		Soil Soil		jze of <u><</u> 2
Cable CA 7.1.4.1- 8:ParameterSoil Designation:Location	Physico@hemii	à à				jze of <u><</u> 2
Cable CA 7.1.4.1- 8: Parameter Soil Designation: Location Textural Classification	Physico@hemi	à à		Soil Soil		jze of <u><</u> 2
Table CA 7.1.4.1- 8:ParameterSoil Designation:LocationTextural ClassificationSand [50 - 2000 µm]	Physico@hemii	à à		Soil Svolf Ranch Frensnos CA, E		jze of <u><</u> 2
Cable CA 7.1.4.1- 8: Parameter Soil Designation: Location Textural Classification Sand [50 - 2000 µm] Silt [2 - 50 µm]	Physico@hemi	à à		Soil Soil Frensnos CA, t 29.7 4.1		jze of <u><</u> 2
Cable CA 7.1.4.1- 8: Parameter Soil Designation: Location Textural Classification Sand [50 - 2000 µm] Silt [2 - 50 µm] Clay [< 2 µm]	Physico@hemi	à à		Soil Svolf Ranch Frensnos CA, to 29.7 25.2		jze of <u><</u> 2
Cable CA 7.1.4.1- 8: Parameter Soil Designation: Location Textural Classification Sand [50 - 2000 µm] Silt [2 - 50 µm] Clay [< 2 µm]	PhysicoChemi 2 2 2 2 2 2 2 2 2 2 2 2 2			Soil Soil Frensno, CA, U Loam 29.7 25.2 8.7		jze of <u><</u> 2
Table CA 7.1.4.1- 8:ParameterSoil Designation:LocationTextural ClassificationSand [50 - 2000 μ m]Silt [2 - 50 μ m]Clay [< 2 μ m]PH in waterPH in waterPH in 0.01 PT CaCl2 (1:1)	PhysicoChemi 2 2 2 2 2 2 2 2 2 2 2 2 2		Frest son	Soil Svolf Ranch Frensnos CA, to 29.7 25.2		jze of <u><</u> 2
Cable CA 7.1.4.1- 8: Parameter Soil Designation: Location Textural Classification Sand [50 - 2000 µm] Silt [2 - 50 µm] Clay [< 2 µm]	PhysicoChemi 2 2 2 2 2 2 2 2 2 2 2 2 2		Frest son	Soil Soil Frensno, CA, U Loam 29.7 25.2 8.7		jze of <u><</u> 2
Table CA 7.1.4.1- 8:ParameterSoil Designation:LocationTextural ClassificationSand [50 - 2000 μ m]Sand [50 - 2000 μ m]Silt [2 - 50 μ m]Silt [2 - 50 μ m]Silt [2 - 50 μ m]Clay [< 2 μ m]Silt [2 - 50 μ m]PH in waterSilt [2 - 50 μ m]PH in 0.01 M CaCl ₂ (1:1)Organic Matter (%)*Organic Carbon (%)	Physico@hemii		Frest son	Soil Solf Ranch Frensnos CA, g 29.7 29.7 25.2 8.7 7.8		jze of <u><</u> 2
Table CA 7.1.4.1- 8:ParameterSoil Designation:LocationTextural ClassificationSand [50 - 2000 μ m]Sand [50 - 2000 μ m]Silt [2 - 50 μ m]Silt [2 - 50 μ m]Silt [2 - 50 μ m]Clay [< 2 μ m]Silt [2 - 50 μ m]PH in waterSilt [2 - 50 μ m]PH in 0.01 M CaCl ₂ (1:1)Organic Matter (%)*Organic Carbon (%)	Physico@hemii		Frest son	Soil Soil Frensno, CA, U 29.7 25.2 8.7 7.8 1.67		jze of ≤2
Table CA 7.1.4.1- 8:ParameterSoil Designation:LocationTextural ClassificationSand [50 - 2000 μ m]Silt [2 - 50 μ m]Clay [< 2 μ m]Clay [< 2 μ m]Textural ClassificationSand [50 - 2000 μ m]Silt [2 - 50 μ m]Clay [< 2 μ m]Textural ClassificationSand [50 - 2000 μ m]Silt [2 - 50 μ m]Textural ClassificationSand [50 - 2000 μ m]Sand [50 - 2000 μ m]	Physico@hemii 200 200 200 200 200 200 200 2		Frest son	Soil Soil Prensnok CA, E 29.7 20.7 20.7 20.97 20		jze of ≤2

(not reported)

B. Study Design

1. Experimental Condition

Corresponding to the interded application rate a defined amount of test substance was added to aliquots of soil (100 g of ary weight). The amount of soil corresponded to a soil layer of 5 cm taking into account a surface area of 19 c cm² in the leaching column. The soil was air dried and sieved to a particle size of ≤ 2 mm. An aliquer of the radiolabelled substance was diluted in acetonitrile and added to a soil subsample. After mixing and evaporation of the solvent this subsample was added to the total amount of soil and the total sample was thoroughly mixed in a tumbling mixer.

After mixing the whole amount of soil, two batches were processed (extracted and analysed) directly



after the application (day 0). Five batches were filled into incubation flasks. The soil moisture was adjusted to 75 % of the water content at a pressure of 1/3 bar and the flasks were closed with a trap attachment filled with calcium hydroxide for collecting volatile organic compounds and carbon dioxide. The flasks were incubated for 30 days under dark aerobic conditions at a temperature of 20 °C \pm 2°C

After the incubation period, two batches were analysed (day 30). Two soil samples were transferred to the top of two soil columns, which had been packed over a thin bottom layer of sand and quartz wool to a height of 30 cm with untreated soil. Considering the cross section of the column and a simulated rainfall of 508 mm, the flow rate of 0.1 M calcium chloride solution was adjusted to 200 ml per day A total volume of 996 ml was passed through the columns and collected in 10 fractions of equal volume and stored at low temperature until processing. Volatile compounds formed in the headspace of the C columns were purged with air into the attached traps \mathbb{Q}

After draining the columns were put in a freezer and the frozen soil was pushed out of the gass tubes. The frozen soil column was cut into a top section of aged soil and 5 segment of about even size constituting the untreated soil. The deepest soil segment contained also the bottom layer of sea sand

2. Analytical Procedures

Aliquots of the soil extracts were investigated by TLC on silion get using one solvent system and on RPsilica gel using two solvent systems Components were visualised by autoractiography, radioactivity scanning with quantification and in the case of unlabelled reference substances by reaction on the TLC plate in an iodine chamber or by spraying with cobalt If-thio ganate

All extracts were radioassayed Carbon dio orde trapped in the calefum hydroxide of the trap attachment was released with hydrochloric acid in a closed apparatus, and absorbed in a scintulation cocktail for the determination by LSC Volatiles trapped in the polyurethane plug were extracted with ethanol and determined by LSC. Soil samples were air-dried and milled The arount of radioactivity was determined by combustion of hornogenised alignots. L \bigcirc

Results and Discussion

A. Data

The distribution of radioactive in the two columns can be seen in Table CA 7.1.4.1-9. The characteri-

The distribution of fadioactive in the two columns can be seen in Table CA 7.1.4.1-9. The cl sation of redioactivity in the agent soil and soil columns can be seen in Table CA 7.1.4.1-10.

0



Table CA 7.1.4.1- 9: Distribution of [cyclohexyl-1-14C]-spiroxamine in Wolf Ranch soil under anaerobic conditions [% AR]

[cyclohexy]	l-1- ¹⁴ C]-spiroxamine	Column 1	Column 2
Valatilaa	During incubation	1.4	· · · · · · · · · · · · · · · · · · ·
Volatiles	During leaching	< 0.01	<0.01
$(^{14}CO_2)$	Other volatiles	< 0.01	
	Aged soil segment	68.1	71.9 2 2
	0-6 cm	4.5	
Sail an	6-12 cm	0.2	$\begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $
Soil ex- tracted	12-18 cm	0.1	
liacieu	18-24 cm	<0	
	24-30 cm	Q0.1	
	Subtotal	<u>م</u>	
	Aged soil segment		
	0-6 cm	A. 200	
	6-12 cm	$\sqrt[3]{0.2}$	
Soil bound	12-18 cm		$O' \downarrow O' \downarrow O' $
	18-24 cm	6° & <00° ~° /	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	24-30 cm	§ @ <0.1 . S	0^{+} 0^{+} 0^{-} 0^{+
	Subtotal	\$ \$19.9 D &	
Leachate			
Total		94.4 [•]	<u> </u>

Table CA 7.1.4.1- 10: Ageing of [cyclonexy] -14Cf spiroxamine and quantitation of compounds in the top soil gayer, soil segments and leachate [% AR]

				ž jų	<u> </u>			
6	Ŭ,	S a	L N	Applied F	adioactivi	ty 👋		
Compound	Day	Day 30K		Column &			Column 2	
Compound			Aged	Ç ^Y 0-6 🛇	Leach-	Aged	0-6	Leach-
			& soil*	∕ cm∂*	Leach-	soil*	cm**	ate
Volatile (¹⁴ CO ₂)	Øn.d. [™]	al.4 «		£.4			1.4	
Spiroxamine	39.9	^{≪65.2} ⊕ 1.2 [≪]	66.2	3.6 ♥ 0.₩	0.004	69.9	1.6	0.017
M01 (desethyl)	_ @n.d. Č	∑° 1.2°	0 .7	∑° 0.¥⊘	م @.d.	0.8	0.1	n.d.
M02 (despropyl) 😞	2.0	Ø <u>.</u> 8	0.5 ×	Q,1	⊿n.d.	0.6	0.1	n.d.
M03 (N-oxide)	35.9	Ø1.1 🔬	1 () (6)	9.5 🔊	0.028	0.5	0.6	0.029
Unknown	Q.2 (§ n.dØ	`19.d.	₯ <0.1℃	n.d.	n.d.	< 0.1	n.d.
Diffuse 🔊	°0.5	n.g.	k [©] n d ∾ [©]		n.d.	n.d.	n.d.	n.d.
Extracted/identi-	78.3	568.3		4.5	0.05	71.9	2.4	0.14
fied		<u>~ ~ ~</u>		»				
~~~		×~~	$\mathcal{A}$	)″			1	
Non-extracted *	17,6	s <b>20</b> 8.5	© 17,2,°	2.3	0.12	18.5	1.3	0.03
Filter	nØ	َدُ ³ 0.5	n.Q.	n.d.	n.d.	n.d.	n.d.	n.d.
Aggravated Cond.	n.d. 9538	13	n.Q. 0.81	0.08	n.d.	0.93	0.06	n.d.
Total Recovery	955	<b>_%95.</b> 7 ~Ç	<i>U</i>	94.4			96.3	<u> </u>
n.d. N&data	0							

Sop soil Dayer

First soft/segment Whue presented as mean of the applied radioactivity. *** S.

# **B. Material Balance**

The total recovery of radioactivity ranged from 94.4% to 96.3% AR.



#### **B.** Volatile Radioactivity

[Cyclohexyl-1-¹⁴C]-spiroxamine was slowly mineralised to CO₂. During the incubation period 0630 days the portion which was degraded to ¹⁴CO₂ was measured to be about 1.4% of the applied radioactivity. The formation of ¹⁴CO₂ during the leaching period was <0.1 %. Volatile organic compounds were not detected (<0.1%).

#### C. Aged Soil prior to leaching

A total of *ca*. 65% of unchanged parent compound was found in the soft after an aging period of  $20^{\circ}$  days. In addition, three degradation products were detected in the organic extracts which chromatographically agreed with the reference substances M01 (desethyl), M02 (despropyl) and M69 (N-carde). Each of the metabolites amounted about 1% of the applied radioactivity in the soil batches incubated for 30 days. At termination of the aging period, 1.4% of the applied radioactivity was mineralized to ¹⁴C/₂.

#### D. Leachate

Based on the applied radioactivity, the amount of radioactivity measured in the total water was 0.17% for both columns included in the leaching experiment. The amount of unchanged parent combound as determined to be <0.01% in column 1 and 0.02% of the applied radioactivity in column 2. The major residue was found to be M03 (N-oxide representing 0.03% of the applied radioactivity in both column leachates.

#### E. Leaching soil column

After termination of the overhead irrigation 92.9 and 4.7% of the applied radioactivity were recovered from the aged soil segment of column 1 and 2, respectively. The total amount of radioactivity translocated into segments 1 to 5 (0-30 cm) was measured to be 4.4 to 7.5% only.

Only those segment extracts containing >1% of the opplied adioactivity were analysed by TLC, i.e. the aged soil segment and segment 1 (6% cm) of both columns. Parent compound was the major residue detected in the extracts. The metabolite pattern was identical to the organic soil extracts of the day 30 incubation batches.

HI. Conclusions The mobility of [cyclobexyl-6⁴C]-spiroxamine and its degradation products was investigated by a column leaching experiment in one soil: Wolf Ranch (loam; pH 3.8, 0.97% OC) following ageing for 30 days under aerobic conditions at 20°C and 75% water content (1/3 bar) in the dark. [Cyclobexyl-1-¹⁴C]spiroxamine was applied to the soil at a nominal application rate of 500 g a.s./ha (equivalent to 1.0 mg/kg).

A total of 26 - 69 % of unchanged spirokamine was found in the soil samples at day 0 until the end of the ageing period of 30 days. The corresponding mineralisation rate to carbon dioxide was 1.4 % of the AR after the ageing and leaching procedure.

Based on the applied radioactivity, the amount of radioactivity measured in the total leachate was 0.17% for both columns. The amount of unchanged parent compound was determined to be <0.01% in column 1 and 0.02% of the applied radioactivity in column 2. More than eight metabolites were detected in the leachate extracts. The major residue was found to be M03 (N-oxide) representing 0.03% of the applied radioactivity in both column leachates. As a result, [cyclohexyl-1-¹⁴C]-spiroxamine is classified as being immobile in soil after aging.



#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to guidance which was acceptable at the time of. The study is consider valid to assess the mobility of [cyclohexyl-1-¹⁴C]-spiroxamine in soil.

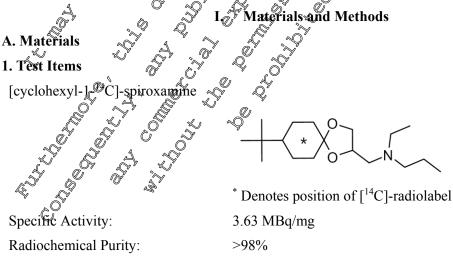
Data Point:	KCA 7.1.4.1.1/03
Report Author:	
Report Year:	
Report Title:	Versickerungsverhalten (ohre Alterung) einer KWG 4168 Galtigen Man- zenschutzmittelformulierung im Boden gemaess BBA-Anförderungen
Report No:	<u>M-006196-01-2</u>
Document No:	$\underline{M-006196-01-2}$
Guideline(s) followed in	BBA Ref.: Leaching Dehavi Bar of Plant Protection Products (4-2)
study:	1986 Part IV 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Deviations from current test guideline:	1986 Part IV
Previous evaluation:	No, submitted, not evaluated
GLP/Officially recog-	Yes, conducted under GLP/Officially recognized testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yest y y y y y
Executive Summary	

The leaching behaviour of formulated [cyclobexyl-1 C]-spiroxamine (EC500) was investigated without ageing in three different soils: Speyer 2.1 (sand, pH 5,3, 0.57% OC), Speyer 2.2 (loamy sand, pH 6.3, 2.48% OC) and Speyer 2.3 (soudy loan, pH 6.6, 1, 44% OC). Leaching behaviour was investigated under aerobic conditions at 20-25°C and 40% moisture holding capacity in the dark. [Cyclohexyl-1-¹⁴C]-spiroxamine was applied to the soil at a prominal application rate of 30 g a.s./ha.

The columns (rength # 30 cm) were constantly if gated with about 399 ml water each over a period of 48 hours and were protected against light influence, as was the leaching water. The leaching fractions were analysed by means of light scientilation measurement.

Soil samples were shown to be biologicably viable at the start of the study.

Because only traces in a range of 0.01% to 0.09% of the applied radioactivity could be determined in the leaching water, no further analysis of the leachate was performed. According to the classification spiroxamine (9s EC \$00) was classified as "immabile"





Isomer A:B

#### 56%: 44%

## 2. Test System (soil)

The soils were taken from wooden containers (which in the warm season are kept in the open and in the winter in the greenhouse) before the start of the experiment, where the soils are stored under plant cover. The field-fresh soils were dried in air and sieved through a 1 mm sieve. The study was performed using one test soil as characterised in Table CA 7.1.4.1-11.

<b>Fable CA 7.1.4.1- 11:</b>	Physico-chemical propert	ies of test soil	5 A 68
Parameter		Soil 6	
Soil Designation:	Speyer 2.1	Speyer 2 3	Speyer 2.3
Location	Germany	Germany O	Q Germany
Batch	Sp 1121 🔬	° F 23994	0° > Sp 3121 >
Sampled for the study	01.03.95		
Textural Classifica- tion (DIN 19682)	Sand	Coamy sand	Sandy kam
Sand [63 - 2000 μm] (%)	Sand 5 88.50 5 94 9.4 5	• F 23994	\$4.3 \$4.3
Silt [2 – 63µm] (%)		Comy sand A Comy sand A T79.7 C T T T T T T T T T T T T T	
Clay [< 2 μm] (%)	Q.4 Q.4 Q.4 Q.4 Q.4 Q.4 Q.4 Q.4 Q.4 Q.4	0 ³ ⁴ 7.2 ⁰ ⁶ ⁶	ÖÎ0.8
pH in water			\$v° ≪ / 0.0
Organic Matter (%)*		Q ⁴ .28 _€	2.48
Organic Carbon (%)		2.4® [*]	1.44
Cation Exchange Ca pacity (meq/100 g	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array}{} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $		12.5
40% of max. water capacity (g/100 g dry soil)			n.d.
Soil Miscobial Bio- mass (mg C/kg dry soil) Start of study			312

n.d. Not determined * Calculated y multiplying openic carbon content by 2/24 (not reported)

# B. Study Design

# 1. Experimental Conditions

A formulation (EC 500) was used that contained spiroxamine. The (theoretical) active ingredient application rate was 50 g a.s./ha with an active substance content in the formulation of approx. 50 % this resulted in a formulated preduct application rate of 1.5 kg/ha per application. Each experimental batch was based on a solt area of 196 cm² (diameter of the leachate column = 5 cm). This gave an added quantity per solt column of  $c_{c0}$  0.15 mg and was diluted with water. To determine the homogeneity of the application solution before, during and after the addition of the application solution to the soil columns in each case the corresponding quantities (39.5 µl) were taken and measured by LSC counter after dilution. The mean value determined here of 0.527 MBq/soil column (corresponding to 742 g a.s./ha) defines the active ingredient quantity applied per soil column.

The leachate columns consisted of a glass column approx. 45 cm long and with an internal diameter of 5 cm. The columns (2 columns for each soil) were first closed at the bottom end with quartz wool. This



was followed by a sand layer to which fresh, biologically active, air-dried soil sieved through a 1 mm sieve was added to the column in portions and filled to a height of 30 cm with gentle vibration. Soil mass added ranged from 662.7-829.9 grams of soil. After a glass frit had been added, the soils were saturated with demineralised water.

The application solution was added dropwise and the column was protected from high (black gardboard) and irrigation was started. This water quantity dripped slowly and evenly onto the column over a period of 48 h (393 ml/48 h corresponds to approx. 0.137 ml/min, the water was pumped with a peristaltic pump).

The total leachate per column was collected in one fraction. After investion had finished, the column was left to drip (dripping time: approx. 5 hours). This fraction was also collected in a marrow peckee glass vessel and added to the leachate fraction.

#### 2. Analytical Procedures

The leachates were first centrifuged for 15 minutes and speed of 2000 rpm. For this, the entire leachate was transferred for each sample quantitatively into a centrifuge braker. The collection vesselow as then rinsed 3 times with ca. 3 mL water each time. As slight turbidity was still prosent after centrifugation, the entire solution was filtered through a folded filter. The centrifuge beaker was ripsed 3 times with ca. 3 mL water each time.

After stirring, the radioactivity of the leachates (without centrifugation filtration) was determined using an LSC under alkaline and acid conditions.

Besults and Discussion

#### A. Data

The analysis data showed that only very small quantities or radioactivity were bonded to soil particles in the leachate as shown in Table CN 7.1.4,1- 12, Soil samples were shown to be biologically viable at the start of the study

# Table CA 7.1.41-12 Badioactivity in leachates after filtration [% AR]

		i da		
<u>A</u>	🗸 Soit 🖉		Mean value of %	of radioactivity applied
	Spewer 2.1	ø, o		0.04
	Spreyer 205	×		0.01
v	speyer 2.3		& A ⁷	0.09
l.	N A Q	2 2	<u>o.</u>	

Conclusions

The leaching behaviour of form ated [weloheavil-1-wel]-spiroxamine (EC 500) was investigated without ageing in three different soils: Speyer 2 (sand, pH 5.3, 0.57% OC), Speyer 2.2 (loamy sand, pH 6.3, 2.48% OC) and Speyer 2.3 (sandy loan, pH 66, 1.44% OC). Leaching behaviour was investigated under aerobic conditions of 20-25°C and 40% moisture holding capacity in the dark. [Cyclohexyl-1-¹⁴C]-spiroxamine was applied to the soil at a nominal application rate of 750 g a.s./ha.

The columns (length = 30 cm) were constantly irrigated with about 393 ml water each over a period of 48 hours and were protected against light influence, as was the leaching water. The leaching fractions were analysed by means of liquid scintillation measurement.

Soil satoples were shown to be biologically viable at the start of the study.

Because only traces in a sange of 0.01% to 0.09% of the applied radioactivity could be determined in the leaching water, no further analysis of the leachate was performed. According to the classification 1 spiroxamine (as EC 500) was classified as "immobile".



#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to BBA guidelines. The study is considered valid to assess the molecular cyclohexyl-1-¹⁴C]-spiroxamine in soil.

# CA 7.1.4.1.2 Column leaching of metabolites, breakdown and reaction products

Adequate soil sorption parameters for all major soil metabolites of the active substance spiroxamine (as defined under Point CA 7.4.1) are provided under Point CA 7.1.57.2, consequently column teaching studies with any metabolites are not required.

### CA 7.1.4.2 Lysimeter studies

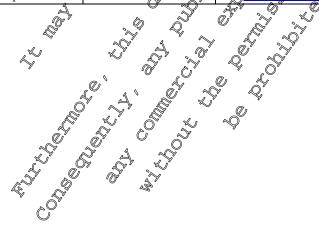
Adequate soil sorption parameters for the active substance spirovamine and all major soil metabolites (as defined under Point CA 7.4.1) are provided under Points CA 7.1.3.1.1 and CA 7.1.3.1.2. Furthermore, determination of the predicted invironmental concentration in groundwater conducted under Point CP 9.2.4 do not indicate groundwater concentration exceeding the relevant trigger levels, consequently lysimeter and/or field leaching studies with the active substance or any metabolites are not required.

# CA 7.1.4.3 Field leaching studies

Adequate soil sorption parameters for the active substance spiroxamine and all major soil metabolites (as defined under Point CA 7, 41) are provided under Points CA 7.1.3.1.4 and CA 7.1.3.1.2. Furthermore, determination of the predicted environmental concentrations in groundwater conducted under Point CP 9.2.4 do no indicate groundwater concentrations exceeding the relevant trigger levels, consequently lysimeter and/or field leaching studies with the active substance of any metabolites are not required.

However, three existing studies investigating the dissipation of pirox amine under field conditions have previously been included under this data point and therefore these studies are included for completeness and as supplemental information.

			<b>~</b>
Substance	Report reference	Document nov	د Comment
Spiroxamine	&CA A1.4.3/	<u> M-006116-01-1</u> O	Submitted for first approval of spirox-
Spiroxamine	KCA 7.1.4.3 02 (	<u>M6006126-01-1</u>	amine, 1999. Reviewed under UP. Consid-
Spiroxamine	KCA 74.9.3/03	<u>M-006127-01</u>	ered valid and acceptable.
4			•





#### Existing studies, previously evaluated

Data Point:	KCA 7.1.4.3/01
Report Author:	
Report Year:	1995
Report Title:	Dissipation of KWG 4168 in soils under field conditions (Germany and Great)
Report No:	RA-2078/93
Document No:	<u>M-006116-01-1</u>
Guideline(s) followed in study:	BBA Guideline IV-4.1 (1986)
Deviations from current test guideline:	Yes (refer below) Some minor deviation(sphot relevant for the reliability of the study (described in study summary)
Previous evaluation:	yes, evaluated and accepted DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog- nised testing facilities:	Yes, conducted under GDP/Officially recognised testing facilities
Acceptability/Reliability:	Yes Q (Y Q Q D C Q Q )
The details of this study a	are fully summarised under point KCA7.1.2.2.1/01
Data Point:	KQX7.1.4.3/02 ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~ ~~
Report Author:	

Data Point:	KGX 7.1.4.3/02 ~ V V V V
Report Author:	1995 <u>0</u> 27 07 07 77 72 27 1995 <u>0</u> 27 77 72
Report Year:	
Report Title:	Dissipation of KWO 41680n soils under field conditions
Report No:	R/A-2002/194 @ 55 5 0 5 4
Document No:	<u>M-006026-017</u> ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Guideline(s) followed in	BBA Guideline IV-4 1 (1986)
study:	
Deviations from current	Some france deviations) not relevant for the cliability of the study (described in
test guidelige:	
Č Č	study-summary)
Previous evaluation:	yes evaluated and accepted
$\sim$	DAR (1997), ROR (2010), RAB (2017)
GLP/Officially recog-	Yes, Conducted under GLP/Officially, recognised testing facilities
nised testing facilities:	A N N A A
Acceptability/Reliability:	DAR (1997), ROR (2010), RAR (2017) Yes, Conducted under GLP/Officially, recognised testing facilities

Acceptability Keliability ? Yes yes with summarised ander point KCA 7.1.2.2.1/02.



Data Point:	KCA 7.1.4.3/03
Report Author:	
Report Year:	1995
Report Title:	Dissipation of KWG 4168 in soils under field conditions (Great Britain and France)
Report No:	RA-2132/94
Document No:	<u>M-006127-01-1</u>
Guideline(s) followed in	BBA Guideline IV-4.1 (1986)
study:	
Deviations from current	Yes (refer below)
test guideline:	some minor deviation(s) not reservant for menerality of the study described in
	study summary)
Previous evaluation:	yes, evaluated and accepted DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GLP/Officially recognised testing factories
nised testing facilities:	
Acceptability/Reliability:	Yes A C C C C

The details of this study are fully summarised under point KCA 7.12.2.1/03.

# CA 7.2 Fate and behaviour in water and sediment

Use of the active substance can potentially dead to the compound reacting surface wher during treatments or *via* soil run-off. The fate and behaviour of the active substance in the aquatic environment has been investigated in laboratory studies according to the data requirements faid down in EC Regulation 283/2013.

### **Overview:**

# Behaviour in the Aquatic Environment

Degradation of spirovamine has been assessed in the equatic environment through standard OECD guideline tests which allow an investigation of the route and rate of abiotic and biotic processes.

Two hydrofysis studies, which have been previously evaluated, are presented and are considered reliable to address the hydrofysic behaviour of spiroxamine. It was found that in a single radiolabelled study investigating hydrofysis in pH 5, 7 and 9 buffers at 25 °C, spiroxamine was stable to hydrolysis at acidic and neutral pH. As pH9 flimited evidence of degradation was presented with observation of M01 (spiroxamine desethyl), M92 (spiroxamine despropyl) and M03 (spiroxamine-N-oxide) reaching a maximum of 1.6, 20 and 0.08 °C R respectively at sindy end (KCA 7.2.1.1/01 (M-006003-01-1))). It should be noted that the study was impacted by poor mass balance at pH 9, raising a number of questions about the reliability of this study. As such, a second study was performed to fully elucidate potential hydrolysis processes.

Furthermore, evaluation of isomer specific hydrolytic behaviour was also investigated in KCA 7.2.1.1/02 (M-00002-01-1). At 30 ^(C) it was found that there was some limited potential for isomer specific behaviour but, due to the slow rate of hydrolysis, these processes are not considered relevant for the overell understanding of spiroxamine behaviour in the aquatic environment. Investigations into potential preferential degradation of spiroxamine in the OECD 308 and OECD 309 systems are being conducted in order to provide a thorough understanding on potential isomer-specific behaviour and how this impacts the risk assessment in terms of use of an isomer Uncertainty Factor (UF) in the risk assessment (EFSA, 2019).

The molar absorbance coefficient of spiroxamine is <10 L/mol/cm at wavelength 295 nm (ref CA 2.4), therefore photolysis in aqueous solution is not expected to be a significant pathway. In the studies available, the half-life of spiroxamine in light exposed samples was calculated to be equivalent to 200 days midday sunlight at 40°N (KCA 7.2.1.2/01 (M-006004-01-1)). No significant metabolites were observed.



The calculated quantum yield for spiroxamine is  $6.42 \times 10^{-4}$  molecules per photon and it can be concluded that photolysis is not a significant degradation mechanism for spiroxamine. Overall, abiotic processes represented by hydrolysis and photolysis are not considered to be the primary mechanism of spiroxamine degradation in the aquatic environment.

In order to investigate biological degradation of spiroxamine, three water/sediment studies have been performed, of which two were previously evaluated during the last spiroxamine renewal. In KCA 7.2.2.3/01 (M-006015-01-1), the route of radiolabelled spiroxamine was investigated in two water sediment systems (Hoenniger water and Stilwell) at 20 °C for up to 100 days. Spiroxamine rapidly dissipated from the water phase to the sediment phase, with no major metabolites formed in the Hoenniger water sediment system. In the Stilwell system, spiroxamine dissipated rapidly from the water phase with the formation of M03 (spiroxamine-N-oxide) as a major metabolite, notably observed at 11.3% R at 6 DAT in only the Stilwell system. Since M03 (spiroxamine-N-oxide) was not observed as a major metabolite in any of the other 5 water sediment test systems, and was only observed above trigger levels at 0-2 DAT in the Stilwell system, this is considered to be a study artefact and is not presented in the proposed route of degradation in aquatic systems (Figure 72-1).

In a second study (KCA 7.2.2.3/04 ( $\underline{M-393324}$ ,  $\underline{0} + 1$ )), radiolabelled spiroxamine was incubated in Anglerweiher and Hoenniger water sediment systems at 20°C. For 118 days. Consistent with the previous study, spiroxamine rapidly dissipated from the water phase with the observation of M66 (spiroxamine acid) as the only major metabolite reaching 25.6% AR in the water phase and 7.9% AR in the sediment phase of the Anglerweiher system.

 $\bigcirc$ In order to address new data requirements on isorber behaviour (FOCUS, 2019), a new water sediment study was conducted in Emperor Dake and Calwich Abbey water sediment systems (KCA 7.2.2.3/07 (M-763128-01-1)). In this study the degradation of individual isomers of radiolabelled spiroxamine was studied in addition to standard achiral analysis. As the chiral analysis was constrained by analytical challenges, the chiradanalysis is cartently being malised and is not available to submit at this time but will be provided to the RMS upon completion. The achiral analysis demonstrated similar findings as reported by KCA7.2.2.3/04 (M*303224-01-1). Spiroxamine dissipated rapidly from the water phase to the sediment where it degraded to the major metabolite MO6 (spiroxamine-acid) at 28.2 %AR in the water phase and 16.3% AR in the sediment phase of the Calwich Abbey system (KCA 7.2.2.3/07 (M-763128-01-1)). Degradation in the Calwich Abbey system followed a similar profile to Emperor Lake bot with less overall depradation. For Calword Abbey, significant replicate variability was observed at 14 and 30 pAT which impacted the reliability of kinetics fits. The proposed route of degradation in aquatic systems is presented in Figure 12-1. Degradation of spiroxamine in water/sediment systems also led to the formation of the collowing migor metholites: M01 (spiroxamine-desethyl, maximum 4.3% ARy and Ar02 (spiroxamine-desprops), maximum 3.2% AR). Although other minor metabolites were sometimes observed none exceeded levels of 3% AR at any time. Notably, M03 was not observed confirming the hypothesis that M03 formation in KCA 7.2.2.3/01 (M-006015-01-1) was not reproducible and is a study artefact.

In order to establish relevant endpoints for risk assessment, the water sediment data was assessed following the FOCUS kinetics guidance (2014). The spiroxamine persistence  $DT_{50}$  values in the total system ranged from 1.4-1 N8 days and  $DT_{90}$  values ranged from 83.7-628 days. Modelling  $DT_{50}$  values for spiroxamine ranged from  $f_2$ .6-1,000 days, with a geometric mean of 157.9 days in the total system established for use in risk assessment. The 1,000 days default  $DT_{50}$  was applied to the total system Calwich abbey is no reliable onetic fit could be established as a consequence of the significant replicate variability at  $f_3$  and  $f_3$  DAF preventing the identification of the breakpoint for hockey stick kinetics. As such, the geometric to be very conservative.

The spiro amine persistence  $\text{Diss}T_{50}$  values in the surface water were very short with rapid dissipation of spiro amine from the water to phase to the sediment phase.  $\text{Diss}T_{50}$  ranged from 0.27 – 7.69 days and  $\text{Diss}T_{90}$  values ranged from 2.5-36.4 days. Modelling  $\text{Diss}T_{50}$  values ranged from 0.47-8.35 days, with a geometric mean of 1.52 days in the surface water.



Dissipation of spiroxamine in sediment could not be accurately fitted to a kinetic model in three of the six test systems resulting in the use of a number of FOCUS default endpoints. As such, the spiroxamine persistence DissT₅₀ values in the sediment phase ranged from 24.3-1,000 days and DissT₉₀ values ranged from 191-3,320 days. Modelling DissT₅₀ values ranged from 72.0-1,000 days, with a geometric mean of 269.9 days in the sediment.

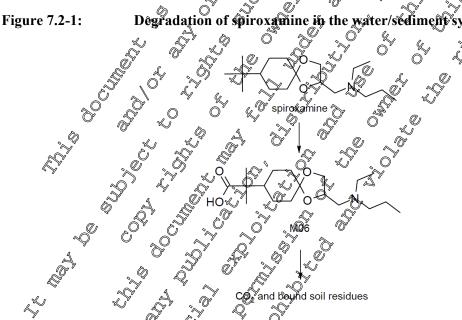
For the M06 (spiroxamine-acid) persistence values in the total system, an acceptable fit could only be determined for one of the test systems (as a consequence of a lack of a decline phase) resulting in a number of presented FOCUS default endpoints. The total system gave persistence DT values of 47 1,000 days and DT₉₀ values ranged from 156 – 3,320 days. M06 (spectra and a modelling total system gave a geomean DT₅₀ value of 293.6 days (f.f  $\neq$  0.453) for use in risk assessments

For M06 (spiroxamine-acid) persistence in surface water DissT56 values could only be established in two of four trials, resulting in a number of presented FOCUS default endpoints and anged from 801. 1,000 days and DissT90 values ranged from 156-3,320 days. 406 (spiroxartine-acid) modelling water phase also gave two established DissT50 values from the four soils resulting in mumber of presented FOCUS default endpoints, ranging from 3248-1,000 days

For M06 (spiroxamine-acid) persistence values in the sediment phase, an acceptable fit could only be determined for one of the four test systems resulting in a number of presented FO@US detault endpoints. The sediment phase gave a range of DissT values of 89.2 1,000 days and a range of DissT value of 296 – 3,320 days. M06 (spiroxamme-acid) modelling sediment phase gave a range of DissT₅₀ values from 89.2 - 1.000 days.

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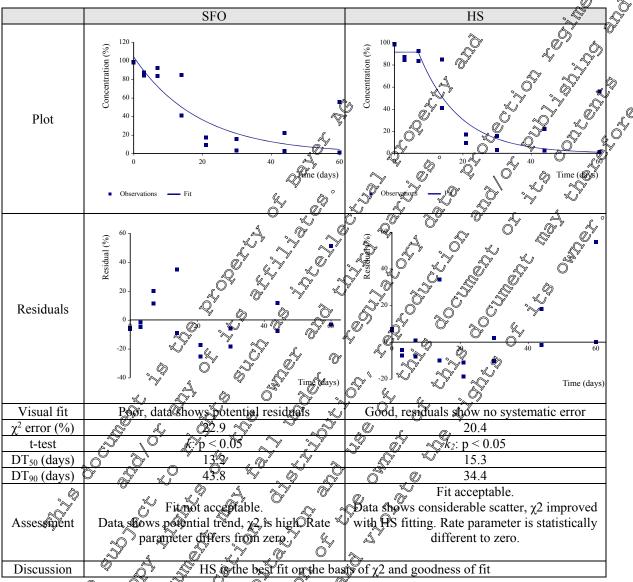
The proposed route of degradation in aquatic systems is presented in Figure



The behaviour of spiroxamine has also been investigated at two concentrations in pelagic water systems, with both achiral and chiral analysis performed (KCA 7.2.2.2/01 (M-763130-01-1)). At the time of submission, only the achiral results were available for submission, and this demonstrated that spiroxamine can degrade rapidly in pelagic water systems, with both concentrations degrading with a DT₅₀ of approximately 10 Hays. Of note the 100 µg/L system showed evidence of an 8 days lag phase prior to entering the decay phase (see Table CA 7.2-1) indicating the presence of a microbial population capable of upregulating entrymes to degrade spiroxamine. This mechanism was also attributed to the significant data scatter seen in the  $100 \,\mu g/L$  system. No degradation was observed in sterile controls. The major metabolites observed were found to be M01 (6.7% AR; desethyl), M02 (7.9% AR, despropyl), M03 (38.4% AR, N-oxide), M05 (9.2% AR, hydroxy), M06 (42.5% AR, acid), desamino-M06 (9.9% AR, acid), M11 (5.9% AR, desethyl acid) and M12 (9% AR, despropyl acid).



Table CA 7.2-1:Evidence of a lag phase for degradation of spiroxamine at high concentra-<br/>tions in pelagic systems



The pattern of metabolism in the  $\hat{OPCD}$  309 study was found to be significantly more extensive than the OECD308 study, indicating that in the presence of radiment spiroxamine degrades more slowly as a consequence of partitioning rapidly out of the aqueous phase to the sediment layer and a reduction in bioavailability. In the absence of sediment, the DQ₅₀ of spiroxamine degradation was significantly <40 days indicating that spiroxamine should not be considered persistent in aquatic systems but also demonstrating the importance of the ediment layer in the fate and behaviour of spiroxamine in the aquatic environment. Chiral analysis of spiroxamine in the OECD309 study are on-going at the time of submission but will be included at a later date, including a discussion on any potential UF.

# CA 7.2.1 Route and rate of degradation in aquatic systems (chemical and photochemical degradation) CA 7.2.1 Hydrolytic degradation

The hydrolysis of spiroxamine has been investigated in two studies (KCA 7.2.1.1/01 and KCA 7.2.1.1/02) which were evaluated during the previous EU review.

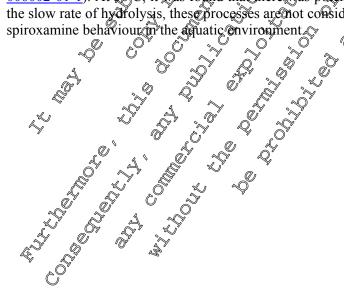


Sub- stance	Report refer- ence	Document no.	Test material used	Comment
Spirox- amine	KCA 7.2.1.1/01	<u>M-006003-01-1</u>	[cyclohexyl-1- ¹⁴ C]-spiroxamine	Submitted for first approval of pi- roxamine, 1999. Reviewed under UP. Considered valid and accepta- ble.
Spirox- amine	KCA 7.1.3.1.1/02	<u>M-006002-01-1</u>	Non radiolabelled spiroxamine	Submitted for first renewal of spi- roxamine, 2010. Reviewed ander UP Considered valid and accepta bre.

Two hydrolysis studies which were previously evaluated in the last renewal are presented. It was found that in a single radiolabelled study investigating hydrolysis in pH 5, 7 and 9 buffers at 25°C, that spiroxamine was stable to hydrolysis at acidic and neutral pH. At pH9, limited evidence of degradation was presented with observation of M01 (spiroxamine desetavi), M02 (spiroxamine despropyl) and M09 (spiroxamine-N-oxide) as metabolites reaching a maximum of 1.6, 2 and 4.08 %AR respectively at study end (KCA 7.2.1.1/01 (M-006003-01-1)). Of note, the study was impacted by poor mass balance at pH 9 which raises a number of questions about the reliability of this study. As such a second study was performed to fully elucidate potential by drolysis processes.

In a second study, hydrolysis of non-radiolabelled spiroxamine was in estigated in pH4, 7 and 9 buffers at 50°C for 8 days (Tier 1 test). By contrast, in this study spiroxamine was found to be stable to hydrolysis at pH 7 and 9 but showed some hydrolytic degradation at pH 4, with the Tier 2 test at pH4 at environmentally relevant temperatures demonstrating that the hydrolysis rate was limited. Under acidic conditions and at elevated temperatures ( $50^{\circ}$ C) metabolites M15 (spiroxamine-ketone) and M28 (spiroxamine-aminodiol) are observed, however these are not expected to form at significant concentrations at environmentally relevant temperatures (KGA 7.2, 1.1/02 (M-006002,01-1)), Overall, the two studies highlight potentially different hydrolytic behaviours of spiroxamine with the observations of KCA 7.2.1.1/01 (M-006092-01-1)) for pH9 potentially unrehable given the poor recovery. The outcome of KCA 7.2.1.1/02 (M-006092-01-1)) demonstrated potential hydrolytic behaviour at pH 4 forming metabolites M15 and M28 which notably aligns with the outcome of the high temperature hydrolysis study (CA 6.5.1/01 M-441):01-04-1). Overall, this suggests that the outcome of KCA 7.2.1.1/02 (M-006002-01-1)) is reliable and that spiroxamine showly hydrolyses at pH4 forming M15 and M28.

Further valuation of somer specific hydrolytic behaviour was also investigated in KCA 7.2.1.1/02 ( $\underline{M}$ -006002-01-1). At 36°C, it was found that here was potential for isomer specific behaviour, but due to the slow rate of hydrolysis, these processes are not considered relevant for the overall understanding of spiroxamine behaviour in the aguatic onvironment.





Data Point:	KCA 7.2.1.1/01
Report Author:	
Report Year:	1995
Report Title:	Hydrolysis of KWG 4168 in sterile aqueous buffer solutions
Report No:	PF4074
Document No:	<u>M-006003-01-1</u>
Guideline(s) followed in	EPA Pesticide Assessment Guidelines, Subdivision N - Chemistry: Environmen-
study:	tal Fate §161-1 Hydrolysis Studies
Deviations from current	Yes. Hydrolysis conditions not in accordance with OECD 507
test guideline:	<u><u>v</u><u>Q</u><u><u>v</u><u>v</u><u>v</u></u></u>
Previous evaluation:	yes, evaluated and classified $\sqrt{2}$
	DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GLPOfficially recognised esting facilities
nised testing facilities:	
Acceptability/Reliability:	Supportive only

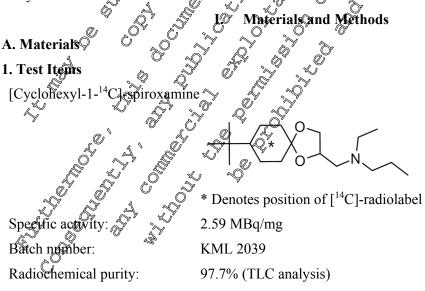
#### **Executive Summary**

The hydrolysis of [cyclohexyl-1-¹⁴C]-labelled spiroxamine was investigated at 25  $\pm$  1°C at pH 557 and 9, in the dark, under sterile conditions [¹⁴C] labelled spiroxamine was dissolved in sterile buffer at a nominal concentration of 1 mg/L.

Samples were removed immediately after treatment and after 3, 7, 94, 20, 24 and 20 days. Sterility of test samples was confirmed at the beginning and end of the 25°C test. Due to low mask balance recoveries at some time points in p14 9 buffer, a second experiment using this buffer was conducted, with samples removed at 1, 7, 14, 22 and 30 days.

Radiochemical balances were quantitative in all samples. Buffer samples were analysed by TLC to identify the compounds present, based on comparison of retention times with known concentration of test substance and analytical standards Multiple TLC technolous were used as confirmatory methods.

Spiroxamine did not degrade agnificantly in the sterile pH 5 and 7 buffer solutions after 30 days at 25°C, however decline of approximately 15% was seen after 30 days in the pH 9 buffer solution in the second experiment. This indicates that spiroxamine is hydrolytically stable under acidic and neutral conditions, and hydrolyses slowly under basic conditions. M01 (spiroxamine-desethyl), M02 (spirox-amine-despropyl) and M03 (spiroxamine-N-oxide) were detected in small amounts in the second experiment in pH 9.0 buffer, reaching maxima of 1.69, 2.27 and 4.08% AR respectively at the end of the study.





#### 2. Sterile Buffers

The buffers used were: pH 5 (0.02M acetate), pH 7 (0.02M phosphate) and pH 9 (0.02M borate) and were prepared as follows:

pH 5 – 0.04 M sodium acetate solution brought to a volume of 250 mL with water and adjusted to pH 5.0 using 0.04 M sodium hydroxide or acetic acid.

pH 7 – 74 mL of 0.04 M sodium hydroxide was added to 125 mL of 0.04 M potassium dihydrogen phosphate solution, brought to 250 mL with water. pH is adjusted to 7.0 using 0.04 M sodium hydroxide or phosphoric acid.

pH 9 – 0.04 moles of boric acid was dissolved in 1 L  $\infty$  0.04 M potassium chloride solution. To  $\beta$ 's mK of this solution, 53 mL of 0.04 M sodium hydroxide was added and brought to 250 mL with water. The pH was adjusted to 9.0 with 0.04 M sodium hydroxide or boric acid.

All buffer solutions used filtered Milli-Q water were diluted to 0.07 M and steriozed prior to use by autoclaving.

#### **B. Study Design**

#### 1. Experimental Conditions

The hydrolysis of [cyclohexyl-1-¹⁴C] labelled spiro amine was investigated at  $25 \pm 1$  °C, at pH 5, 7 and 9, in the dark, under sterile conditions. [oyclohexyl-1-¹⁴C]-labelled spiro amine was dissolved in sterile buffer at a nominal concentration of 1 mg/L. The appendix solubility of spiro amine was above the test concentration (see Point CA 25).

Due to poor material balances at D days after treatment, an additional experiment at pH 9.0 was conducted, also using 0.02M borate buffer made in the same way as described above.

#### 2. Sampling

Duplicate aliquots of samples were removed immediately after treatment and after 1, 3, 7, 14, 20, 24 and 30 days. Sterility and pH officest samples was confirmed using additional samples from 0, 14 and 30 days after treatment.

The additional experiment at pH 9.0 was sampled in diplicate after 7, 7, 14, 22 and 30 days, with additional samples at 14 and 30 days for sterility testing

# 3. Analytical Procedures

Aliquots were removed and directly analysed by LSC. Samples were analysed by TLC without concentration was used to identify compounds present, based on comparison of retention times with known concentration of test substance and, in some cases, analytical standards (for example metabolites). Three different TLC systems were used for the main experiment:

1) Normal phase, using acetonarile/water/trathylappine (80/18/0.5, v/v/v) solvent system

2) Normal phase, using diethoromethane methanel methylethylketone (60/20/10, v/v/v) solvent system

3) Normal phase, using chlorotorm/methanol/methylethylketone (100/10/20, v/v/v) solvent system

Two further HC systems were used for the supplementary experiment at pH 9.0:

1) Normal phase, using apetonitorle/water/ammonia (25%) (80:18:2, v/v/v) solvent system

2) Reverse phase, using n-fix ane/dichloromethane/2-propanol/ammonia (30/70/10/2, v/v/v) solvent system on the first ph, and chloroform/ethanol (50/50, v/v) on the second run.

Radioactive zones were analysed by a Bio-Imaging analyser, and the limit of detection (LOD) was for a single peak  $\geq 1\%$  of applied radioactivity (corresponding to 0.008 mg a.s./L). There are metabolite values below 1% AR given for the additional experiment at pH 9.0, however as none of the values are approaching 10% (max individual value of 5.70%) they are simply given as reported.



Identity of spiroxamine was also confirmed by concentrating, running on TLC system 2) above twice (the second time using material eluted with methanol from the main radioactive zone on the TLC plate from the first run), and then using GC/MS.

#### 4. Determination of degradation kinetics

The reported hydrolysis half-life of spiroxamine in pH 5, 7 and 9 aqueous buffers was calculated based on a regression analysis of spiroxamine residues as determined by TLC.

#### II. Results and Discussion

#### A. Data

The results of the HPLC analysis of aqueous buffer wilution are summarised in Dable CA 7.2, P.1-1 to Table CA 7.2.1.1-4.

Table CA 7.2.1.1-1:	Characterisation of	f radioactivity	in pH 5	.0 aqueous	buffer solu	tion [% AR]	

			$\bigcirc$		~~	<u>~~</u> 0		ſ	<u> </u>
Compound	Donligato	$\sim$ Inerplation time (BAT) $\sim$ $\sim$ $\sim$ $\sim$ $\sim$							
Compound	Replicate	0		×~3 _~	7	14	<b>20</b>	24	30
	А	96.43	<b>99</b> .81 %	×100.14	101,06	100.37	≫101.6 <b>8</b> ≫	100.75	<b>2</b> .57
Spiroxamine	В	100.92	Q101,68/	102.74	29.06	KJ01.63	99 <b>G</b>	100.75	400.96
	Mean	98.68 ^O	100,75		A00.06	101.0	109.68	<b>@100.75</b> ©	100.27
	Α	97 <i>.</i> <b>9</b> 5	101.20	101.52	102,37	99.65	¥02.85¢,	J 101.57	100.78
Total radioac-	В	102.04	£J02.990		100.29	¢01.81	100,70	102.21	101.91
tivity	С	~~ · ~		<u>'0</u> "	~- ¢	102.64	<u>_</u>	0 [×] -	105.63
	Mean	100%	102,09	<b>4</b> 92.73 a	r 101.33∕∕	101,36	<b>101.78</b>	101.89	102.77
		0	s ľ			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		/	

DAT: days after treatment All values expressed as mean percentage of applied radiactivity %

\$ 1

Table CA 7.2.1.1-	2% Chara	acteristation	<b>M</b> radioact	ivity in pH	7.0 aqueous buffe	r solution [% AR]

Commonwel	Replicate		<del>v</del> ř v	· · Nn	cubation	time (DA	ľ)		
Compound		U ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		. <b>.</b>	ິ 7 🖉	ÿ 14 [€] √ ^v	20	24	30
l		97.98	9 <b>%4</b> 0	Ø9.04	97.78	102,09	99.93	102.94	100.42
Spiroxamine	B	10\$37	<b>A</b> 99.96	¥102.00	100.26	27.33	98.85	104.96	103.14
	Mean	. 99.68	©98.68 [©]	100,52	~99.02 ^	<b>999.21</b>	99.39	103.95	101.78
	, Ø	©)∮8.63 [™]	98.09	<b>\$99</b> .69	≪98.25 [©]	0 101.60	100.56	104.04	103.09
Total radioac-	B B	10137	<u>1</u> 00.63	ر) 102.0 🗸	10026	101.86	99.46	106.33	105.96
tivity	C A	Û.	ĵ - ĵ?	r <u>0</u>		97.86	_	-	102.02
	Mean	<b>\$100.0</b>	99. <b>36</b>	100.85	<b>99.26</b>	100.44	100.01	105.19	103.69

DAT: days after treatment All values expressed as mean percentage of applied radioactivity (BAR)

# Table CA 7.2.1.1-3: Characterisation of radioactivity in pH 9.0 aqueous buffer solution – first

Commound	Donligato			Incubation time (DAT)						
Compound		> <b>V</b> ‰ /`	í¥	3	7	14	20	24	30	
J.	A S	90.88	8.12	89.93	104.0	101.20	99.61	101.67	71.33	
Spiroxamine	Mean	190.78	101.54	88.18	103.79	99.40	99.05	106.64	72.35	
		<b>95.83</b>	99.83	89.06	103.90	100.30	99.33	104.16	71.84	
		^ø 94.70	102.13	89.93	105.04	101.04	100.07	102.68	72.63	
Total radioac- tivity	𝔅 B 🏷	105.30	105.66	90.05	105.43	102.20	99.55	107.59	72.71	
tivity S	C	-	-	-	-	100.04	-	-	73.07	
Ô	Mean	100.0	103.90	89.99	105.23	101.09	99.81	105.14	72.81	

DAT: days after treatment

All values expressed as mean percentage of applied radioactivity (% AR)



	ond expe	i intene [70					_Ŵ	$\gg$
Commonwel	Darkaata			Ş				
Compound	Replicate	0	1	7	14	22	_030	Q,
	А	93.36	88.03	89.79	83.71 🔍	80.60	82.40	
Spiroxamine	В	101.62	91.58	91.64	89.90 🖉	87.11	87.82	
	Mean	97.49	89.81	90.72	86.84	83.86 💍	8591	ĈQ
M01 (anirow	А	0.59	0.33	n.d.	0,82	0.51 🏷	. °∿I.29 ~~	P
M01 (spirox- amine-desethyl)	В	0.65	0.44	n.d.	Ø.70	0.72	1.90	
amme-desetilyi)	Mean	0.62	0.39 "	<i>v</i> –	<b>60.76</b>	<b>\$</b> .62 ~	1,60	Ő
M02 (spirox-	А	0.40	0.58	n.d.	1.43	_01.40 ×	D12	×
amine-despro-	В	0.44	0.35	n.d.	k kan	1.06	2.42	
pyl)	Mean	0.42	0947	- >	<u>∘</u> ¶.32	× 1\23	Q 2.27	
MO2 (animor	А	1.29	&2.60 Ø	° 4,51	3.19	چە.70 ^م ى	3%83	
M03 (spirox- amine-N-oxide)	В	1.41	© 2.40 €	<u>م 22.</u>	× 3,708	2.40r	4.32	
amme-n-oxide)	Mean	1.35 🦼	2.50	@ <b>3.8</b> 7 Q	3.49	4.05	<b>2 4.08</b>	
Diffuse radiase	А	0.08 🖑	"n.d. "	n.	1.06	2,98	^{1.24}	
Diffuse radioac-	В	0.12	_°≈\$0.01_©	.0.46	0 n.d. 7	\$0.15 <b>1.5</b>	đ.đ.	
tivity	Mean	<b>9</b> .9	2 - 2	~ <b>.</b>	1 <b>0</b> 6	1.5	<b>1.24</b>	
	А	Q5.76 🕜	≠ 91°.5∕3	[%] 94.25	<b>%0</b> .21	<u>9</u> 1\$79	90.88	
Total radioactivity	В	₹ <b>04.2</b>	Ø4.77 💍	r 95,32	095.48	Ø1.44 ^	96.46	
	Mean	¢ 100.9	093.15	<b>9</b> 24.79	92.85	~ ⁹ 91.3 <b>2</b>	93.67	

 Table CA 7.2.1.1-4:
 Characterisation of radioactivity in pH 9.0 aqueous buffer solution – second experiment [% AR]

n.d.: not detected, DAT: days after beatment

All values expressed as percentage of applied radioactivity v% AR)

#### **B. Material Balance**

Good radiochemical balances were achieved with mean recovery of applied radioactivity of 100.0 to 102.77% AR for pH2, 99,26 to 105.19% AR for pH 7, 72.81 to 105.23% AR for pH 9 samples from the first experiment. Due to the mass balance talling below values recommended in the guideline, data from this first experiment using pH 9 buffer has not been considered further. From the second experiment in pH 9.0 buffer recoveries of 91.32 to 1000% AR were achieved. The pH values and sterility of samples were maintained throughout the study.

# C. Transformation of the Test Substance

Spiroxamine was stable to hydrolysis at 0H 5 and 7. Due to poor mass balance, values from the first experiment using pH 9 buffer were not considered, however decline of *ca*. 15% spiroxamine was seen using pH 9 buffer in a second experiment TLC analysis confirmed that spiroxamine was the major compound defected M01 (spiroxamine desethy), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) were detected in small amounts in the second experiment in pH 9.0 buffer, reaching maxima of 1.60, 2.27 and 4.08% AR respectively at the end of the study.

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# D. Degradation Kinetics

In the report, hydrolysis harf-lives in pH 5, 7 and 9 buffers were calculated by extrapolation using singleexponential first order kinetics. The reported degradation rates are sufficient to demonstrate that spiroxamine is stable to hydrolysic at pH values of 5 and 7 and is only slowly hydrolysed at pH value 9.

### Conclusions

The hypholysis of [¹⁴C]-spirovamine was studied using sterile aqueous buffer solutions at pH 5, 7 and 9 incubated at  $2^{39}$ C for a 30 day period.

**₩**Ĩ.

Sphoxamine did not degrade significantly in the sterile pH 5 and 7 buffer solutions after 30 days at 25°C, however, decline of approximately 15% was seen after 30 days in the pH 9 buffer solution in the second experiment. This indicates that spiroxamine is hydrolytically stable under acidic and neutral conditions, and hydrolyses slowly under basic conditions. M01 (spiroxamine-desethyl), M02 (spirox-



amine-despropyl) and M03 (spiroxamine-N-oxide) were detected in small amounts in the second experiment in pH 9.0 buffer, reaching maxima of 1.60, 2.27 and 4.08% AR respectively at the end of the study.

#### Assessment and conclusion by applicant:

Study does not fully meet the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) USEPA (EPA): N, 161, 1 (similar to required guides line, minor differences). The study is considered supplemental to asses the hydrolysis of spiroxample as a function of pH as a consequence of poor mass balance at pH 9, 0

Data Point:	KCA 7.2.1.1/02
Report Author:	
Report Year:	
Report Title:	Hydrolysis of KWG 4168 (Spires amine, proposed) as a gunction of pH
Report No:	
Document No:	<u>M-006002-04</u> x x x x x x
Guideline(s) followed in	OECD guidefine for the testing of chemicals No 511: Hydrolysis Studies
study:	
Deviations from current	Yes a g g g g g g g g g g g g g g g g g g
test guideline:	Yes Residues: Hydrolysis conditions not in accordance with OCCD 50%
	Fate: Some minor deviation(s) not relevant for the reliability of the study (de-
	scribed in study summary)
Previous evaluation:	Signature and accepted 4 and a construction of the second se
A. 11	
GLP/Officially recog	Yes, conducted under GLO/Officially recognised testing facilities
nised testing facilities.	
Acceptability/Reliability: (	$\sum Yes \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma} \xrightarrow{\gamma}$
Ú al	

### Executive Summary

The hydrolysis of non-labelled spiroxamine was investigated at  $50 \pm 0.5^{\circ}$ C at pH 4, 7 and 9, over 8 days in the dark under sterile conditions. After II test was also conducted at pH 4 and 50°C (over 22 days) and 30% (over 102 days). Non-labelled spiroxamine was dissolved in sterile buffer at a nominal concentration of 1 mg/Q

Samples were reflected immediately after treatment (*ca.* 12 hours) and after 8 days in the preliminary test at 50°C. In the tie 11 test, duplicate abquots from the 50°C test were removed *ca.* 12 hours after treatment and after 0.8, 1, 025, 2, 3.29, 6, 7.29, 15 and 22 days. From the 30°C test, duplicate aliquots were removed *ca.* 12 hours after treatment and after 0, 15, 22, 33, 75 and 102 days. Temperature and pH were monitored throughout, and sterility of test samples was confirmed at 0, 15 and 22 days incubated at 50°C, and 9, 45, 22, 33, 75 and 102 days incubated at 30°C.

Buffer samples were analysed by GC-MS to dentify the compounds present, based on comparison of retention times with known concentration of test substance. Breakdown products were identified using HPLC-MS.

Spiroxamine did not degrade significantly in the sterile pH 7 and 9 buffer solutions after 8 days at 50°C (corresponding 6 a half-life 6 1 year at 25°C). In a tier II experiment in pH 4 buffer solution, decline of approximately 80% was seen after 22 days at 50°C, and decline of approximately 50% was seen after 102 days at 30°C. This indicates that spiroxamine hydrolyses slowly under environmentally relevant conditions. (temperature and pH). At low pH and at high temperature spiroxamine hydrolysed under acidic conditions. Metabolites M15 (spiroxamine-ketone) or 4-tert-butylcyclohexanone in the report and M28 (spiroxamine-aminodiol) or N-ethyl-N-propyl-3-aminopropane-(1,2)/aminodiol in the report were detected in pH 4 buffer, although they were only quantified at 22 DAT after incubation at 50°C, at 3.95



and 4.35 mg/L respectively.

#### I. Materials and Methods

### A. Materials

## 1. Test Items

Non labelled spiroxamine

Batch number:

Chemical purity:

920522ELB01 99.0% (GLC analysis, isomer A 53.0% and isomer B 46.09

## 2. Sterile Buffers

The buffers used were: pH 4 (0.01) (0.01) pH 7 (0.01) physical phy

pH 4 – 2.105 g/L citric acid, adjusted to pH 4 Susing Sodium Hydroxide.

pH 7 – 3.5831 g/L disodium prosphate, adjusted to pH 7.0 using phosphoric acid.

pH 9 – 3.8118 g/L sodium (etraborate, adjusted to pH 9.0 using phosphoric acid.

All buffer solutions used filtered Mille Q water and were sprilized at 90°C prio to use.

### B. Study Design

# 1. Experimental Conditions

In a preliminary test, the hydrolysis of non-fabelled spiroxamine was investigated at  $50 \pm 0.5$  °C, at pH 4, 7 and 9, in the dark, under sterile conditions. Spiroxamine was dissolved in sterile buffer at a nominal concentration of 10 mg/L. According to the report, the aqueous solubility of spiroxamine isomer A is 14 mg/k and isomer Bas 10 mg/L at 20 °C and pH 60, with solubility rising steeply with decreasing pH.

A tier II test was conducted at pH conly temperatures  $0^{+}50 \pm 0.5$  and  $30 \pm 0.5^{\circ}$ C and all other conditions the same the preliminary test.

# 2. Sampling

In the preliminary test, diplicate aliquous of sample were removed *ca.* 12 hours after treatment and after 8 days. Temperature and pH were monitored throughout, and sterility was confirmed from aliquots taken at the same times as quantification samples.

The ther II test, duplicate arquots from the 50°C test were removed *ca*. 12 hours after treatment and 0.8, 1, 1.25, 2, 3.29, 6, 7.29, 15 and 22 days was sampled in duplicate. From the 30°C test, duplicate aliquots were removed *ca*. 12 hours after treatment and after 5, 15, 22, 33, 75 and 102 days. Temperature and pH were monitored throughout, and sterify was confirmed at 0, 15 and 22 days incubated at 50°C, and 0, 15, 22, 33, 75 and 102 days incubated at 30°C.

# 3. Analytical Proceedires

Aliquots were removed and analysed by GC-MS without concentration, based on comparison of retention times with known concentration of test substance. The carrying gas was helium and column was a 15m+4m fused silica closed coupling, I.D. 0.25 mm.

In order to identify breakdown products, reverse-phase HPLC-MS using a LiChrospher 100 Diol column, mobile phase of water+25% NH₄OH (8/2, v/v) and acetonitrile (starting gradient of 10/90, v/v).



This was reported for samples from 22 DAT at 50°C only.

#### 4. Determination of degradation kinetics

The reported hydrolysis half-life of spiroxamine in pH 4 aqueous buffers was calculated based on linear regression of spiroxamine residues as determined by GLC using the software StorgraphicsPlus 3.0

#### II. **Results and Discussion**

#### A. Data

The results from the preliminary test are summarised in Table CA 72.1.1-5 to Table Results from the Tier II test are summarise in Table CA 7.2.1.1-8 to Table CA 7.2.191-9

Table CA 7.2.1.1-5: Residues in preliminary test at 50°C in pH 4.0 aqueons buffer solution [mg/L]

	[8/-	-1		`	, <u>"</u> 0"		, °C	ð		4
Compound			Č	Incubati	on time	(DÁŤ)		S	e e	4
Compound			0 4			0	ð,	8		
Spiroxamine A			9.62		× ~	× A		3.31	Į.	
Spiroxamine			5.22	$\mathcal{T}$		Å.	, N	າໝີ		A A A A A A A A A A A A A A A A A A A
(isomer A)			<u> </u>			*	Ř	239	Ş	0
Spiroxamine					~ ~	Ø Å		0.92 5	Š. 4	)
(isomer B)		Ĺ	<b>%</b> .40 0	~ ~	, s	í d		0.92		
DAT: days after treater	atment	<u>a</u>			, P	Å	×	~O~	1	
All values expressed	d as mg/L	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	°~		(C -		~ [©]	8	×	
$\Lambda$ Isomer $\Lambda + Is$	omer B	17			¥,	,O ^V	Ő .		U	

Isomer A + Isomer B

Table CA 7.2.1.1-6: Résidues in preliminary test at 50° G in pH 7.0 agreous buffer solution Jmg/Ll Ô Ôĥ C

		× .
Compound	Dicubation time (DAT)	1
Compound		8
Spiroxamine		8.27
Spiroxamine 📎		4.49
(isomer A)		4.47
Spiroxamine		3.78
(isomer B)		5.78
DAT: days after tre	atment by a by in a	
All values expresse	d as seg/L	

А

Isomer A + Isomer B

#### Residues in preliminary test at 50°C in pH 9.0 aqueous buffer solution Table CA 7.2 Č, $[m \hat{g} \hat{L}] = \hat{h}$ íQ, ß

4						
Compound	🕺 🖉 🖉 Incubation time (DAT)					
Compound		8				
Spitoxamine A	4.88Q ~~	5.05				
Spiroxamine (isomer A)		2.80				
Spiroxamine (isomer B)	2.17	2.25				
DAT: days after tre						

All values expressed as me

Pisomer



		Incu	Incubation time (DAT)					
0	5	15	22	33	75	102		
	0	0 5	Incul 0 5 15	Incubation time (I           0         5         15         22	Incubation time (DAT)           0         5         15         22         33	Incubation time (DAT)           0         5         15         22         33         75		

Table CA 7.2.1.1-8:	Residues in Tier II test at 30°C in	pH 4.0 aqueous buffer solution [mg/L]	
---------------------	-------------------------------------	---------------------------------------	--

Compound			Incu	bation time (	DAI)		
Compound	0	5	15	22	33	75	1.02
Spiroxamine (isomer A)	5.55	5.60	6.38	5.16	5.39	<b>3</b> 4.97	\$?83 b
Spiroxamine (isomer B)	4.94	4.92	4.67	3.98	3.05	1.60	
Spiroxamine A	10.49	10.52	11.05	<u>9</u> .14	8.44	6.57 %	
DAT: days after the All values express A Isomer A +	sed as mg/L			- C - K			

Table CA 7.2.1.1-9: Residues in Tier II test at 59°C in pH 4.0 aqueous buffer solution [mg/I

				$\sim$	~	7 0. "	I A A A A A A A A A A A A A A A A A A A		, 4	$ \rightarrow $
Compound		Incubation time (PAT) O								
Compound	0	0.8	10	1.25	Ľ	3.29	۵ ۵	3.29	. 15 🧃	22
Spiroxamine (isomer A)	7.50	6.45	6463	591	<b>5</b> .84	<u>0</u> 4.69	©4.84	4.06	¥ 3.16	1.92
Spiroxamine (isomer B)	6.34	5.34	<b>≪4.9</b> 7	°~,4.35_″	¥4.04	2.93	2.45	1.86	0.96	0.94
Spiroxamine ^A	13.84	11.79	M1.60	¥10.26	9.88	7,62/	Ţ:29	5,92	×3.92	<b>2</b> .26
M15 (ketone)	-	- Q	-~	Z.		× V	8-	Q"-	Ş - (	3.95
M28 (aminodiol	-				⊀ <b>)</b> - ∧	Ø - 💉	ð -	- 6	- Q	4.35
DAT: days after treatment										
All values expressed as mg/I	L ,					L	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0		
A Isomer A + Isomer B					L.			8	5	
	, ¥	4				<i>Q</i> ) *	l a	(( .	))	

#### B. Transformation of the Test Substance

Spiroxamine was stable to hydrolysis at pH 7 and 9. There was a discrepancy between the applied test substance and that recovered by analysis at pH 9 to the preliminary test, however, the report explains that this loss was due to absorption to the filter. At pH 4 losses of around 66% of test substance were observed after 8 days at 50°C during a rier II test, metabolites M15 (spipoxamine-ketone) and M28 (spiroxamine-amprodio) were detected in pH 4.0 buffer, although they were only quantified at 22 DAT after incubation at 50 °C (3.95 and 435 mg/C respectively). The report considers the concentrations of these two metabolites correspond to a degradation of spiroxamine of 80% by the end of the study. At 30°C in pH4 buffer, recovery of 4.70 mg/L dotal spiroxantine after 102 days incubation indicates a degradation of around \$9%.

#### C. Degradation Kinetics &

Spiroxamine was stable (i.e. hat life i year at 25°C) to hodrolysis at pH 7 and 9. At pH 4, half-lives at 20°C for isomer A and B of 790 and 120 days, respectively were calculated in the report. The reported degradation rates are sufficient to demonstrate that spiroxamine is only slowly hydrolysed.

#### ÂÎI. 🗞 Conclusions

The hydrolysis of [¹⁴C]-spiroxamine was studied using sterile aqueous buffer solutions at pH 5, 7 and 9.

Spiroxamine did not degrade significantly in the sterile pH 7 and 9 buffer solutions after 8 days at 50°C (corresponding a half-life of 1 year at 25°C). In a tier II experiment in pH 4 buffer solution, decline of approximately 80% was seen after 22 days at 50°C, and decline of approximately 50% was seen after 102 days at \$0°C. This insticates that sphoxamine hydrolyses slowly under acidic conditions. Metabolites M155 spiro amine ketone and M28 (spiroxamine-aminodiol) were detected in pH 4 buffer, although they were only quantified at 22 DAT after incubation at 50°C, at 3.95 and 4.35 mg/L respectively.



#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to study guideline(s) OECD 111 (required guideline). The study is considered valid to assess the hydrolysis of non-radiolabelled spiroxamine as a function of pH.

#### CA 7.2.1.2 Direct photochemical degradation

The molar absorbance coefficient of the active substance spiroxamine is <10 L/mol/cm acwavelength 295 nm (ref CA 2.4), therefore studies investigating the direct photolysis of the active substance in aque ous solution are not needed according to the data requirements laid down in Commission Regulation (EU) No 283/2013. However, two existing studies are available and have therefore been included for completeness. One study (KCA 7.2.1.2/01) investigates the direct photolysis of the active substance in aqueous solution to address the data point. A further study (KCA 7.2.1.2/02) calculates the quantum yield for photo-degradation as supporting thata. Both studies were evaluated during the previous EU review.

		a			$\sim$	O`		L.V	$\sim$	A.
Substance	<b>Report reference</b>	Q,	Documen	Çno. 👡	ý	K)	<u>ک</u> (	Comment	Ş.	0
Spiroxamine	KCA 7.2.1.2/01	y I	@20060@#	<u>-01-1</u> ©"				first appro		
Spiroxamine	KCA 7.2.1.2/02		<u>1-006008</u>	- <u>01</u> 0	Ô			viewed un		
			"0"	õ,	ď	Q'e	red	d and acc	ptable	•

In accordance with the data requirements defined by 5C Regulation 283/2013, for aqueous photolysis studies included under Point CA7.2.1.2, metabolites are considered major if the exceed 10% AR, otherwise metabolites are considered photor.

	5
Dete Deinte	KCA/7.2.1/2/01 / 2/ 2/ 2/
Report Author	
Report Year	
Report Title:	Photolysis of KWG 4168 in aqueous solution
Report No:	RF4075
Document No:	$4 - 006 0 - 10^{\circ} $
Guideline(s) followed in	USER $(=ER)$ : Sec $(N 162-2;$
study:	
Deviations from current	
test guideline.	
Previous evaluation:	yes, evaluated and accepted
	DAR (1997), RAR 2010, RAR (2017)
GLP/Officially recog	Xes, conducted order GP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:"	Yes O Q

## Executive Summary

The aqueous photolysis  $\mathcal{O}$  [cyclohexyl- $\mathcal{P}$ -1⁴C]-spiroxamine was investigated after exposure to artificial light in sterile 0  $\mathcal{O}$  M phosphate buffer solution at pH 7 for up to 15 days continuous irradiation. [Cyclohexyl- $\mathcal{K}$ - $\mathcal{A}$ C]-spiroxathine was dissolved in buffer at a concentration of 1.33 mg/L with 0.1% acetonitrile present as a  $\mathcal{K}$ -solvent.

Quartz sample tubes were irradiated in a Heraeus Suntest apparatus equipped with a Xenon lamp with filters to block infrared light and irradiation below 280 nm. Light exposed samples were incubated at 25  $\pm$  1°C with continuous temperature monitoring. Dark control samples were run concurrently for 15 days under the same conditions in quartz vessels wrapped in aluminium foil to prevent irradiation.



Irradiated samples were removed after 0, 2, 5, 7, 12 and 15 days after treatment, and dark controls were removed at 15 days after treatment.

Triplicate aliquots were taken for LSC to quantify the radioactivity present in solution. Buffer solutions were analysed by Thin Layer Chromatography (TLC) using three separate methods run against reference standards to confirm quantification and identity.

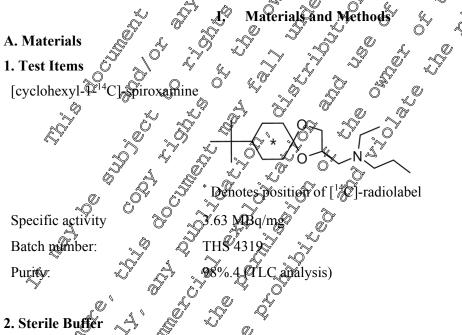
Light intensity was measured by radiometer and uranyl oxalate actinometer. The actinometer is prepared using 0.01M uranyl nitrate and 0.05M oxalic acid, with samples irradiated for 10 minutes and analysed via titration with 0.05 N KMnO₄ solution.

Recovery of applied radioactivity was 94.29 to 100.0% for light exposed samples, and 97 52% for dark control samples.

Spiroxamine exhibited slow degradation in lighter posed samples and represented 78.22% of applied radioactivity after 15 days continuous irradiation. No significant degradation was detected in the dark control samples, with spiroxamine accounting for 9573% scapplied radioactivity at the end of the incubation period.

Several separate peaks below 10% were detected in ifradiate Samples and were identified. M03 (spiroxamine-N-oxide) reached a maximum of 4.01% AR at 5 DAT. M02 (spitoxamine-despropyl) eached a maximum of 4.47% AR at 15 DAD still tising at the end of the study. M01 (spiroxamine-desethyl) reached a maximum of 4.53% AR of 12 DAT, though recoveries also include some A of M05 (spiroxamine-hydroxy). M05 (spiroxamine-hydroxy) reached a maximum of 3.13% AR of 12 DAT, though it is noted that this corresponds to isomer B of this metabolite only

The  $DT_{50}$  of [¹⁴C]-spiroxamine in Fight exposed samples was calculated to be equivalent to 236 days midday sunlight at 40°N. Dark incubations did not show an appreciable decline



The study was carried on in 0.00 M phosphate buffer pH 7.0, with an electrical conductivity of 0.6 mS.

## B. Study Design

# 1. Experimental Conditions

The aqueous photolysis of [cyclohexyl-1-¹⁴C]-spiroxamine, was exposed to artificial light in sterile 0.01M phosphate buffer solution at pH 7 for up to 15 days continuous irradiation. [cyclohexyl-1-¹⁴C]-spiroxamine, was dissolved in buffer at a nominal concentration of 1.33 mg/L with 0.1% acetonitrile present as a co-solvent. This application rate is based on the maximum rate of 2 kg a.s./ha,



distributed in an assumed water layer of 15 cm (standard assumption is a 30 cm water layer, which would correspond to 0.667 mg/L). Application solution was made up and dispensed into 20 quartz yessels, 12 of which were irradiated in a Heraeus Suntest apparatus equipped with a Xenon lamp with fatters to block infrared light and irradiation below 280 nm. The average intensity of this lamp over the study period is 11.1 mW/cm². Light exposed samples were incubated at  $25 \pm 1^{\circ}$ C and the temperature was monitored continuously. Dark control samples were run concurrently in two of the quartz vessels, wrapped in aluminium foil to prevent irradiation and subject to the same conditions as irradiated samples. The remaining vessels were used for sterility checks, measurement of pH, or retained in case of losses or the need to identify metabolites.

#### 2. Sampling

Irradiated samples were removed after 0, 2, 5, 7, 12 and 15 days after treatment and dark controls were removed at 15 days after treatment. At each time point the pH and temperature were measured.

Sterility of test samples was confirmed at the beginning and end of the study period.

#### 3. Analytical Procedures

Triplicate aliquots were taken for LSC at each sampling point to quantify the radioactivity present in solution.

Buffer solutions were analysed using three different TLC methods without concentration, and chromatographed against reference standards to confirm results and identify metabolites:

A) Normal phase using an acetonitrile/water/25% aromonia ( $\frac{80}{18}$ ,  $\frac{v}{v}$ ) solvent system

B) Normal phase using a chloroform/methanol/25% amfaonia (65/28/\$v/v/x) solvent system

C) Reverse phase using an n-hexane/dichloromethane/2-propanol/ammonia (30070/10/2, v/v/v/v) solvent system for the first run, and a choroform/ethane/1 (5050, v/v) solvent system for the second run.

Radioactive zones of the TLC plates were measured using a Bio-imaging Analyser. The detection limit for a single peak in the solutions was  $\geq 0.6\%$  of applied radioactivity.

One isomer of 2005 (spiroxamine-hodroxy had the same chromatographic behaviour as M01 (spiroxamine-desethyl) with TLC method A). For simplification of the evaluation it was assumed that the isomers were formed in a ratio of 50:50, similar to the ratio of the diastereoisomers of the applied [¹⁴C]-Spiroxamine. To validate the assumed ratio the ratio of the isomers of metabolite M02 (spiroxaminedespropyl) was determined from BAT 15 and found to be 45.55. This indicates that for M05 (spiroxamine-hydroxy) a possible error of quantification by using a ratio of 50:50 is regarded as negligible. Therefore metabolite M01 (spiroxamine-desethyl) was quantified by subtracting the amount corresponding to 50% of M05 (spiroxamine-hydroxy) (amount of separate isomer) from the total peak (sum of M01 and 50% of M05)

Light introsity was measured by radiometer and uranyl oxalate actinometer. The actinometer is prepared using 0.01M uranyl purate and 0.05M oxalc acid with samples irradiated for 10 minutes and analysed via titration with 0.05 N KMnO4 solution

## 4. Determination of degradation kinetics

The reported balf-life of spice xamine in light exposed samples was calculated by regression using mean values for each time point. The light intensity of the lamp was compared to reference values for midday summer winlight at 40 % in order to correct to the period of equivalent full 12 hour days of natural irradiation.

A. Data

#### II. Results and Discussion

The recovery and distribution of radioactivity in light exposed and dark control samples is presented in Table CA 7.2.1.2-1 and Table CA 7.2.1.2-2.



Table CA 7.2.1.2-1:	Distribution of radioactivity in irradiated samples incubated at pH	7 and
	25°C [% AR]	<i>a</i> , °

Commoned	Replicate		Ir				
Compound	-	0	2	5	7	12	Ø15 ⁴
	А	98.90	89.46	79.73	87.98	81.13	81.780
Spiroxamine	В	97.40	90.59	85.22	86. <b>30</b>	75.10	74%
	Mean	98.15	90.02	82.48	<b>8</b> Å14	78.16	78.22
MO2 (aninemenine	А	1.40	1.00	5.00	¥.63	3,58	°~2.67
M03 (spiroxamine- N-oxide)	В	1.11	0.82	3.02	¢ [*] 2.05	¢40	3.770
IN-OXIGE)	Mean	1.26	0,91	4.01	1.84	<b>3.99</b>	
M02 (spiroxamine- despropyl)	А	0.12	¢.95	2.42	3.01	3.62	<u>9</u> .64
	В	0.12	A.31	2.1₩	\$3.51 ×	4.60	5.29
	Mean	0.12 🔍	1.63	2.27	<b>3.26</b>	<b>4.11</b>	4,4
M01 (spiroxamine- desethyl)	А	0.22 🕵	1676	ي 2.48	3.43	© 4.63~	<b>368</b> 4
	В	0.20© [*]	<u>9</u> 47 ×	J 2. <b>29</b>	<b>Ø</b> .46 n	¥ 4. <b>4</b> 3	<u>4</u> .93 。
uesettiyi)	Mean		~1. <u>6</u> 10	2Q8	⁰ 3.44	4053	@ [*] 4.39
M05 (cnirovomino	А	ĭ₩.d.	2.31	الم∂1.53	2.08	≪_1.69	2,8,8
M05 (spiroxamine- hydroxy)	В	n.d, N	<i>,</i> 1229 🔬	1.340	220	\$ ⁷ 4.56	2.62
liyuloxy)	Mean	n.d, '~	<b></b>	1,43	<u></u> 02.14	303	2.50
	A K	0@0	≫"2.25	<u>^</u> 3∕03 ⊘	1.86	\$.65 🔬	3.39
Diffuse radioactivity	В 🖓	Ø.12 Ø	133	S ⁷ 1.41 O	201	⁽⁶⁾ 4.82 ⁽	6.39
	Mean	<b>. ≪ 0.26</b> Ø	<b>3</b> .69	1.72	<b>2</b> .16 🚿	3.93	4.89
		^{* %} 101094	, 98.73 ^A	9 <i>3</i> 949	©99.92	91 <b>9</b> 30	97.70
Total radioactivity	B	<b>98</b> .95 🍙	∛ 96. <b>60</b> °	95.39	× 99.29	Ø97.91	97.67
-	°∼ Mean₄	Ø100.0	97,67	_{∿≫} ∿94.29∕√ຶ	<b>99.</b> 99	Sec. 61 (1997) 97.61	97.69
.d.: not detected, DAT: d .ll values expressed as mg	ays after treatment		çiy (% ÂK)			) %	

# Table CA 7.2.1.25: Distribution of radioactivity in dark control samples incubated at pH 7 and 25°C [% ARk

	$\cap' \cup \cup$	
Compound	Replicate	Incubation time (DAT)
		<b>15</b> <b>94.49</b>
		94.49
Spiroxamine	S ^B S ^B	96.98 95 73
	Nean C	95.73
	Mean Mean	2.05
M03 (spiroxamine-N-oxede)	A Mean N	1.15
M03 (spiroxamine-N-oside)	Mean 🕎 🗸	1.60
M02 (spinoxamine-desprapyl)	AN AG	n.d.
M02 (spiroxamine-despropyl)		n.d.
	Mean ~	-
		n.d.
M01 [®] (spiroxamine-deseth [®] )	[™] BO [™]	n.d.
	Mean	-
	Ă Ă	n.d.
M05 (spirosamineshýdroxs)	_ ∧O B	n.d.
	Mean	-
XY Z A Y	А	0.50
M01 (spiroxamine-deseth@) M05 (spiroxamine-bydroxx) Diffuse radioactivity	В	0.46
M05 (spirosamine by droxs)	Mean	0.48
Total fadioactivity	Α	97.04
Total adioactivity	В	98.59
	Mean	97.82

n.d.: not detected, DAT: days after treatment

All values expressed as mean percentage of applied radioactivity (% AR)



#### **B.** Material Balance

Recovery of applied radioactivity was 94.29 to 100.0% for light exposed samples, and 97.82% control samples.

#### **C. Degradation of Parent Compound**

Spiroxamine exhibited slow degradation in light exposed samples and represented 78.22% ARomean after 15 days continuous irradiation. No significant degradation was detected in the dark control safeples, with spiroxamine accounting for 95.73% of AR (mean) at the end of the incubation period.

Several separate peaks below 10% were detected in availated samples and were dentified. MOX (spin) roxamine-N-oxide) reached a maximum of 4.01% AR (mean) at 5 DAT M02 (Spiroxamine-despropu) reached a maximum of 4.47% AR (mean) at 15 DAT, still rising at the end of the study. Mol (spiroxamine-desethyl) reached a maximum of 4.53% AR (mean) at 2 DAT, though receiveries also include isomer A of M05 (spiroxamine-hydroxy). MO5 (spiroxamine-hydroxy) seached maximum of 3.13% AR (mean) at 12 DAT, though it is noted that this corresponds to somer B of this metabolite only. None of the metabolites were observed in significant amounts,

#### **D.** Degradation Kinetics

The  $DT_{50}$  of [¹⁴C]-spiroxamine in hight exposed samples was calculated to be 50.5 days incidiation to the test conditions, equivalent to 236 days midday surfight ab 10°N Bark ocubations did not show an appreciable decline, therefore, DT₅₀ was not calculated for dark controls. DT₅₀ volues have not been recalculated as they sufficiently show that photolysis in aqueous solution is slow

Conclusions The results of this study indicate that aqueous photosis is not a major mode of pssipation of [14C]-spiroxamine under the test conditions employed. The  $DT_{50}$  of  $[^{14}C]$ -spire amine in light exposed samples was calculated to be equivalent to 236 days midday sonlight at 40°N. No significant metabolites were observed.

#### Assessment and conclusion by applicant:

Study weets the current guidance and the requirements in 283/2013. The study was conducted to study guide One(s) (USEPA (=EPA): N, 162-2 (similar to required guideline). The study is considered wild to assess the direct photolysis of [cyclohexyl-1-14C]-spiroxamine

the first of the second second



Data Point:	KCA 7.2.1.2/02
Report Author:	
Report Year:	1994
Report Title:	1994 Determination of the quantum yield and assessment of the environmental hat life of the direct photodegradation of KWG 4168 in water (buffer pH 7)
Report No:	PF4001
Document No:	<u>M-006008-01-1</u>
Guideline(s) followed in	Phototransofrmation of Chemicals in Water, Part A; Direct Phototransfor-mation,
study:	UBA (1992)
Deviations from current	None $\nabla Q$
test guideline:	
Previous evaluation:	yes, evaluated and accepted $O'$ DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GOP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes O O Z Z Z

#### **Executive Summary**

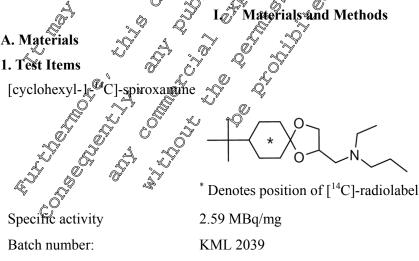
The aqueous photolysis of [cyclohexyl- $p^{44}$ C] spiroxamine was investigated in conjunction with the actinometer uranyl oxalate after exposure to artificial light in aqueous solution at 25 °C. The test was performed in either 0.01M acetate (pH4), phosphate (pH 7) and borate (pH5) buffer solutions for UV-VIS absorption spectrum data, or phosphate buffer (pH 7) for photolysis and quantum field measurements. Test item was incubated for up to 500 minutes continuous inadiation, whilst the actinometer was incubated for 10 minutes continuous irradiation before or after the test frem. [ 4 C]-spiroxamine was dissolved in deionised water at a nominal concentration of 20 mg/L in acetonitrile.

Quartz vessels (one per time point) were irradiated of a mervy-go-round apparatus equipped with a UV emission lamp (filtered to block infrared light and irradiation below 295 cm) maintained at 25±1 °C. No dark control sample were included

Irradiated samples containing test item were removed after 9,50, 100, 150, 200, 250, 300, 350, 400, 450 and 500 minutes of continuous irradiation Actinometer solutions were irradiated separately for 10 minutes either prior b, or after, test item solution irradiation.

UV-VIS absorption spectra of test solutions in buffers were analysed directly using a UV-VIS-spectrophotometer. Test solutions in water were analysed directly by reverse phase HPLC without concentration. Actinometer solutions were analysed by titration &

The calculated quantum yield for spiror amine is  $6.42 \times 10^{2}$  molecules per photon under the test conditions employed. The stimated range of environmental  $DP_{50}$  under summer sunlight, estimated in GC SOLAR and the Frank and blop for models is 247 day > 1 year.





Purity:

>99% (HPLC analysis)

#### 2. Test solutions

- The UV-Vis absorption spectrum experiment was performed using:
- 62 mg/L spiroxamine in 0.02M acetate buffer (pH 5.0)
- 31.0 mg/L spiroxamine in 0.02M acetate buffer (pH 5.0 acetonitrile)
- 12.4 mg/L spiroxaimine in 0.02M phosphate buffer (pH 7.0)
- 155 mg/L spiroxaimine in 0.02M phosphate buffer (pH 7.0)/acetopitrile ( $(1/1, \sqrt{x})$ )
- 12.4 mg/L spiroxamine in 0.02M borate buffer (PH 9.0)/acetopttrile (1/1
- 12.4 mg spiroxamine in water/acetonitrile (
- 31.0 mg spiroxamine in water/acetonitrile
- 62.0 mg/L spiromxaine in water/acetophtrile

The photodegradation experiment was carried out using a nominal 4.20 mg/L spiroxantine, dissolved in acetonitrile in 0.02M photokets have a spiror and a spiror a acetonitrile, in 0.02M phosphate buffer pH7.0. Actinometer solution contained 0.01M uranyl ions and 0.05M oxalic acid in water.

#### **B. Study Design**

#### 1. Experimental Conditions

The UV-Vis sorption spectra, photolysis and quantum yield of [cyclohexyl-16]C]-spiroxamine, was investigated by comparison to a chemical actinometer when exposed to artificial light in sterile buffer solutions for up to 500 minutes continuous irradiation Quartz vessels with a 1 cm optical path length were irradiated on a meny-go, found apparatos with a UV samp filtered to block infrared light and irradiation below 295 mm) maintained at 25-1 °C. For photolysis and quantum yield, 22 vessels with test item solution were used, in two separate experiments.

## 2. Sampling

Irradiated samples were removed after 0, 50, 100, 250, 200, 250, 300, 350, 400, 450 and 500 minutes irradiation. Actinometer solutions were irradiated separately for 10 minutes either prior to, or after, test item solution irradiation.

## 3. Analytical Procedures

UV-VIS absorption spectrowere analysed using a DMS90 spectrophotometer. Test item was quantified using reverse-phase HPLC with a Lightrosoft RP. Select B column, gradient elution of water/acetonitrile/phosphoric acid (95/5/0.2, v/v/v) and acetomoriale (starting gradient 90/10, v/v) with RAMONA 4 radio detector. The Aimit of Detection (LOD) was not reported.

Samples with actinometer were analysed by furation with manganese sulphate*H2O in (1 M) sulphuric acid and potassium permangenate (001M) solution.

Light intensity was measured by radiometer and uranyl oxalate actinometer. The actinometer is prepared using 0.0 m uranvi nitrate and 0.05M oxalic acid, with samples irradiated for 10 minutes and analysed via titration with 0.05 M KMtrO4 solution.

# 4. Determination of degradation kinetics

Environmental half-life of spiroxamine was estimated using two models - GC-SOLAR and an arithmetic model developed by Frank and Klöpffer. Model versions were not given in the study report. Within GC-SOLAR, direct photo-transformation at the surface of pure water was assumed at 30°N, 40°N, 50°N and 60°N latitude with clear sky and typical ozone concentrations. The Frank and Klöpffer model calculates



environmental half-lives for conditions in central Europe (corresponding to 50°N latitude).

#### II. **Results and Discussion**

#### A. Data

The recovery of radioactivity in irradiated samples is presented in Table CA 7,

Table CA 7.2.1.2-3:	Distribution of radioactivity 25°C	in irradiated	samplesincub	ated appH '	7 and 🧔
	25°C	(ČA)			Y Q

					S	)	a.Y		No.	Ś		()
					Irradiat	ion tim	e (mun)		,¢	20- 20-	2	Å
	0	50	100	150	200	250	<b>300</b>	350	<b>ð</b> 400	Q450 🔎	Ĵ ⁵ 00 🖗	1
Experiment 1 (mg/L)	4.20	3.94	3.91	3.93	3.82	3.95	∛ 3.71¢	° 3.86	4.03	3.84	4.0\$ 4.10	
Experiment 2 (mg/L)	4.19	4.19	4.15	3.98	4.10	4	3:99	3,95	4.06			
				×		Ĵ.	Å . (			$\sim$		
Experiment 1 (% applied) ^A	100.0	97.1	99.5	97.40		98.1	97.6	98,4	98.Q	97	98.7°	
Experiment 2 (% applied) ^A	100.0	100.4	<b>6</b> 00.1	99.6	J00.1 %		₽ Ĉ		• <i>0</i> 1	∲99.6 ¢	99.1	
Mean	100.0	98.8¢	99.80	98.5¥	99.2 ^y	98.7	973	98.3	989	98,5	98.9	

^AIn these cases '% applied' refers to recoveries compared to 0 DAG

#### B. UV-VIS absorption properties of test item

All the UV-Vis absorption spectra of spiroxantine in different aqueous schritions water/acetonitrile; buffers pH 5, 7 and 9) showed one comparatively low absorption maximum in the low range of UV at about 190 to 200 nm (s-values from, 180 to max. 8, 392 L/mole cm, band width to max. 215 nm).

The absorption properties indicate that direct interactions of spiroxamine in aqueous solution with the sunlight in the troppsphete are possible, but only to a very low extent.

## C. Quantum xield

The quantum yield of spiroxamine is calculated as  $6.42 \times 10^{-4}$  molecules degraded per photon.

## D. Environmental half-life 🕺

Ő The full range of hat lives of spir amin from GC-SOLAR and the Frank and Klöpffer models is 247 days - >1 year.

Ľ

Conclusions

The calculated quantum you'd for spirox anine 56.42  $3^{-4}$  molecules per photon under the test conditions employed. The estimated range of environmental DT₅₀ under summer sunlight, estimated in GC SOLAR and the Frank and Klöpffer models is 24 days - > 1 year.

## Assessment and conclusion by applicant

Study meets the current guidance and the requirements in 283/2013. The study is supporting information.

The strict was conducted to determine the quantum yield of the active substance using the ECETOC method. The study & considered valid to assess the quantum yield of the active substance [cyclohexyl-1-20-spitoxamine.



## CA 7.2.1.3 Indirect photochemical degradation

Data to address the data requirement for indirect photochemical degradation are not required since  $\hat{h}e$  molar absorption coefficient  $\epsilon$  is < 10 M/mol/cm.

#### CA 7.2.2 Route and rate of biological degradation in aquatic@ystems

Use of plant protection products containing the active substance spiroxamine may result in contact with aquatic systems, therefore the route and rate of biological degradation in aquatic systems has been in vestigated in laboratory studies according to the data requirements and down in EC Regulation 283/2013.

In accordance with the data requirements defined by EC Regulation 283/2013, for studies investigating the route and rate of biological degradation in aquatic systems included under Point (A 7.2.2, metabolites are considered major if they exceed 10% AR or exceed 5% on consecutive sampling intervals or exceed 5% and are rising at the end of the study, otherwise metabolites are considered minor.

## CA 7.2.2.1 "Ready biodegradability"

A study investigating the ready biodegradability of the active substance spiroxapine in standardised laboratory studies has not been performed instead the face and behaviour of the active substance in aquatic systems is investigated in studies performed under Point CA 7.2.2.3 and a classification or "not readily biodegradable" is assumed.

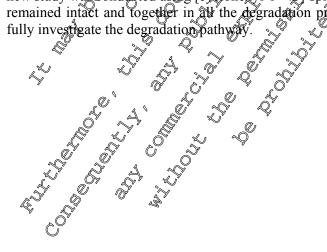
# CA 7.2.2.2 Aerobic mineralisation in surface water

Use of plant protection products containing the active substance spirox amine may tesult in contact with aquatic systems, therefore the activity mineralisation in surface water has been investigated in laboratory studies according to the data requirements laid down in FO Regulation 283/2013.

No existing studies are available investigating the aerobic mineralisation in surface water of spiroxamine and therefore one new study was conducted (KCA  $7_c^{2/2}.2/00$ ). The study was primarily to fulfil the data requirement bullalso to address the new requirements of EFSA  $2019^1$ .

Sub- stance ence	Bocument no Test material	Comment
Spirox KCA 7.3 2.2/01 amine		New data not yet reviewed under UP.

The aerobic mineralisation in surface water of spiroxamine had not been previously investigated. The new study was conducted using [cyclohex) $\oplus$  1-¹⁴ ( spiroxamine only, however as the two ring moieties remained intact and together in all the degradation products observed this is considered sufficient to fully investigate the degradation pathway.





Data Point:	KCA 7.2.2.2/01
Report Author:	
Report Year:	2021
Report Title:	[14C]-spiroxamine: Aerobic mineralisation in surface water - Final interimeter of
Report No:	VC/19/056
Document No:	<u>M-763130-01-1</u>
Guideline(s) followed in	(EU) No. 283/2013
study:	(EC) No. 1107/2009
	$\bigcirc OECD 309 \bigcirc \bigcirc$
Deviations from current	None Q Q Q X L
test guideline:	
Previous evaluation:	No, not previously submitted Q
GLP/Officially recog-	No, not conducted under CLP/Officially recognized testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes y y y y y

#### **Executive Summary**

**1,3 The study was still ongoing at time of dossier submission therefore an interim report has been submitted and summarised. The main delays relate to i) the identification of the component tertatively named desamino-spiroxamine-acid for which an authentic reference standard is being synthesised burnot available yet (once this reference standard is available some elements of the confirmatory analysis in a secondary system will need to be completed, i.e. TLC and MS) if data fegarding chirality are still ongoing. This work will be submitted in the final report for the study (estimate August 2021).

The aerobic mineralisation of [cylonexyl.  $f^{4}C$ ]-opiroxamine was investigated in a "faelagic" test system (natural fresh water) at 20 ± 2°C, for a period of 59 days. The study was carried out using water from Carsington Water, a reservoir that stores water that is purped from the River Derwent. Spiroxamine was dosed at nominal concentrations of 10 and 100 µg/k

Natural water (100 mL) was added to individual 250 mL glass contral flasks immediately after arrival at the test site (approximately 1 day after collection). Each flask was attached to a flow through system with volatile maps attached the water was stirred constantly and treated with the [cyclohexyl-1-¹⁴C] spiroxamine test item. The flask were treated as soon as possible after filling to minimise any decline in biological activity relative to the natural system. The application rates averaged 10.4 and 103.4  $\mu$ g/L. For each of the two test concentrations, duplicate flasks and their associated traps were removed at 0, 3, 7, 14, 21, 30, 45 and 59 days.

The redox potential, pH and dissolved oxygen content of the water in the reference flasks dosed with the non-labelled form of the test item was measured at regular intervals during the incubation. Single sterile control samples were taken for analysis at 29 and 58 days (100  $\mu$ g/L level only).

The positive and solvent control samples showed rapid mineralisation of the [ 14 C]-benzoic acid. The total mean recoveries of radioactivity at the end of the incubation at 59 days were 80.7% and 72.9% AR for the positive and solvent control, respectively. This demonstrated that the level of biological activity in the test system was sufficient. There was mormal degradation seen in the sterile control water phases with spiroxamice accounting for 90.6% AR and 93.2% AR in the day 29 and 58 day samples, respectively.

The overall material balances were good for both test concentrations: 96.7% and 94.5% AR for 10 and 100  $\mu$ g/L respectively. The total radioactivity in volatile traps at 59 days was: 2.9% and 2.7% AR for 10 and 100  $\mu$ g/L, respectively.

At both dose levels mean recoveries of spiroxamine declined rapidly from 94.3 % AR (mean, 10  $\mu$ g/L) and 98.4% AR (mean, 100  $\mu$ g/L) reaching 0.2% AR for the lower dose concentration system at 59 DAT. For the 100  $\mu$ g/L dose level spiroxamine levels decreased from 98.4% AR (mean) (100  $\mu$ g/L) at the start, however, were variable for the remainder of the study with large differences between replicates from the same sampling interval, with this variability resulting in an apparent rise in mean levels at the



last sampling point to 28.4% AR (mean).

The metabolite M03 reached a maximum (mean) value of 38.4% AR on day 21 at the 100 µg/L @se level and similarly reached a mean of 35.6% AR on day 45 at the 10  $\mu$ g/L dose level.

The metabolite M06 reached a maximum of 42.5% AR after 30 days at the 10 mg/L dose level before declining to 28.6% AR by the end of the study. At the 100 µg/L dose level the maximum value of 148% was reached after 59 days.

Mean levels of the despropyl and desethyl acid metabolites M12 and M11 never exceeded 5% AR for the 100 µg/L dose level, but at the 10 µg/L dose level both exceeded 5% AR for the tast two sampling intervals at days 45 and 59.

DT₅₀ and DT₉₀ values for the degradation of spiroxanine in the biotic samples were calculated according to the FOCUS guidance document on degradation kinetics. An input data set was defived from theirdividual data for each time point and each concentration. SFO model was selected as the best fit kinetic in both cases.

1 able CA 7.2.2	2.2-1: Summ	iary of Deg Ks0 and Deg Loo watters
System	Kinetic Model	$DT_{50}$ (days) $DT_{90}$ (days) $\chi^2$ error $\chi^2$ error $\chi^2$ Prob >t
10 µg/L	SFO	1.3 37.6 31.4 6 00.948 402E-07
100 µg/L	SFO	₩3.4 @ @ 44.4 @ 6 23.0 0 0.73 Ø 5.34E-04
	. Q	1. Materians and Methods
A. Materials		1. Materians and Methods

Table CA 7.2.2.1:	Summary of Deg 🖧	and Deg T ₂₀ Walus
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1. Lest ltems
Lavalahawil 1 14 Prair Amir 2 1 2 2 2 2 2 4
Cyclonexyl-1- Cy-spirotanine
Specific Activity. 4.26 MBq/mg (34.4 mCi/mmol, 1,273 MBq/mmol)
Radiochemical Purity: 98,3% (FPLC as determined in study at the time of applica-

#### 2. Test System (water tem

The study was performed using one surface water system as characterised in Table CA 7.2.2.2-2. The study was carried out using water from Carsington Water, a reservoir that stores water that is pumped from the River Derwent. Water was collected by bucket and filtered through 100  $\mu$ m filter into a 20 L

container.



Parameter	Water system
Surface water system designation:	Carsington water
Geographic Location	A 300 ha hectare reservoir that stors water that is pumped from the River Derwent at Ambergate and smaller quantities of water draining off grassland surround the reservoir
City	Carsington Water,
Country	QUK Q Q L
Geographical co-ordinates	SK 24813 49995 Q O
Wa	iter characteristics
pH, at sampling depth	\$ \$ 8.56 \$ \$ \$ \$ \$
Dissolved oxygen concentration, at the time of treatment (mg/L)	
Total organic carbon (ppm)	
Hardness (mg equiv CaCO ₃ /L)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
Nitrate content (mg/L)	V 2 2 2 07 2 07
Phosphorus content (mg/L)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
B. Study Design	

#### Table CA 7.2.2.2-2: Physico-chemical properties of the surface water

#### 1. Experimental Conditions

The aerobic mineralisation of fcyclohexyl-1, C]-spiroxamine was investigated under aerobic conditions in a pelagic surface water system (Carsington water) over operiod of 59 days. [Cylohexyl-1-¹⁴C]spiroxamine was dowed at nominal concentrations of 10 and 100 µg/L.

Natural water (100 mL) was added to individual 250 mL gbss concal flasks immediately after arrival at the test site (approximately 1 day after contection). Each flask was attached to a flow through system with volatile traps attached (KOH and PU foam bang). We water was surred constantly and treated with the [cyclohexyl-1-¹⁴C] spiroxamine test item. The flasks were treated as soon as possible after filling to minimise any decline in biological activity relative to the natural system. The actual application rates averaged 10.4 and 105 4 µg/k.

Sterile test systems were prepared to determine influences on the degradation of the test substance induced by hydrolysis. Therefore, the respective test systems (surface water, test vessels and trap attachments) were sterilized by autoclaving for 39 minutes at 120°C.

Positive control flasks treated with [¹⁴G] benzoic acid at a nominal dose rate of 10  $\mu$ g/L were used as control items to verify that the test water showed a good level of biological activity as it is known to mineralize rapidly increases solven control flasks were treated to show the effects of the addition of organic solvent into the test system.

#### 2. Sampling

Duplicate flacks and their associated traps were removed at each sampling interval. Samples were taken at zero time and following 3, 7, 14, 21, 30, 45 and 59 days incubation. The volatile traping solutions were removed aceach sampling point and analysed.

A series of control fasks were treated and incubated:

- Sterile Controls: Single samples containing sterilised water were treated at the 100  $\mu$ g/L level and incubated under sterile conditions for 29 and 58 days prior to analysis. These controls were used to enable differentiation between biotic and abiotic degradation of the test item.
- Positive Controls: Satisfactory biological activity of the water was demonstrated using flasks



treated with [phenyl-U-¹⁴C]-benzoic acid at a nominal dose rate of 10  $\mu$ g/L. The samples were incubated for 59 days, with their associated traps being changed after 1, 2, 6, 9, 13, 15, 21, 28, 45 and 52 days.

•Solvent controls: The solvent control samples were prepared, incubated and sampled as for the postitive controls. These were additionally dosed with the same volume of organic solvent (5 and actonitrile) as used for the treatment of the spiroxamine dosed flasks.

The redox potential, pH and dissolved oxygen content of the water in the reference flasts doset with the non-labelled form of the test item was measured at regular intervals during the incubation.

#### 3. Analytical Procedures

The analysis of water samples to determine the total radioactivity present was determined LSC. Flask washes were performed on day 45 and day 59 samples (including day 58 sterile and day 59 positive and solvent control flasks) by adding acetonitrile to the conical flasks and agitating. The acetonitrik was decanted and radioactivity analysed by LSC analysis

The 10  $\mu$ g/L water samples were concentrated and analysed by high performance liquid chromatography (HPLC) and the 100  $\mu$ g/L water samples were analysed near by high performance liquid chromatography. Selected samples were also analysed by Liquid Chromatography Mass Spectrometry (LC-MS) to confirm the presence of spiroxamine and the main metabolites

Trap solutions were removed for analysis at each sampling time and activity quantified by LSC. The identity of the radioactivity in the potassium hydroxide traps was characterised by the addition of barium chloride to representative trap samples and LSC analysis. The PU bangs was extracted with acetonitrile and supernatant analysed by LSC.

TT1 1 1 1 1 1		· ~ 1	· el · / 10	are summarised below:
I he key analytical teo	chniques and ed	iuinvanent used	INADIS SURGY	are summary sed below.

LSC Packard TriCate Liquid Scintillation Counters (dpm automatically calculated per quench
HPLC Agilent 1260 infanity HPPC system: X-Bridge Shield C18 250 x 4.6 mm column
HPLC Q Agilent 1260 infinity HPLC system, X-Bridge Shield C18 250 x 4.6 mm column
HPLC Agilen 1260 in the KPCC system; Phenomenex EUX-AMP 150×4.6mm 3µm particles
TLC $\sim$ Merck Silicagel 60 F ₂₅₄ ; (Nextinal phase)
LC-MS Thermo Dexacting Obitrap Mass Spectron Greer
Aleated Dectrospray/Atmospheri Pressure Chemical Ionisation Source (HESI/APcl)

# 4. Determination of degradation kinetics

 $DT_{50}$  and  $DT_{90}$  values for the degradation of spiroxamine. In the natural water were determined following the recommendations of the FOCUS work group, with calculations performed according to the FOCUS guidance document on degradation kinetics. The kinetic evaluations and the statistical calculations were determined using the software package CAKE (v3.3).

The goodness of fit of the estimated data to the measured data was assessed by visual inspection and based on a scaled error, based on a chi-square  $\chi^2$ ) test. The significance of the estimated parameters was also confirmed by a single sided test. A scaled error (chi²Err%) of less than 15% is generally considered a good fit whilst et-test probability of < 0.05 (> 95% parameter significance) is considered sufficiently small.

# A. Data

#### **Results and Discussion**

The oxygen content of the water in the flasks averaged 99.95% saturation (range 98.90% to 100.20%), while the redox potentials relative to the standard silver/silver chloride/4M KCl electrode averaged +250.82 mV (range +215.60 to +271.50 mV). The pH of the water in the reference flasks averaged 8.42 (range 8.33 to 8.55). These results show that the test water remained aerobic and within the environmentally relevant pH range throughout the study.



The distribution and characterisation of radioactivity for each water system incubated at 20°C following application of [cyclohexyl-1-¹⁴C]-spiroxamine are summarised in Table CA 7.2.2.2-3 to Table CA 7.2.2.2-6.

#### Table CA 7.2.2.2-3: Degradation of [cyclohexyl-1-14C]-spiroxamine at 20° Cunder aerobic conditions in Carsington water surface water system – Jow dose (10 µg/L) [mean % AR] R ۵

						A	. Oʻ		9
			]	Incubation	time (DA)			N Q	_
	0	3	7	<b>A</b>	21 🖉	30	_045 ~C	<b>59</b> 0	S.
Water phase	99.5	96.2	94.0	<u>91.5</u>	92.5%	95.9 🖌	\$93.4°	26-0	Š
Flask wash	n.p.	n.p.	n.p. 🧹	Øn.p.	цср.	n.p. "O	1.3	P.4	•
PU bung extract	0.0	0.2	0.2	0.2	0.3	0.30 ⁹	€0	0.9	
Ethylene glycol trap	0.0	0.1	0.1	0.1	> 0.0	0.0	0.2	Q.S.	
2M KOH trap 1	0.7	0.7	<b>Q</b> .7	َکْ 0.7 کُ	0,∜∕	×0.8	₽ 1.0×	×¥⊻ĩ	
2M KOH trap 2	0.5	0.6	Ø.6 🚽	0.6	<b>1</b> .7	Ø 0.6 Ø	<b>Q</b> .7	م 0.7 م	
Total volatiles	1.2	1.6	1.6 🔊	<u>_</u> 166	Q1.7	1.8		Ø 3.0 ×	
Total % AR	100.7	97.7	95.6	~93.1	> 93, <b>9</b> →	<b>\$0</b> .7	📞 97.6 [∾]	97,5	
<b>Overall mean ± SD</b>		Ũ	it is a second s		± 2.6				
n.p.: not performed		R				<del>d d</del>	Ő,	. <u> </u>	

Table CA 7.2.2.2-4: Degradation of [cyclohexyl-1-OC]-spir oxamine at 20°C under aerobic conditions in Carsington Water surface water system high dose (100 µg/L) [mean % AR]  $\sim$ "W Ô

n

Water phase Flask wash PU bung extracy Ethylene glycol trap 2M KOH trap 1 2M KOH trap 2 Total volatiles Total % AR Overall mean ± SD n.p. not performed * Excluding Serile sam	0.0 0.16	3 9424 0.2 0.2	© 94.4 n.p. 0.0	14) 92.4~ n.p. 66	32 32 90.8 90.8 90.8 90.8 90.9 20.9 20.9	time 07 29 Ster- ile 94.9 ngr. 20.0	9124 9124 0.7 0.7	90.1 3.7 1.2 0.2	<b>58</b> <b>ster-</b> <b>ile</b> 89.9 6.0 0.1 0.1	<b>59</b> 88.4 2.2 2.1 0.2
Ethylene glycol tran	\$\cong 0 \cong \co	3 9424 0.2 0.2	7 0 0 0 0 0 0 0 0 0 0 0 0 0	92.4~ 92.4~ n.p.~ ¢.6	32 32 90.8 90.8 90.8 90.8 90.9 20.9 20.9	29 ile ( 94.9 ng. 	9124 9124 0.7 0.7	90.1 3.7 1.2	ster-           ile           89.9           6.0           0.1	88.4 2.2 2.1
Ethylene glycol tran	98 8 n.p. 0.0 0.14	9404 n.p. 0.20 0.0	© 94.4 n.p. 0.0	92.4~ 92.4~ n.p.~ ¢.6	~0.9 ©0.1	20.0 0.0	9124 9124 0.7 0.7	90.1 3.7 1.2	ile 89.9 6.0 0.1	88.4 2.2 2.1
Ethylene glycol tran	98 8 n.p. 0.0 0.14	9404 n.p. 0.20 0.0	© 94.4 n.p. 0.0	92.4~ 92.4~ n.p.~ ¢.6	~0.9 ©0.1	20.0 0.0	9124 9124 0.7 0.7	90.1 3.7 1.2	89.9 6.0 0.1	2.2 2.1
Ethylene glycol tran	0.0 0.16	0.2 0.0	0,30°	86 86	~0.9 ©0.1	20.0 0.0	0.7 0.1	3.7 1.2	6.0 0.1	2.2 2.1
Ethylene glycol tran	0.0 0.16	0.2 0.0	0,30°	86 86	~0.9 ©0.1	20.0 0.0	0.7 0.1	1.2	0.1	2.1
Ethylene glycol tran	0.0	00	00	× 80	~~~0.1	20.0 00/	0.1			
Ethylene glycol trap 2M KOH trap 1 2M KOH trap 2 Total volatiles Total % AR Overall mean ± \$0 n.p. not performed * Excluding Serile som	0.60 .0.1	0.0 0.1 0.4 9078	00	° 0.0 → 0.2 0 4 √	©0.1 0.3©	$0.0^{\circ}$	0.1	0.2	0.1	0.7
2M KOH trap 1 2M KOH trap 2 Total volatiles Total % AR Overall mean ± © n.p. not performed * Excluding Gerile sam	\$0,1 0.1 99.0 \$	Ø.1 0.1 < 0,4 9@*8 ≤	$\frac{0.1}{0.5}$	0.2 0.2 0.4 S	0.3	0.1	0.2			
2M KOLCtrap 2         Total volatiles         Total % AR         Overall mean ± SD         n.p. not performed         * Excluding Serile some	0.1 \$ 0.1 \$ 99.0	0.1 5 0.4 9078 3	0.1	0,4	A S		0.3	0.3	0.2	0.4
Total volatiles Total % AR Overall mean ± §D n.p. not performed * Excluding Serile som	0.1~ 99.0	0,4, 9/21×8 3	0.5		¥.¥	0.1	0.1	0.1	0.1	0.1
Total % AR       Overall mean ± \$0       n.p.     not performed       *     Excluding Serile some	99.0	GØ⊉% \%	<u></u>	°40,8	<u>1.4</u>	∕≫0.2	1.3	1.8	0.3	2.8
Overall mean ± SD n.p. not performed * Excluding Serile som	A	3.8.0 °	≫ <b>9</b> 4.9	≫93.3 _©	[≫] 92.2 [~]	95.1	92.6	95.5	96.1	93.
n.p. not performed * Excludingsperile som			∕ ູ≪		94.S±	<b>2.3%</b> *				
2M KOH trap 1 2M KOH trap 2 Total volatiles Total volatiles Total % AR Overall mean ± SD n.p. not performed * Excluding Serile sam 4 4 5 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7										



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Table CA 7.2.2.2-5: Characterisation of [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions in Carsington water surface water system – low dose (10  $\mu$ g/L). [% AR]

	[0	% AR]							. 4	Ő
<b>a</b> 1	Rep-			I	ncubation	time (DA	(T)		- A	0 [×]
Compound	licate	0	3	7	14	21		45	<u>59</u>	
Spiroxamine	Α	99.0	76.6	54.3	45.3	41.7	4.0	< 0.1	05	
1	В	89.5	78.8	69.8	33.6	39.5	<u>\$</u> 9.4	0.9	<b>39</b> .1	Ô
	Mean	94.3	78.9	63.1	40,1	40.6	×7.0	Ø:4/	°∼°0.2 ~	Į į
M12 (spirox-	Α	< 0.1	< 0.1	< 0.1	<b>S</b> .1	< 0.1 (	2.1	A.S.2	¥ 4.70	_(
amine-despro-	В	< 0.1	< 0.1	< 0.1	<0.1	<0.1	3.0	, © 2.8 🔊	5¥	1
pyl acid)	Mean	<0.1	<0.1	<0.1	<ol> <li>&lt;0.1</li> </ol>	<0,1	2.6	9.0	5.0	$\bigvee$
M11 (spirox-	Α	< 0.1	< 0.1	<0.1	<0.1	<b>Q</b> .1	&° 2.7 ∜	\$.5	⁰ 6.5 L	7
amine-de-	В	< 0.1	< 0.1	<0.20	<0.1 *	≫<0.1 @	1.7 ⁹	N96.0	5,30°	
sethyl acid)	Mean	<0.1	<0.1	<b>≶0.1</b> ́	~0.1 ֊	<0,1 [×]	202	ð 5.7 ×	5,9	
M06 (spirox-	Α	< 0.1	< 0.1	പ്.7 (	6.7	26/0	a) 1.1 a	4,5		
amine-acid)	В	< 0.1	< 0.1	<0.1	5,3	20.3	O 53.8	ðø.3	24.4 °	
	Mean	<0.1	<0.1	0.9	_^6.1 _	23.2	42,5	20.4	28.6	
Desamino-	А	< 0.1	2.3	2,3	a 5.1 L	4,4	°⊗°0	7.3	40.4	
M06*	В	< 0.1	203	\$ 53 \$	3.3%	\$5.9	2.8	5	06.0	
(desamino-spi-				6 42.3 6	s s		2.8		Ò	
roxamine-	Mean	<0.1 🔍	2.3	2.3	<b>4.2</b>	× 5.2	24	6.2 ×	8.2	
acid)		<i>a</i> .				Å	$\sim$			
M05 (spirox-	Α	<0,0	×0.1	0.6	Suit	<i>6</i> 80	3.0 Ö	ġ,a	1.1	
amine-hy-	В	<0 <u>%</u> i (	<0.1	₹¥ <0.£	5.6	¶y 12.3°∧	9.8	<0.1	0.9	
droxy)	Mean	<b>650.1</b> C	) [×] <0.1		4.5	9.2	6A ,	0.4	1.0	
M03** (spirox-	А	`≫<0.1⊴	7.2	37.6	🗡 16.77°°	4.2	∞25.7 ∞	» <u>38.3</u>	30.0	
amine-N-ox-	В ≪	$<00^{\circ}$	<b>6</b> .8	011.18	23,2	×5.0 «	2.6	33.0	37.0	
ide)	Mean	<0.1	≫7.0_@	14.4	×¥9.9	⁰ 4.6 ⁰	[∞] 14.2″	35.6	33.5	
M02 (spirox-	Å	<u>√</u> <0.1, 0	) <0,1		° 3.1 °	6,2	<b>d</b> 0.1	< 0.1	0.8	
amine-despro-	°S™B _ \	[∪] <0.1° ^y	_<0.Ĭ	×0.1 ×	4.05	6.8	<i>∽</i> \$75.4	1.9	< 0.1	
pyl)	Mean	<0.1		@´0.8 ເ ⁽⁾ >	~3,5	6.5	≈ 7.7	0.9	0.4	
M01 (spirox- O	AS ^Y	≪2.3	6.5	7.90	~~6.4 C	ີ 2.1 ©	2.4	<0.1	< 0.1	
amine-de- Ø sethyl)	B	2.4	5,4	÷.9	© 6.1	378	2.6	1.1	< 0.1	
	Mean		<b>6</b> .1	6.6	6.3	<b>Ž</b> .9	2.5	0.5	<0.1	
Unknown	Ą	<0.1	<u>č0.1</u>	$> <0.1^{\circ}$	₹0.1 %	<0.1	<0.1	<0.1	<0.1	
	®″	<u>√</u> 5.7 _	$\sim <0.1^{\circ}$	<u> &lt;0</u> √1	×<0.1 ≈	×0.1	1.2	<0.1	0.3	
	Mean	<u>a</u> 2.9 <i>Q</i> ′	<0,1	≸ <b>0.</b> 1	<u>&lt;0</u>	<0.1	0.6	<0.1	0.2	
Minor metabo-	` A	, <05°	<u>ب</u>	`≪>≤0.1	LS .	0.7	1.2	12.2	8.7	
lites***	BC	\$7,7	×1.0~	<0.1	0.9	< 0.1	2.3	2.8	10.0	
4	Mean	<u>2.9</u>	1.2°	<b>69.1</b>	^{0°} 1.2	0.4	1.7	7.5	9.3	
Total %	A 🧳	101	96.8	≈ 94.2 ≪	92.4	91.2	94.1	93.7	94.2	
	B	97.6	94.6	§ 90,15×	84.6	90.5	95.7	93.0	91.9	
	Mean	<b>99.5</b>	⁹ 94.4	89.2	86.1	89.8	92.9	93.4	93.0	
* Tentative	ID by LC	-XIS continn	ation agai	nst reference	standard per	nding				
** Sum of th	ree region	-XIS continn s exceeding 4.1	w.C	<u>é</u>						
* Tentative Sum of th None ind				~~~						
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Table CA 7.2.2.6: Characterisation of [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions in Carsington water surface water system – high dose (100 μg/L) [% AR]

	['	% AR]										<i>i</i> o <i>i</i> o
					Inc	ubation	time (DA	AT)	<b></b>		6	D'
Compound	Repli ate	0	3	7	14	21	30	29 ster-0	45	58 (* ster-	-59	
	A	98.1	84.2	92.3	84.8	@A	3.1	<b>ilt</b> 90.0	2.6 ^{a)}	93.2 °₅	A Y	Ô
Spiroxamine	В	98.7	87.2	83.5	40.8		15.5	n/a	220	a a		
	Mean	98.4	85.7	87.9	62.8	13.3	ĄJ.	<b>90.0</b> ^{b)}	( <b>1</b> 2.4 ^a )	<u></u>	28.4ª	1
M12 (spirox- amine-	A	<0.1	<0.1	<0.1	Q0.1	<u> </u>	1.5		₹ <u>7.</u> 30	<0 <i>2</i> 5		
despropyl	B	< 0.1	< 0.1	<0.1	√ <0.	<0,1	10	n a	Q.5	n/a	2.4	
acid)	Mean	<0.1	<0.1	<0.1	<b>&lt;64</b> ∿≲0.1	<b>69</b>	<b>P.3</b>	<b>⊗0.1</b> ^{b)} <0.1 №	<b>4.1</b>	<b>∕&lt;0.1</b> ^{b)} <0.€		
M11 (spirox- amine-de-	A B	<0.1	<0.1 <0.1	.≴071 ≪<0.1.″	×<0.1	≥2.1 V<0.1°	1.5	, O`	6.6 0.4		03 .6	-
sethyl acid)	D Mean	<0.1 <0.1	<0.1	<0.1 <0. <b>\$</b>	<0.1 <0.1	1:0/	1.3%	nka ≶0%1 ^{b)}	<b>0</b> .4	<u>∢</u> n/a <b>≪0.1</b> ^{b)}	<b>2.1</b>	
• /	A	<0.1	<0.1 <0.0	<0.x <0.1	~0%1 ~0%4	<b>1:0</b>	<b>8</b> .7	≫0.1 ^b ≈	§ 18.0	<0.1%	15.0	
M06 (spirox-	B	<0.1	s <b>0</b> .1	<0.1	1.0	1.5	×13.7	n/aÔ	8.8	.n/a	14.6	
amine-acid)	Mean	<0.1	<0.1	Q<0.1		4.6	11.2	<( <b>b</b> )	13.4	<0.1 ^{b)}	14.8	
Desamino-	A	<0. k	1.9~	<0.1	0.0	<u>9</u> ,4	<b>JQ</b> _3	<0.1 b	8.9	≪0.1 ^b	2.8	
M06*	В	<0.1	Ł.2	j A	£4.6	10.5	≪9.2 ×	n/a 🗞	5.2	n/a	9.2	
(desamino- spiroxamine- acid)	Mean	°≈0.1		0.7 S	2.64	9.9.9		۵ ۵ _۵	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<0.1 ^{b)}	6.0	
M05 (spirox-	A	<0.0	SQ.¥	<del>6</del> 0.1	S.1	<b>₹</b> 0.7	$O_{2.0}$	₹1.1 °C	3.1	0.1 ^b	1.9	
amine-hy-	B	≰0.1	Ø.1	<b>X</b> 0.1	~<0.1	⅀1.0℗	0.8	n/a Î	0.4	n/a	< 0.1	
droxy)	Mean	Q.1 (	×0.1	<0,∫>	0.6	0.8	b,¥	<b>√</b> (, <b>I</b> ^{b)}	1.7	<b>0.1</b> ^{b)}	0.5	-
M03** (spi-			3.5	~001 ³⁷	1,8	40.0	\$3.9	≪0.1 ^b	35.8	1.0 ^b	5.2	
roxamine-N-O	4/12	0.9	2.4	4/.8	Ø <b>2</b> 8.1	≫36.7 ¢	28.2	n/a	36.2	n/a	46.2	-
oxide) 👸	Mean	0.1	3.2	<b>≜</b> 2.4 ∼	<u>×14.70</u>		36,1	<0.1 ^{b)}	36.0	<b>1.0</b> ^{b)}	25.2	
M02 (spirøx-	A	<0.1	1.1		1,4,		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.4 ^b	2.3	0.4 ^b	1.7	-
amone-	B, Ø	<0.0)	0.7	19	<u> </u>	×8.4 ×	8.6	n/a	7.3	n/a	3.2	
despropyl)	Mean	<b>&lt;0.1</b>	<b>0:9</b>	<b>00.4</b>	<b>3.9</b>	<mark>ي 7.4</mark> اً 1¢&	<b>7.9</b> 3.4	<b>0.4</b> ^{b)} 0.7 ^b	4.8	<b>0.4</b> ^{b)}	<b>3.0</b> <0.1	-
M04 (spirox-	B	<u>₄&lt;0.1</u> ≥<0.1	<u>~0.1</u> <0.10	<u>~0.8</u> <0.1	r 0.7⊚ 1¢5∕	130, 4,2	<u> </u>	0.7° n/a	1.1 2.3	0.9 ^b n/a	<0.1	-
amine-)	Mean	<0.1	<0.10 ≪0,1	~0.3. @Q4	$\mathbb{Q}$	3.1 ²	<b>2.6</b>	0.7 ^{b)}	2.5	0.9 b)	5.5 1.6	-
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	TVICAIP	<u>~0</u>					2.0	0./ /	2.2	0.7 /	1.0	J



					Inc	ubation	time (DA	AT)			
Compound	Repli ate	0	3	7	14	21	30	29 ster- ile	45	58 ster- ile	, and a second
M01 (spirox-	А	0.6	3.0	1.5	2.6	5.7	3.8	2.7 ^b	≫≶0.1	1.9 ^b	₽2.7 <u>,</u>
amine-de-	В	< 0.1	3.0	2.6	8.6	7.0	5.4	n/a 🔏	\$ 6.6	n/a	1,200
sethyl)	Mean	0.3	3.0	1.3	4.3	6.4	4.6	2.7 b) [©]	3.3	1,2 ^{b)}	20
Minor metab-	Α	< 0.1	<0.1	< 0.1	< 0.1	5.8	6.3	<0, b	8.8	0 .1	4.5
olites***	В	< 0.1	< 0.1	< 0.1	0.8	A2	5.0	∠n/a	2.9 🦼	^> n/a ^>	v 5.9
ontes	Mean	0.3	<0.1	0.8	1.7	₹5.0	5.7	©≮0.1 ^{b)}	5.4°	0.2	5.
	А	98.7	94.2	94.6	92.7		91.0	94.9 ^b	97,5 O	905.1 b	O ^a)
Total % AR	В	99.0	94.7	94.3	20:2	90.6		yn/a ≪	97.5 ¢	n/æ	92. 1
	Mean	98.8	94.4	93.8 候	, 92.4 ô	° 90.85	" 91,4 <i>"</i>	94,96)	97(3 ^{a)}	95,1 ^{b)}	92.7 ^{a)}

b) Sterile sample, no duplicate sample collected

Not applicable n/a

Tentative ID by LC-MS confirmation against reference standard pend

** Sum of three regions

None indivi dually exceeding 3.0

B. Material Balance

The overall material balances were 96.7% and 94.5% for the 10 (ange 99.1 to 80.7%) and 100 µg/L (range 92.2 to 99.0%) samples, respectively. The sterile control samples yielded a mean recovery of 95.1% and 96.1% AR at day 29 and day 58, respectively. The positive and solvent control samples showed a mean recovery of 76.8% AR after work up at day 59.

C. Mineralisation

Mineralisation to CO2 was low in piroxamine treated samples from both dose levels (1.7 and 0.5% ARmaximum at the 19 and 100 µgd levels, respectively Formation of volative organic compounds (VOC) was insignificated as demonstrated by value of $\leq 0.3\%$ AR at all sampling intervals for both concentrations in degradation fest systems as well as in sterfle test system. An additional small amount of volatile radioactivity (maximum 1, 0 and 2.1% AR for the 10 and 100 µg/L jevels, respectively) was recovered in the PK bungs (assumed related to parent spiroxarsine),

Rapid mineralisation in the positive control flasks (treated with ¹⁴C-benzoic acid) demonstrated that the test water had acceptable levels of biological activity for the test.

D. Degradation of Parent Compound

For both test-item dose levels and all interval are visit majority of the activity was recovered in the water phase with 88.4% AR (mean) being the lowest proportion recovered in the water phase.

At both dose levels mean recoveries of spire amine declined rapidly from 94.3 % AR (mean) (10 µg/L) and 28.4% AR (mean) (100 µg/L feaching 0.2% AR for the lower dose concentration system. For the 100 µg/L dose level spiroxamine levels decreased from 98.4% AR (mean) (100 µg/L) at the start, however, were variable for the romainder of the study with large differences between replicates from the same sampling interval, with this variability resulting in an apparent rise in mean levels at the last sampling point to 28,4% ARQ meany As this is only an interim report, clarity may be provided once the study reaches termination.

The netabolic MO2 reached a maximum (mean, n=2) value of 38.4% AR on day 21 at the 100 μ g/L dose Vevel and similarly reached a mean of 35.6% AR on day 45 at the 10 µg/L dose level.

The metabolite M06 reached a maximum of 42.5% AR after 30 days at the 10 µg/L dose level before declining to 28.6% AR by the end of the study. At the 100 μ g/L dose level the maximum value of 14.8% was reached after 59 days.



Mean levels of the despropyl and desethyl acid degradates M12 and M11 never exceeded 5% AR for the 100 μ g/L dose level, but at the 10 μ g/L dose level both exceeded 5% AR for the last two sampling intervals at days 45 and 59.

There was minimal degradation seen in the sterile control water phases with spirexamine accounting for 90.0% AR and 93.2% AR in the day 29 and 58 day samples, respectively.

**3 Additional work is being conducted on the confirmatory analysis (including synthesis of a authentic reference standard to support the tentative identity of the desamino-spiroxamine-acid component; TI confirmation in a secondary analytical system and MS confirmation).

E. Degradation Kinetics

The results of the kinetic fitting are summarised Table CA 7.2.22-1. For both dose devels, the SFC model gave a good fit for the data, with good r-softare and chi-square@alues and a low prop >t. values of 11.5 and 13.4 days were determined for the low and high dose-level, respectively

F. Isomers of Parent Compound

**1 Additional work is currently being conducted on the chiral analysis of the samples for parent spooxamine. This work will be submitted in the final report for the study (currently coport included is an interim report).

The aerobic mineralisation of [c@lohex\$4-1-14CP-spirg&amin@w elagic" test system (natural fresh water) at $20 \pm 2\%$ for a period of 59 days.

Conclusions

Mineralisation to CO₂ was now from both dose levels.

Spiroxamine was degraded extensively. At the lower concentration, spiroxamine was degraded with a DT₅₀ value or 11.5 days (SFO) and comprised 15% after DAT 45. Af the higher concentration, there was a lag phase to the degradation and more variation observed between replicates (average levels ranged between 9.9° and 28.4% AR over the period 24 to 59 days.

The metabolite M03 reached a maxm (mean m=2) (alue of 8.4% ÅR on day 21 at the 100 μ g/L dose level and similarly reached a mean of 35,6% AR on day 45 at the 10 µg/L dose level. The metabolite M06 zeached a maximum of 42.5% AR after 30 days afthe 10 ug/L dose level before declining to 28.6% AR by the end of the stody. At the 100 µg/L dose level the maximum value of 14.8% was reached after 59 days. Mean levels of the despropy and desethyl acid metabolites M12 and M11 never exceeded 5% AR for the 100 ag/L dose level, but at the 10 µg/L dose level both exceeded 5% AR for the last two sampling intervals at days 45 and 59 @

DT₅₀ values of 11.3 and 13 days were determined for the low and high dose-level, respectively using SFO kinetics.

Very little hydrolysis was observed in the sterile samples (>90% spiroxamine after DAT 59, most prominent degradation product was metabolite M01 (spiroxamine-desethyl, max 1.8% AR)). \sim

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Assessment and conclusion by applicant.

Study meets the current guidance and the requirements in 283/2013.

The study was conducted to Study guideline(s) OECD 309 (required guideline). The study is considered valid to assess the aerobic mineralisation of [cyclohexyl-1-14C]-spiroxamine in surface water.

à CA 7.2.23 Water/sediment study

Use of plant protection products containing the active substance spiroxamine may result in contact with aquatic systems, therefore the fate and behaviour of the active substance in water/sediment systems has been investigated in laboratory studies according to the data requirements laid down in EC Regulation



283/2013.

The fate and behaviour of the active substance in water/sediment systems was investigated in six studies (KCA 7.2.2.3/01 to KCA 7.2.2.3/06) which were evaluated during the previous EU review. In addition, two new studies are available for renewal, (KCA 7.2.2.3/07) conducted to address the new data equirement since the previous evaluation and also to address the new requirements of OFSA, 2019¹ and (KOA 7.2.2.3/08) has been conducted to provide an up-to-date kinetic assessment of degradation rates observed in all water/sediment studies to modern requirements (FOCUS 2014).

Sub- stance	Report refer- ence	Document no.	Test material used	Comment of S
Spirox- amine	KCA 7.2.2.3/01	<u>M-006015-01-1</u>	[cocclohexyl-1-	
M03 (spirox- amine-N- oxide)	KCA 7.2.2.3/02	<u>M-006094-01-1</u>	[cyclohexyl-] ¹⁴ Clespiroxanine ¹⁴ Clespiroxanine ²	The second and accepted to the second
M03 (spirox- amine-N- oxide)	KCA 7.2.2.3/03	M-032872-01-1		
Spirox- amine	KCA 7.2.2.3/04	M-903324-01-1 C	[1,3 @roxolane-4-	Submitted for the strength of spi-
Spirox- amine	KCA 7.2.2.3/05 🔏		n.a. K	UB Considered valid and accepta-
Spirox- amine	KCA 7.2.2.3	<u></u>	[Sclohex91-1-	J J Je.
Spirox- amine	KCA 7 2.3/07	<u>M. 063128@1-1</u> (interim rpt)	[cyclohexyl-1- ¹⁴ Coppiroxemine	Rew data not yet reviewed under
Spirox- amine	KC@ 7.2.2.3/08	<u>M-763141-01≯</u>		

The fate and behaviour of the active substance spiroxamine in water/sediment systems has been investigated in a total of sit/systems. Previously evaluated studies have been conducted using both [cyclohexyl-1-¹⁴C]-spiroxamine and [1,3-dioxorane-4,¹⁴C]-spiroxamine and show a consistent degradation pathway for the division of the studies and very little to no separation of the two possible radiolabelling positions, therefore the new water/sediment study was sufficiently conducted using [cyclohexyl-1-¹⁴C]spiroxamine-and very little to no separation of the two possible radiolabelling positions, therefore the new water/sediment study was sufficiently conducted using [cyclohexyl-1-¹⁴C]-

pathway for the daration of the studies and very little to no separation of the two possible radiolabelling positions, therefore the new water/sedfment study was sufficiently conducted using [cyclohexyl-1-¹⁴C]-spiroxamine-only.



New studies, not previously evaluated

Data Point:	KCA 7.2.2.3/07
Report Author:	
Report Year:	
Report Title:	[14C]-spiroxamine: Route and rate of degradation in aquatic sediment systems under aerobic conditions at 20°C - Interim report
Report No:	VC/19/057
Document No:	<u>M-763128-01-1</u>
Guideline(s) followed in study:	Commission Regulation (EU) No. 283/2013 in accordance with Regulation (CC) No. 1107/2009 OECD 308
Deviations from current test guideline:	$\begin{array}{c c} \hline OLCD 508 & & & & & & & & & & & & & & & & & & &$
Previous evaluation:	No, not previously submitted a star of the
GLP/Officially recog-	Yes, conducted under GDP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes Q Q Q Q Q Q Q Q Q Q

Executive Summary

The route and rate of degradation of spiroxamine was investigated in two different water/sediment systems (Calwich Abbey, silt loam; Emperor Lake, sandy loam both from the United Ringdom) under laboratory aerobic conditions at 20°C. The lest system was designed to provide a laboratory representation of a "worst case" scenario resulting from direct overspray or fun-off of the test substance into a stationary body of water. Cylindrical metabolism flasks of 6° cm inner diameter were filled with a layer of sediment to a depth of 3 cm (50° dry weight minimum) and overlying water (*ca.* 225 to 250 ml) added to a depth of 2° cm above the sediment surface giving cratio of approximately 1:4 v/v.

[Cyclohexyl-1- $\frac{1}{10}$]-spiroxamine (radiochemical purity 99.6%) was applied to the surface of the water overlying sedment at a target rate of 84.8 kg of a 5 per flask, which was equivalent to a field application rate of 750 g/ha (assuming a water body depth of 30 cm).

Humidified air was passed through each treated flask continuously to maintain aerobic conditions (the air inlet tube in each task was just under the water layer surface). Effluent gas was then passed through traps containing etholene glycol and aqueous potassium hydroxide for the collection of volatile organic components and carbon dioxide respectively. A further trap consisting of a polyurethane foam bung, was placed in the head of the vessels

Duplicate treated samples of each water sediment system were removed for analysis after 0, 1, 3, 7, 14, 30, 42, 62, 46 and 100 days of incubation.

Overlying water was carefully decanted into a grass vessel containing appropriate amounts of acetonitrile, and the remaining sediment was transferred to a suitable container for extraction by rinsing with portions of the extraction solvent. Sediment samples were extracted four times at room temperature with acetonitrile/water/35% ammonia solution 8020/1 v/v/v.

The overall recoveries of applied radioactivity ranged from 92.7 to 103.0% AR for the two test systems. The overall mean material balance was 97.1 and 99.5% AR for the Calwich Abbey and Emperor Lake water/sectiment systems, respectively.

The thean proportion of total radioactivity extracted from sediment samples and in the overlying water declined slowly over time from 100.9% AR at 0 DAT to 78.1% at 100 DAT in the Calwich Abbey system. The Emperor Lake system declined similarly, from 100.1% at 0 DAT to 79.5% at 100 DAT. Unextracted residues (bound residues) increased slowly throughout the incubation, reaching maximum levels of 10.7% AR in Calwich Abbey at 100 DAT and 12.4% AR in Emperor Lake at 76 DAT.



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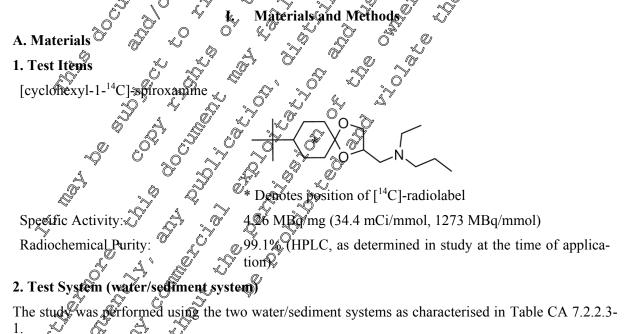
Significant radioactivity was detected in the PU bungs in both systems from 30 DAT, reaching maximum levels of 9.5% AR in Calwich Abbey at 30 DAT and 5.6% AR in Emperor Lake by 100 DAT. Subsequently, selected samples of PU bung extracts from both systems were analysed by HPLC and the volatile radioactivity was confirmed to be volatile ¹⁴C-spiroxamine. The level of applied radioactivity recovered in the volatile traps was $\leq 4.9\%$ AR for both water/sediment systems over all sampling intervals and was detected in the KOH trap and was assumed to be carbon dipxide (not confirmed as <5% AR).

Following application of [cyclohexyl-1-¹⁴C]-spiroxamine spiroxamine showed rapid dissipation in the water phase of both systems, declining from 79.9 - 83.9% AR (mean of duplicate samples) at 0 DA to <1.0% by 76 DAT. In the Calwich Abbey system, the amount of spiroxamine in the sediment increased \bigcirc to 45.4% AR after 7 DAT and subsequently decreased to 30.0% AR after 100 DAT. In the Emperature Lake system, the amount of spiroxamine in the sediment increased to 69.2% AR after 42 DAT and subsequently decreased to 58.6% AR after 100 DAT.

Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine was accompanied by the formation of one major degradation product M06 (spiroxamine-acid: max 44.5% AR at 2 DAO) and several other minor metabolites M01 (spiroxamine-desethyl: max 4.3% AR at 100 DA1), M02 (spiroxamine-despropyl: max 3.2% AR at 30 DAT), M03 (spiroxamine-N-oxide: max 2.3% &R at 7 DAT) M11 (spiroxamine-desethyl acid: max 3.3% AR at 76 DAT) and M12 (spiroxamine-despropyl acid: max 3.0% AR at 62 DAT). Some other minor unidentified metabolites were observed but none of which exceeded a total of 3.0% AR at any sampling interval.

 DT_{50} values for the degradation of spiroxamine were calculated in the report, however, a re-evaluation of the degradation kinetics in accordance with FOCUS guidance focument on degradation kinetics (FO-CUS 2014), was performed in the performed under point KCA \mathcal{F} 2.2.2.48 (<u>Mc763141-01-1</u>).

Additional work is currently being conducted on the chiral analysis of the samples for parent spiroxamine. This work will be submitted in the final report for the study currentity report included is an interim report) and will be supplied as part of a top up dbmission (estimate August 2021).





Parameter	Water/sedin	ment system
Water/sediment system designation:	Calwich Abbey	Emperor Lake
Geographic Location		
City	Calwich, Staffordshire ^A	Chatsworth, C Derbyskipe ^
Country	UK x	
Sedir	ment characteristics	Sandy koam ⁷² ⁷² ⁷² ⁷² ⁷² ⁷² ⁷²
Textural Classification (USDA)	Silt loam	Sandy war a
Sand [50 - 2000 µm] (%)	20 Q	
Silt $[2 - 50 \ \mu m]$ (%)		
Clay [< 2 μ m] (%)	& <u>6 9 5 5</u>	Sandy boam 72 0 72 0 71 0 72 0
pH	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
in H2O (1:1)	, @ , Ø.2 Q , O	05.2 Å
in 0.01M CaCl2 (1:1)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	30° 4.9° 50°
Organic Matter (%)*	× × 8.44 × ×	
Organic Carbon (%)	· ~~ ~~ ~~ ~~ ~~ ~~~~~~~~~~~~~~~~~~~~~	5 S1.8 Q
Cation Exchange Capacity (meq/100g)	6 7 10.5 °	6.7
Cation Exchange Capacity (meq/100g) Sediment moisture content (w/w @)	T & 18005 &	5 5 5 5 5 5 5 5 5 5
Soil Microbial Biomass (mg or C/100 g sedi ment)		
Initial, DAT 0	2 ³ 0 ⁴ 759 ⁴ ¹	^م رج 15.4
Final, 100 DAT 120 😓 🖉 🦉	<u>34.1</u> <u>y</u> <u>k</u>	17.7
	ter characteristics	
pH, at the time of the atment		7.5
Dissolved oxygen concentration, at the time of treatment (mgP)	5.5 5 5 3.0 0	4.7
		6.7
$U_{1} = 1$		33
Nitrate content (mg/L)	2.5 ×	0.6
Phosphorus content (mg/L)	0 12	1.7

Table CA 7.2.2.3-1:	Physico-chemical	properties of the water	sediment systems
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* Calculated by multiplying organic orbon clottent by J.724 (for reported)

A Location krown free of pesticide use for at leas 5 yrs and used within 17 days from sampling.

The test soils were handled in accordance with SO 5667-12 and 5667-15 prior to use.

B. Study Design

1. Experimental Conditions

The behaviour of [cyclohexyl; ¹⁴C] opiroxamine was investigated in two contrasting sediment water systems ('Calvich Abbey' and 'Emperor Lake') over a period of 100 days.

The test system was designed to provide a laboratory representation of a "worst case" scenario resulting from direct overspray of run-off of the test substance into a stationary body of water and then subjected to aerobic conditions. Tests were performed in flow through systems consisting of glass vessels (500 fbL, *cab* cm internal diameter) each containing a sediment layer (3 cm depth) and an overlying water layer (12 cm) i.e. a water to sediment ratio of 4:1 v/v and attached to an ethylene glycol trap to collect organic volatiles followed by two potassium hydroxide traps (2M) to collect carbon dioxide. A further trap consisting of a polyurethane foam bung, was placed in the head of the vessels.

Water/sediment system samples were pre-acclimatised to the incubation conditions (dark, 20°C) for 8-10 days before application of the test substance (within 17 days of sampling).



[Cyclohexyl-1-¹⁴C]-spiroxamine was applied to the surface of the water overlying sediment at a target rate of 84.8 μ g of a.s. per flask (in a small volume of solvent), which was equivalent to a field application rate of 750 g/ha (assuming a water body depth of 30 cm).

Additional samples for each soil were treated with an equivalent amount of blank solvent only to pointor microbial activity at the beginning and end of the incubation period.

Additionally sediment extracts and surface water samples were separately analysed using a chiral HPLC method. This work is currently on going and will be submitted in the final coport for the study (currently report is interim) as soon as possible

2. Sampling

Duplicate samples for each water/sediment system were removed for analysis after 0, 1, 3, 7, 14, 30, 42, 62, 76 and 100 days of incubation. Untreated samples were analysed for biomass at the beginning and end of the experiment.

3. Analytical Procedures

Overlying water was carefully decanted into a glass vessel containing appropriate amounts of accionitrile, and the remaining sediment was transferred to a suitable container for extraction by rinsing with portions of the extraction solvent. Sediment samples were extracted four times at room temperature with acetonitrile/water/35% ammonia solution 80/20/1 v/v/v, by addition of solvent, vigorous, mechanical shaking and centrifugation. Radioactivity in extracts was determined by liquid scintillation counting (LSC). Aqueous samples and combined sediment extracts was determined by liquid scintillation counting (exceptions were some 1 and 3 DAT sediment samples containing low amounts of fadioactivity) by direct injection by reverse phase HPLC with radio-detection. Degradation products were identified by comparison of the retention times of reference standards. The LOD/LOD of the HPLC method was estimated to be 0.28/0.90% AR. Confirmators analysis using an atternative technique was conducted by TLC with co-chromatography against reference items on selected samples.

Volatile radioactivity in volatile traps was quantified by ESC. Any radioactivity in the polyurethane foam bung was extracted using acconitric and quantified by ESC. Carbon dioxide in the potassium hydroxide traps was not confirmed as <5% AR

Following homogenisation, non extractable residues (NERS in extracted sediments were determined by combustion.

4. Determination of degradation kinefics

The degradation kinetics of data within this report are subject of a separate modelling study. DT_{50} and DT_{90} values for the degradation of spiroxamine and its metabolites have been re-calculated from the reported data following the recommendations of the ROCUS work group (FOCUS 2014²). Full details are provided in the report under point KCA $\frac{7}{2}$.2.3.08 (M-763141-01-1).

J. Results and Discussion

A. Data

The distribution of radioactivity for each water/sediment system incubated at 20°C following application of [cyclohexel-1-14] -spire amine are summarised (as overall means) in Table CA 7.2.2.3-2 and Table CA 7.2.2.3-3.

The characterisation of radioactivity for each water/sediment are summarised (as overall means) in Table CA 7.2, 23-4 and Table CA 7.2.2.3-8. The characterisation of radioactivity for each separate layer for each water/sediment are summarised (as individual replicates) in Table CA 7.2.2.3-5 to Table CA 7.2.2.3 For the Calwich Abbey system and in Table CA 7.2.2.3-9to Table CA 7.2.2.3-11 for the Emperor Lake system.



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Table CA 7.2.2.3-2: Recovery and distribution of radioactivity following treatment of Calwich Abbey system with [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic . conditions [mean % AR]

			, ,	1					
Compound				Inc	cubation	time (DA	(T)		
Compound	0	1	3	7	14	30	42	<i>~</i> 62	76 100
Overlying water	83.9	86.9	83.8	48.5	44.8	42.1	32.4	@26.6	30.9 27,8
Sediment extract	17.1	11.3	15.7	46.9	47.2	37.6	48.0	52.0	50 .2 \$0 .3
(sub-total)	100.9	98.2	99.6	95.3	92	79.7	80.4	78.6	81.1 78.1
PU bung*	n.a.	n.a.	n.a.	1.0	1.	9.5	Ø.2	6.0 (3.2 4,0
Volatile traps**	n/a	n.d.	n.d.	n.d.	n.d.	0.4	s≫1.5	3.6 [©]	49 07
Non-extractable radioactivity	0.4	0.4	0.5	2.5	3.9	3.7Q	6.5	AS .	8.6 0 10.7
Total AR	101.4	98.6	100.0	98.&	97.8	93 ⁄.2	92.7	95.7	97,7 252

n.a.: not analysed, n.d.: not detected, DAT: days after treatment

n.a.: not analysed, n.d.: not detected, DAT: days after treatment a solution of the second se Overall total recovery = 97.1% AR

All values expressed as mean percentage of applied radioactivity (% AR)

Table CA 7.2.2.3-3: Recovery and distribution of radioactivity following treatment of Emperor Lake system ofth [cyclohess/l-1-14C]-spiroxamine at 20°C under aerobic conditions [mean % AR]

	con	annons	V 0	<i>C</i>	Ű,	S d	0 _0	Û,	°	
Compound		Q	Å,	The The	abation		(T) (T)	ð	K	
Compound	0			⊘ 7	° 14 🕅	30 ⁰ ×	⊘ @302	<u>62</u>	O´76	100
Overlying water	79.9	88.0	≶∕97.6	47 8	3600	23.4 🗋	م\$15.1 %	25.76	9.8	9.0
Sediment extract	20.3 %	11.9	4.6	46.3	£56.5	⊗61.9 ≪) 73 <u>.</u> 29	60.4	75.9	70.5
(sub-total)	100,2	9959	192.3	694.2 ≫	©92.4 Ô	× 87¢4	88.3	86.1	85.7	79.5
PU bung*	n (a/	ða.	≪n.a	0.2	1,2,7	200	2.0	4.8 ⁴	2.2	5.6
Volatile traps**	"Ma	🕻 n.d. 👌	n.d	0.1	Q)Ĭ	@0.4	0.8	^v 0.8	2.7	2.1
Non-extractable radioactivity		1.	\$0.0 \$	A.2	>>> 5.2 √	<u>s</u>	Ţ.S	6.4	12.4	10.1
Total AR	1007.1	Q 0.9	Q _{02.3} %	98.6	920	\$ \$.8	@99.0	98.0	103.0	97.3

n.a.: not analyzed, n.d.: not detected, DAD: days after treatment * shown to comprise parent spuroxamine. ** radioactivity associated with first carbon dioxide trap

Overall total recovery = 99 5% AR All values expressed as mean percentage of applied radioactivity (% AR) \$

R 4: Characterisation of radioactivity following treatment of Calwich Abbey Table CA 7.2.2.3 system with [cyclobexyl-1 C]-spiroxamine at 20°C under aerobic condi-Utions mean % ARY - Overview of means

*) <u>~</u> ~			- @					
Composit			Š		No Inc	ubation	time (DA	(T)			
Compound		A A	-Q.	3	<u>مَ</u> 7	/ 14	30	42	62	76	100
Total ,	w	\$ \$3.9	A86.9	× 83.9	48.5	44.8	42.1	32.4	26.6	30.9	27.8
- AN	S	17.0	v 11. 3 ≫	15Q	26.8	47.2	37.6	48.0	52.0	50.1	50.3
Spirox-	W.,	× 83.9	85,6	81.8	£ 39.5	11.1	12.8	0.4	0.5	0.2	n.d.
amine	Š	17.0	Ø1.3	S15.7 🖉	₿ 45.4	42.6	28.8	29.6	36.5	31.7	30.0
M01	Ŵ	n.d.	0.3	0.3	0.6	0.2	0.9	n.d.	n.d.	n.d.	n.d.
(desethyl)	S	💭 n.d. 💭	n.d.	n. Q .	1.4	1.0	0.6	1.3	2.5	2.2	2.4
M02	Ŵ	n.d.	ØÅ	0.3	0.6	0.5	1.1	n.d.	0.1	n.d.	n.d.
(despropyl)	Š	n.d.	A .d.	n.d.	n.d.	1.5	1.6	0.4	1.6	1.2	1.8
MOSY 🖉	w	Shid Sa	nd	0.6	0.8	0.2	n.d.	n.d.	n.d.	n.d.	n.d.
(kydroxy)	S	n.d.	n.d.	n.d.	n.d.	0.5	n.d.	n.d.	n.d.	n.d.	n.d.
M03 ©	w	n.d.	0.1	n.d.	2.3	0.7	1.4	n.d.	n.d.	n.d.	0.2
(N-oxide)	s	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M06	w	n.d.	n.d.	0.1	3.1	26.5	21.9	28.2	21.2	27.0	23.8
(acid)	S	n.d.	n.d.	n.d.	n.d.	0.9	6.5	16.3	9.9	13.2	16.0



Compound					Ind	cubation	time (DA	T)			
Compound		0	1	3	7	14	30	42	62	76	100 °
M11 (des-	W	n.d.	n.d.	n.d.	n.d.	1.2	0.6	1.2	1.6	1.5	jan.d.
ethyl acid)	S	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1.8	And.
M12 (des-	W	n.d.	n.d.	n.d.	n.d.	0.5	0.7	1.3	?}€	1.3	1.4
Propyl acid)	s	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.5	S1.4	n.d.🗳	
Other	W	n.d.	0.4	0.7	1.6	3.9	2.7	1.3	1.6	1,0,	Å Å
unknowns	S	n.d.	n.d.	n.d.	n.d.	0.7	n.d.	n.d.	n.d.	<u>_</u> d	6n.d.

n.d.: not detected, DAT: days after treatment

All values expressed as mean percentage of applied radioactivity (%

Table CA 7.2.2.3-5: Characterisation of radioaction for adioaction for the formation of the comparison system with [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions – water system [% AR] ~ (M)

Compound Replicate 0 1 3 7 14 30 42 62 76 100 A 82.6 76.3 72.1 42.6 39.1 45.2 34.4 29.6 32.9 32.7 Total B 85.3 97.5 95.6 54.4 50.5 34.0 30.7 25.5 29.0 \$22.9 Mean 83.9 86.9 83.9 48.5 44.8 42.1 32.4 26.6 30.9 27.8 Spirox- amine A 82.6 75.1 70.1 36.4 20.8 24.8 0.3 n.d. n.d. M01 Mean 83.9 85.6 85.8 39.5 52.1 42.6 1.4 0.8 0.3 n.d.
A 82.6 76.3 72.1 42.6 39.1 45.2 34.4 29.6 32.9 32.7 B 85.3 97.5 95.6 54.4 50.5 35.0 80.7 25.5 29.0 22.9 Mean 83.9 86.9 48.5 44.8 42.1 32.4 26.6 30.9 27.8 Spirox- amine A 82.6 75.1 77.1 36.4 20.8 24.8 0.3 n.d. 0.3 n.d. M01 B 85.3 96.1 93.6 42.6 1.4 0.8 0.3 n.d.
Total B 85.3 97.5 95.6 54.4 50.5 39.0 80.7 25.5 29.0 22.9 Mean 83.9 86.9 85.9 85.9 48.5 44.8 42.1 32.4 26.6 30.9 27.8 Spirox- amine A 82.6 75.1 70.1 36.4 20.8 24.8 0.3 n.d. 0.3 n.d. Mean 83.9 85.3 96.1 93.6 42.6 1.4 0.8 0.5 0.5 n.d. n.d. 0.3 n.d. 0.3 n.d. 0.3 n.d. n.d. 0.3 n.d.
Mean 83.9 86.9 83.9 48.5 44.8 42.1 32.4 26.6 30.9 27.8 Spirox- amine A 82.6 75.1 70.1 36.4 20.8 24.8 0.3 n.d. 0.8 n.d. B 85.3 96.1 93.6 42.6 1.4 0.8 0.3 n.d. 0.8 n.d. n.d. Mean 83.9 85.6 81.8 39.5 34.1 42.8 0.4 0.5 0.5 n.d.
A 82.6 75.1 70.1 36.4 20.8 24.8 0.3 n.d 0.3 n.d. n.d.<
B 85.3 96.1 93.6 42.6 1.4 0.8 0.5 0.5 n.d. n.d. </td
B 85.3 96.1 93.6 42.6 1.4 0.8 0.5 0.5 n.d. n.d. </td
Mean 83.9 85.6 84.8 39.5 32.1 42.8 0.4 00.5 0.5 n.d. M01 A 9.3 0.3 0.5 0.5 1.6 n.d.
M01 B n.d. (, 0.3) 0.3 (, 0.7) n.d. (, 0.2) n.d. (, n.d. (n.d.
B n.d. () 0.3 0.3 0.4 n.d. () n.d. () </td
Mean n.d 0.3 0.3 0.6 0.2 0.9 n.d. n.d.<
M02 (despropyl) A ndd. 0.5 0.3 0.6 0.9 2.3 n.d. 0.0 n.d. <
(despropyl) B n.d. 0.3 0.3 0.8 n.d. n.d. <t< td=""></t<>
M05 A n.d. n.d
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $
Meann.dn.d 0.3 ↓ 0.8 → 0.2 ≤ n.d. n.d. n.d. n.d. n.d. n.d.
M_{02} $(A = 1.0) H_{02}$ H_{02} H_{02} H_{02} H_{03}
$\begin{array}{c c c c c c c c c c c c c c c c c c c $
$\ x \ _{\infty} = \ x \ _{\infty} \ $
M06 n.d. n.d. 0.2 2.1 13.2 8.8 29.6 24.9 28.6 28.5
(acid) $B = 1.07 II.07 II.0$
(acid) @ Mean and and
M11 (des-
$\begin{array}{c c c c c c c c c c c c c c c c c c c $
\square Miean Niean Niew, Bud. Rad. 1.2 0.6 1.2 1.6 1.5 1.1
M12 (des- M12 (d
¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬¬
Mean rad n.d n.d n.d. 0.5 0.7 1.3 1.6 1.3 1.4
Other A C A. 0.3 0.6 1.3 2.3 4.2 1.3 1.5 1.0 1.4
$B_{\text{min}} = B_{\text{min}} = B_{\text{min}} = 0.5 + 0.5 + 0.7 + 1.8 + 5.5 + 1.2 + 1.3 + 1.7 + 0.9 + 1.1 + 0.9 + 1.1 + 0.9 + 0.9 + 0.1 + 0.9 + 0$
unknowns Alean n.d. 0.4 0.7 1.6 3.9 2.7 1.3 1.6 1.0 1.2

n.d.: not detected, DAC days after treatment



Table CA 7.2.2.3-6:	Characterisation of radioactivity following treatment of Calwich Al	bbey
	system with [cyclohexyl-1- ¹⁴ C]-spiroxamine at 20°C under aerobic of	condi- •
	tions – Sediment system [% AR]	

Compound	Replicate				Inc	ubation	time (D	AT) 🤌		(Ôn' '
Compound	Replicate	0	1	3	7	14	30	42	62	76 [©]	100
	А	17.1	18.4	26.7	52.0	53.5	31.2	46.9	52.0	52.7	49.4
Total	В	17.0	4.3	4.7	41.7	40.9	43.9	49.4	52.0	∂ ¥7.6	\$1.2
	Mean	17.0	11.3	15.7	46.8	47.2	37.6	48.0	52.0	≯ 50. f ∾	50.3
Q	А	17.1	18.4	26.7	50.8	50.2	29.00	27.2	34	33.7	3,10
Spirox-	В	17.0	4.3	4.6	40.1	35.1	286	32.0	38.2	29.7	28.4
amine	Mean	17.0	11.3	15.7	45.4	42.6	28.8	29.6	36.5	31.7	O30.0
M01	А	n.d.	n.d.	n.d.	₹N.1	0.8	🕅 n.d. Ø	°1.1	2.0	2.1	2.4
M01 (desethyl)	В	n.d.	n.d.	0.1	1.6	1.2	1.2	1.5	3.0	2.3	~24
(desettiyi)	Mean	n.d.	n.d.	nkd.	1¢4°	1.9	.0.6	×1.3	Q.5	°~¥.2	׎.4
M02	А	n.d.	n.d.	Dd.	, ¶.d.	A.6	2.2	00.8	<u>م</u> 1.2	n.d. <u>1</u>	2.2 。
M02	В	n.d.	n.d. 🖉		» n.d. (1.3 🗸	1.1	n.d	2.00°	2,50	1.4
(despropyl)	Mean	n.d.	n.d.	n.d.	næd, y	13	1.6	<u>`</u> 0Ğ	1,6	1.2	A .8
1405	А	n.d.	n@	ñ.d.	nCel.	s 6 /9	. () .d.	√ n .d.	¶1.d.	Sh.d.	n.d.
M05	В	n.d.	Red.	n.d.	⊖n.d. ≈	C≫n.d.	n.d. 🔍	n.d. 🖉	n.d.	n.d.	n.d.
(hydroxy)	Mean	n.d. 🖉	n.d. 🤇	🎽 n.d. 🔊	″ n.d. [%]	0.5	n.Ø.,	n.d.	nÆ	n.d.	n.d.
1402	А	n.d.V	n.¢	n.¢	nð	n.đ.	pQ.	, ©d.	Ôd.	°n⊁.d.	n.d.
M03 (N-oxide)	В	ndd.	s_ñ.d.	fØd.	p.d.	ø.d.	On.d.	9ĥ.d. 🐐	∽n.d. %	n.d.	n.d.
(IN-OXIDE)	Mean	n.d.	n.d. 🔉	🕅 n.d.	n.d.	[¶] n.d.	n.d.¢	n.d.,	n.d. ^O	n.d.	n.d.
MOC	A 🔊	n.d	n.d.	n.d	n.d.O	n.d.	nd	16,6	140	13.3	13.1
M06 (acid)	B 🥎	n d.	n.Q.	n Q.	n(d.	1,8	* 13 .1	,^₽ 3.9 ,	\$.9	13.1	19.0
(aciu)	Mean	a.d.	Øŋ.d.	n.d. 4	n.d.	00.9 🖇	6.5	~16.3 (§ 9.9	13.2	16.0
M11 (1		🕅 n.d. 🎽	∮n.d.	n.d. 🔍	n.d 🏑	rn.d.♡	n.d	n.d. 🏸	n.d.	3.6	n.d.
M11 (des- ethyl acid)	B L	n.d	n.eC	n.d.	n o	n@	p.d.	n.d.	n.d.	n.d.	n.d.
euryr aciu)	`	p.ď.	n.d.	n ∂d.	°≈ n .*d.	.	∂n .d. ∝	n.d.	n.d.	1.8	n.d.
M12 (1		n.d.	Sn.d.	n.d.	∛n.d.	n.d. 🖉	🎙 n.d. 🖗	₽ [™] n.d.	1.0	n.d.	n.d.
M12 (des-		Pn.d.	n.d. 🦄	n.dØ	n.d.	n.¢	n.¢	n.d.	n.d.	2.9	n.d.
	Mean	n,đ	n.d.	nd.	n⁄ðľ.	n.d.	n.d.	n.d.	0.5	1.4	n.d.
Outhan a los	A	And.	Q.d.	n.d.	n.d. 🖉	Cn.d.	⊳n.d.	n.d.	n.d.	n.d.	n.d.
Other 🖉	×B ×	Dn.d.	n.d.	» [∿] n.d. ()"n.d. 🖗	1.4	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean L	n.d 🖉	n,dO	n.d.	n.đ	0,4	n.d.	n.d.	n.d.	n.d.	n.d.

, OF Table CA 7.22.3-7: Characterisation of radioactivity following treatment of Calwich Abbey system with [cyclohexy1-1-14C]-spiroxamine at 20°C under aerobic condi-tions – Cotal system % APJ

Calendaria	Replicate	v "Oʻ			Incu	ibation	time (D	AT)			
Compound	Replicates	. O ^y	1×	۲ S	7	14	30	42	62	76	100
	$\mathcal{V} \to \mathcal{A}_{\Lambda}$	å 9 9.7 "	9 4.6	98.8	94.6	92.6	76.5	80.8	81.6	85.5	82.0
Total 🔗		102.2%	r 101 <u>8</u>	^{\$%} 100.3	96.1	91.5	82.9	80.1	75.6	76.6	74.2
Total	«Mean [®]	100,9	98.2	99.6	95.3	92.0	79. 7	80.4	78.6	81.1	78.1
Spirox	A C	99 .7	93.5	96.8	87.2	70.9	53.8	27.5	34.9	34.1	31.7
amine		102.2	100.4	98.2	82.7	36.5	29.4	32.5	39.1	29.7	28.4
	Mean.	^{,*} 100.9	97.0	97.5	84.9	53.7	41.6	30.0	37.0	31.9	30.0
M101 ~~	A	n.d.	0.3	0.3	1.6	1.3	1.6	1.1	2.0	2.1	2.4
MO1 (desetby)	В	n.d.	0.3	0.4	2.3	1.2	1.3	1.5	3.0	2.3	2.4
(uescuryy)	Mean	n.d.	0.3	0.3	2.0	1.3	1.5	1.3	2.5	2.2	2.4



Commonwel	Derlegte				Incu	ibation	time (D	AT)			
Compound	Replicate	0	1	3	7	14	30	42	62	76	100 °
M02	Α	n.d.	0.5	0.3	0.5	2.5	4.5	0.8	1.2	n.d.	22
M02 (deepropul)	В	n.d.	0.3	0.3	0.8	1.3	1.1	n.d.	2.3	2.5	<u>i</u> .4 1
(despropyl)	Mean	n.d.	0.4	0.3	0.6	1.9	2.8	0.4 🥎	» 1. 7	1.2	1.8
M05	А	n.d.	n.d.	0.5	1.1	0.9	n.d.	n.d	n.d.	n.đ	n.d.
(hydroxy)	В	n.d.	n.d.	0.6	0.5	0.4	n.d.	n.ď.	n.d.	, nd.	n.d.
(liyuloxy)	Mean	n.d.	n.d.	0.6	0.8	0.6	n.d.	n.d.	n.d. 🗞	On.d.	n.d. 🔬
M03	Α	n.d.	n.d.	n.d.	0.6	6.8	\mathbf{a}	1	n.d×	n.d	0.5° 11.a.
(N-oxide)	В	n.d.	0.3	n.d.	4.0	0.6	2.6	n.d.	n.C.	n Q.	0.5 11.a.
(IN-OXIGE)	Mean	n.d.	0.1	n.d.	2(3	0.7	Q4″	n.d.	∞ ø.d.	J.d.	A0.2 👔
M06	Α	n.d.	n.d.	0.2	<u>3</u> 2.1	13.9	<u>0</u> 8.8	۰46.3 _م	38.8	¥1.9¢	
(acid)	В	n.d.	n.d.	n.d	¢°4.1	41 Q	48.0	42.7Q	23.5	38,6	38
(aciu)	Mean	n.d.	n.d.	0.1	3.1 °	277	284	44,5	31.2	\$40.3	39.8
M11 (des-	Α	n.d.	n.d.	n.d.	Jisd.	_≪ n.d.	0.6	¥.3	"Т.З	~5.2	™1.1
ethyl acid)	В	n.d.	n.d.		©n.d.		Ø 0.5 🏷	1.1	1.8		1.k°
euryr aciu)	Mean	n.d.	n.d.	n.d	I.	1.2	0,6	1.2	1.6	33	
M12 (des-	Α	n.d.	n.d	n.d/	nd. ∡n.d.	p.Q.	Ø,3 ⁹	°2,6	2.0	1.3	ST.2
Propyl acid)	В	n.d.	n.d.	<u>&n.d.</u>	Kµ.d.	×1.1 .		‰Ó.9_(≥ 1.3 (1.6
r topyr actu)	Mean	n.d.	Ön.d.	√n.d ́	n.d.	7 0.5 7	0.7.5	1.8	3.0	1.3	1.4
Other	Α	n.d,	0.3	0.6	1,3	2.3, Ø)0	40	10	1) D	<u>,</u> ≸.0	1.4
unknowns	В	n_d. ▼ ~@ d.	<u>9</u> .9	0.7	<u>_</u>	(P)0	A. J. 2	P.3	J.7 ,	0.9	1.1
ulikilo wils	Mean	∼nad.	°∼Ø.4	0.7	@1.6	4.6	\$ <u>2.7</u>	1.3	َ≶َ 1.6	1.0	1.2

n.d.: not detected, DAT: days after treatment

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Table CA 7.2.2.3-8: Characterisation of radioactivity following treatment of Emperor Lake sys-tem with [exclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions [mean % AR] - Overview of means

	Ô		\sim	Č,	N a			17			
Commound	×0		0	o «	🖉 🔣	cubation	time (DA	.T) ~~			
Compound C	J	<i>~</i> 0	الاً ^{ال}	3	~7,*	A Ă	O30 🖌	% 42	62	76	100
Total 🔊	W	79.9	88:0	97.7	D .9	36.0	y 25,4°	15.1	25.7	9.8	9.0
Total	S	20 Ý	120	A .7	46.2	\$ 56,4	62.0	73.2	60.4	75.9	70.5
	W	79.9	×\$7.2	, 96.6 🔍			18.6	6.0	14.0	0.3	0.9
amine	S	20 .3	10.5	4:1 ⁰	4 1 ,9	25.0 \$\$.4	² −36.7	69.2	55.4	48.0	58.6
M01	WØ	n.d 🏹	0,2 ,10d.	Ø.3	≪0.4	05	¥ 1.0	0.5	1.2	n.d.	0.4
(desethyl)	S S	n 🖓 🎽	Dd.	Ø.2	≫ 2.2 🚿	1.3	3.0	3.0	1.8	2.1	3.9
M02 🔊	W	@.d.	0.3	¥ 0.3	0.6 2.3 2.1 2.1 0.6	.0.6	0.9	0.7	1.7	0.7	0.3
(despropyl)	S	n.d. 🐧		$0\mathcal{R}$	29	P.3	2.3	1.1	n.d.	0.8	2.1
	W	n.d	0,07	Ø2	°n.d. 🔊	€n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
(hydroxy)	S	n.d.	n.d.	n.d.	n.d	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M03	W	Jr.d.	🖓 n.d. 🛛	n.d. n.d.	n đ⁄	n.d.	0.2	0.3	0.5	n.d.	0.3
(N-oxide)	S	n.d. 🍙	n.d	n.a⊮	m.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M06	Ì.	n.d.	nd.	@v.d.	<i>≰</i> ∕0.5	8.1	3.3	6.2	5.8	7.0	3.8
(acid)	\$s	nd.	H.d.	h 11. u .	🖗 n.d.	n.d.	n.d.	n.d.	3.2	23.0	5.8
M11 (des-	w	, n.d. 🤞	n.d.	n.d©	n.d.	n.d.	0.1	0.2	0.3	0.3	0.4
ethyl acid	S	\approx n.d	n.d. n.d	n.đ.	n.d.	n.d.	n.d.	n.d.	n.d.	0.5	n.d.
M12 (des-	Ŷ	n d.	TQ.	n.d.	n.d.	n.d.	n.d.	n.d.	0.2	0.8	0.8
Propykacid)	≫s	ád.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	W	@n.d. 🕺	y 0.1	0.3	0.6	1.9	1.3	1.2	1.9	0.6	2.2
unknowns	S	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1.5	n.d.

n.d.: not detected, DAT: days after treatment

All values expressed as mean percentage of applied radioactivity (% AR)



Characterisation of radioactivity following treatment of Emperor sys	
with [cyclohexyl-1- ¹⁴ C]-spiroxamine at 20°C under aerobic condition water system [% AR]	s − ∘
water system [% AR]	

Compound	Donligato				Inc	ubation	time (D	AT) 🤌			(\mathcal{I})
Compound	Replicate	0	1	3	7	14	30	42	62	76	100>
	A 81.2 98. B 78.5 77. Mean 79.9 88. A 81.2 98. B 78.5 76. Mean 79.9 87. A 81.2 98. B 78.5 76. Mean 79.9 87. A n.d. 0.2 B n.d. 0.3 yl) B n.d. 0.3 A n.d. 0.4 A n.d. 0.4 pyl) Mean n.d. 0.5 A n.d. 0.5 A n.d. 0.5 A n.d. 0.6 B n.d. n.d. B n.d.	98.7	99.8	56.6	36.5	18.4	18.9	9.2	5.2	15.7	
Total	В	78.5	77.2	95.5	39.2	35.5	32.5	AQ.5	42.1	Â ⁴ .5	
	Mean	79.9	88.0	97.7	47.9	s _▲ 36.0	25.4	42 6 18.9 9 32.5 42 25.4 25 5.8 0 6.1 27 6.0 14 0.5 0 0.5 0 0.5 0 0.5 0 0.5 0 0.5 0 0.5 0 0.6 1 0.6 2 0.7 4 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.6 1 0.7 4 0.6 1 0.7 4 0.8 5 0.5 0 1.4 0 0.5 0 0.5 0 0.5 0 0.5 0 0.5 0 0.5 0	25.7	¥ 9.8°∧	9.0
Swimor	А	81.2	98.1	98.8	53.8	27.4	9.80	5.8	0.7	76 100 5.2 \$5.7 44.5 2.2 9.8 9.0 n.d. 100 0.7 9.8 9.8 9.0 n.d. 100 0.7 9.0 n.d. 0.9 n.d. 0.8 0.7 9.3 n.d. 0.4 0.7 0.3 0.6 0.4 0.7 0.3 n.d. n.d. n.d. 0.6 n.d. 0.7 0.5 n.d. 0.5 n.d. 0.6 1.1 0.9 0.4 0.8 0.8 0.5 4.2 0.8 0.2 0.6 2.2	
Spirox- amine	В	78.5	76.3	94.3	37.8	22.6	275	6.1	2¶.3		m.d.
amme	Mean	79.9	87.2	96.6	48.8	25.0	18.6	6.0	014.0	[∞] 0.3	76 100 5.2 \$.7 4.5 2.2 9.8 9.0 n.d. 1.0 0.7 0.4. 0.8 0.9 n.d. 0.8 0.7 0.4. 0.8 0.4 0.8 0.4 0.7 0.3 n.d. n.d. 0.7 0.3 n.d. n.d. 0.7 0.3 n.d. n.d. n.d. n.d. 0.7 0.3 n.d. n.d. n.d. n.d. n.d. n.d. n.d. n.d. n.d. 0.6 n.d. 0.7 0.5 n.d. 0.5 n.d. 0.6 1.1 0.9 0.4 0.6 1.1 0.9 0.4 0.5 4.2 0.8 0.2 0.6 2.2
M01	А	n.d.	0.2	0.3	\$ 0.4	0.4	¥1.0_¢	°0.5	0.2		
(desethyl)	В	n.d.	0.3	0.4	0.4	0.5	1.10	0.5		ŋ.Ø.	"n.d.
(deseury)	Mean	n.d.	0.3	0,3	0∂ A°	0.5	A.		62 76 100 9.2 5.2 5.7 42.1 4.5 2.2 25.7 9.8 9.0 0.7 n.d. 1.0 0.7 n.d. 1.0 27.3 0.7 n.d. 0.2 n.d. 0.8 1.0 0.8 0.4 2.3 0.7 0.3 1.0 0.8 0.4 1.0 n.d. n.d. n.d. n.d. n.d. 0.5 n.d. 0.3 0.4 n.d. 0.7 0.3 0.5 n.d. 0.5		
M02	А	n.d.	0.4	0 .2	Q .7	Ø.6	A.1 🗞	00.8	1.0	0.8	
(despropyl)	В	n.d.	0.2 🔎	0.3	0.5	0.6 🗸	0.6	0.6	2.30°		0,2%
(despropyr)	Mean	n.d.	0.3	0,3	0.6	0,6	0.9		4 ,7	0.7	
M05		n.d.	n@	_0×2″	nCel.	s_n∕d.	() .d.	<mark>√ p</mark> .d.	An.d.	Sh.d. (n.d.
(hydroxy)	В	n.d.	% 2	Ø.2	on.d. ≈	Çvn.d.	n.d. 🤇	🗘 n.d. 🔬	n.d.		n.d.
(liyuloxy)	Mean		0.1	້ 0.2 ັງ	🖞 n.d. 🌂	n.d.>	n.Ø.		n	n _k d.	100 \$5.7 9.0 100 100 100 9.0 9.0 9.0 9.0 9.0 9.0 9.0 9
M03			n.	n.Ø	nð	ned.	<u></u> ØŽ			°∕1%.d.	0.6
(N-oxide)	В	nd.	⇒ ñ.e.	fl?d.	p.d.	ø.d.	jon.d.	9n.d. 🐐		🖌 n.d.	n.d.
(IN-OXICC)	Mean	n.d.	n.d. 🔬	🕅 n.d.	n.d.	[™] n.d.	¥°0.2 ©	0.3	0.50		
M06		n.d	n.d.	n.d	0.90	5.8 **	45,7	9.8			
(acid)	B N		n.Q.	n Q.	Q 2	10.3	×2.2	× /		10.8	
(acid)	Mean		<i>⊘</i> g.d.	D.d.	0.5	08.1 🖇	3.3	6.2		7.0	
M11 (des-		@n.d. 🎽	∮n.d.	n.d. 🔊	n.d 🖌	r.d.♡	0.3	0.5%	0.4		0.7
ethyl acid)			n.¢	n.d.	n.d	n@	n.d.		0.3	0.5	n.d.
etilyi aela)	<u>Nean</u>		n.d.	n.d.	`∧n.d.	.	Ø.1 🛛	0.2		0.3	
M12 (des-		n.d.	Sn.d.	_n.d. 🧹	∲n.d.	n.d.	🎙 n.d. 🖗		0.5		
Propyl acid)	<u> </u>		n.d. 🦄	n.dØ	n.d.	n.¢	n.¢		n.d.	0.9	0.4
	Mean		n.đ.	n.d.	n Ø.	n.d.	n.d.				
Other	Að		Q.d.	0.3	0.9	*	√ 1.2				
	x B x	Dn.d.	[~] 0.2	°0.3 €	D″ 0.4 [≪]	1.5	1.3				
unknowns	Mean L	n.d.	0,10°	0.3	0%6/	14	1.3	12	10	0.6	22

Table CA 7.22.3-10: Characterisation of radioactivity following treatment of Emperor system with [cyclohexyF1-14C] spiro ramine at 20°C under aerobic conditions – Sediment system [% AR]

Colorand	Replicate	, <u> </u>	Ĩ			ubation	time (D	AT)			
Compound	Replicates	ð″	Î [¥]	Č,	7	14	30	42	62	76	100
($\mathcal{D}^{\circ} A_{\circ}$	21.1 ×	\$2.9 J	°°∕3.3	38.0	55.7	69.5	68.6	73.9	80.8	62.7
Total 🔗		19.5%	21.0	[≫] 6.0	54.5	57.1	54.5	77.8	46.9	70.9	78.3
Total	- Mean 🖗	20.3	12.3	4.7	46.2	56.4	62.0	73.2	60.4	75.9	70.5
Spirox	AC B	QP.1	n.ď.	2.9	34.9	53.2	62.6	64.4	65.3	54.5	52.0
amine		¥19.5	21.0	5.4	48.9	53.5	50.7	73.9	45.5	41.5	65.2
	Mean. 🔨	20.3	10.5	4.1	41.9	53.4	56.7	69.2	55.4	48.0	58.6
	A	n.d.	n.d.	0.2	1.4	1.2	4.1	3.2	2.1	2.6	4.4
Mto1 (desetlasp)	В	n.d.	n.d.	0.3	3.0	1.4	1.9	2.8	1.4	1.5	3.5
(uescuryy)	Mean	n.d.	n.d.	0.2	2.2	1.3	3.0	3.0	1.8	2.1	3.9



C	Durlanda				Inc	ubation	time (D	AT)			
Compound	Replicate	0	1	3	7	14	30	42	62	.d. n.d. .d. 1.6 .d. 0.8 .d. n.d. .d. 1.0 .d. n.d. .d. n.d.	100 °
M02	А	n.d.	n.d.	0.2	1.6	1.2	2.8	1.0	n.d.	n.d.	Å
M02	В	n.d.	n.d.	0.4	2.6	1.3	1.8	1.1	n.d.	1.6	, n.d. /
(despropyl)	Mean	n.d.	n.d.	0.2	2.1	1.3	2.3	1.1	⊳ n.d.	0.8	2.1
M05	Α	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d S	n.d.	n.đ	n.đ
(hydroxy)	В	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.		n.d.
(liyuloxy)	Mean	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	nd.	n.d. 🦏	On.d.	©n.d.∢
M03	А	n.d.	n.d.	n.d.	n.d. (∱n.d.	n.d.		n.d 🗶		n.d 12. d.
(N-oxide)	В	n.d.	n.d.	n.d.	n.d. 🕅		n.d	n.d.	n _o .	nî.Q.	n.d tt.d.
(IN-OXIDE)	Mean	n.d.	n.d.	n.d.	n.d.	0.4	pQ.	n.d.	sav.d.	J.d.	~n.d. ∉
MOG	А	n.d.	n.d.	n.d.	jn.d.	n.d.	Ôn.d.	₀n.d. "	⁰ 6.5	Ž2.7 (j 2.0,©
M06 (acid)	В	n.d.	n.d.	n.d.	Ø n.d.	n.d	n.d	n.d:Q		23	9,65≯
	Mean	n.d.	n.d.	n,d. 🔍	n.d.	n.đ	n.d.	næl.	3,2 √n.d.		\$.8
M11 (des-	А	n.d.	n.d.	n d.	B,d.	n d.	m.d.	4 .d.		1.0	n.d.
ethyl acid)	В	n.d.	n.d.	n.d.	Kn.d.	Ôn.d.	Øn.d. 👌	» n.d. ″	[©] n.d.	n.d	n.de.°
eniyi aciu)	Mean	n.d.	n.d,	n.d.	n.d.	n.d. ~	n.d.	n.¢Ç	n.d.	0,5	nØ.
M12 (des-	А	n.d.	n.d	n.ð≯	n dz	n.Q.	nd.	°n d.	∭n.d.	_≪ n.d.	Jr.d.
Propyl acid)	В	n.d.	nd.	(m, d.	≪ŋ.d.	`≈p.d.	n.d.	Sh.d.	n.d. 🖌		0 [°] n.d.
r topyr actu)	Mean	n.d.	Ön.d.	∽n.d. ൣ`	∽n.d.√	🖓 n.d. 🛛	n.d.	n.d 🛇	n.d	n.¢	n.d.
Other	А	n.d,	🕅 n.d. 🖤	n.d. '	n.d.	n.d.	n Q	nd	n d.	⊾ñ.el.	n.d.
unknowns	В	n_d. [♥]	ŋ, Ø	n Ø.	p.a.	100	al d.	≈ 0 .d.	n.d.	3.0	n.d.
	Mean	~ n ≥d.	°~ny.d.	nď	M.d.	Ln.d.	Sn.d. 🔊	n.d. 🤇) n.d., 🖔	1.5	n.d.
d.: not detected, l	DAT: days after	fréatmen	t S	, n.u.	0	Ś					

Table CA 7.2.2.3-11: Characterisation o	f Adio a	erivity f	Olowin	g treatm	ient 🕅 Emperor system	m
Swith Syclobexyl-1	¹⁴ C]-spi	roxani	ne at 20	°C ande	r perobic conditions -	To-
tal system W AN	ž ~ ~		<i>w</i>		D.	

	<u> </u>	- Solution of the second secon	· •	\sim	N.Y		× .	\sim			
Compound	Donie	~	& .		🖋 Incu	iDation_	time (P	ΑŤ)			
Compound	Replicate	00	۵ 1 🐒	3	70	14	30,	42	62	76	100
Č6	NØA €	1023	101.6	1,03/1	94,6	92.2	\$7.8	87.5	83.1	86.0	78.4
Total 🍾	Bీ≪	28.0	98 .2	101.5	<u>93</u> .7	£2.6 ≈	\$7.0	89.0	89.0	85.4	80.6
Total	Mean	00.1	® 9.9	√102.3 ©	[≫] 94.2≪	*92,4 0	87.4	88.3	86.1	85.7	79.5
C in	A L	∀102. %		101.7	88.7	8057	72.4	70.2	66.0	54.5	53.7
Spirox- amine	S B Mean	98	97.8	99.7	\$0 .8	~76.1	78.1	80.0	72.8	42.2	65.2
		100.1	. 1.7) 100. 7	≫87.7 "	78.4	75.2	75.1	69.4	48.3	59.4
M01	<i>C</i> -	n.d.。	0.2 0)″ 0.5 ©	1.90	[*] 1.7	5.1	3.7	2.3	2.6	5.2
(desethyl) «	B S	n.đ.y	$0,3^{\vee}$	0.65		1.9	3.0	3.3	3.5	1.5	3.5
(desettiyi)	Mean [©]	nd.	0.3	s 9.6	× 2.6	1.8	4.1	3.5	2.9	2.1	4.4
M02	A	-Qa.d.	0.4	§*0.4 ×	≽ 2.3	1.8	3.9	1.8	1.0	0.8	4.6
(desptopyl)	SB A	n.d,	0.2	0.2	3.0	2.0	2.4	1.7	2.3	2.3	0.2
(ucspuopyi)	Mean S	n.d.	0.3	1 56	2.7	1.9	3.2	1.8	1.7	1.5	2.4
M05	\wedge A	n.d.	@ŋ.d.	£0.2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
(hydroxy)		@n.d. ^	Q 0.2 <	Q 0.2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Mean &	<u>n.d.</u>	0.1	0.2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M03	Mean & A O B B	n d.	ñ.a.	n.d.	n.d.	n.d.	0.4	0.6	n.d.	n.d.	0.6
(N-ovide)	Ø [¥] B [∪]	(#.u.	n.d.	n.d.	n.d.	0.8	n.d.	n.d.	1.0	n.d.	n.d.
M03 (N-oxide)	Mean 🧳	n.d.	n.d.	n.d.	n.d.	0.4	0.2	0.3	0.5	n.d.	0.3
Moo (acid)		n.d.	n.d.	n.d.	0.9	5.8	4.5	9.8	11.6	26.0	8.2
(acid)	B 🖉	n.d.	n.d.	n.d.	0.2	10.3	2.2	2.6	6.5	34.1	11.1
	Mean	n.d.	n.d.	n.d.	0.5	8.1	3.3	6.2	9.1	30.0	9.6



Compound	Donligato				Incu	ibation	time (D	AT)			
Compound	Replicate	0	1	3	7	14	30	42	62	76	100 °
M11 (dea	Α	n.d.	n.d.	n.d.	n.d.	n.d.	0.3	0.5	0.4	1.0	n.d.
M11 (des-	В	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.3	0.5	n.d. (
ethyl acid)	Mean	n.d.	n.d.	n.d.	n.d.	n.d.	0.1	0.2 🐧	» 0.3	0.8	0.4
M12 (des-	Α	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d S	0.5	0.6/	10
· ·	В	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	<u>0</u> 29	0.4
Propyl acid)	Mean	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.2 🦏	0.8	© [×] 0.8 🔬
Others	Α	n.d.	n.d.	0.3	0.9 (\$ 2.2	1.2	0.9	1.3	05	4.2
Other	В	n.d.	0.2	0.3	0.4	1.5	1,2	1.4	2,5	29 [°]	4.25
unknowns	Mean	n.d.	0.1	0.3	96	1.9	_Ω3 [×]	1.2	×1.9	ð 2 .1	2.2

n.d.: not detected, DAT: days after treatment

B. Material Balance

The material balance (mean) at each sampling interval ranged from 92.7 to 103.0% AB for the two test systems. The overall mean material balance was 97.1 and 99.5% AB for the Calwich Abbey and Emperor Lake water/sediment systems, respectively.

C. Extractable and Non-Extractable Residues

The mean proportion of total radioactivity extracted from sedtment samples and in the overlying water declined slowly over time from 100.9% AR at 0 DAT to 98.1% at 100 DAT to the Calwich Abbey system. The Emperor Lake system declined similarly, from 100.4% at 0 DAT to 79.9% at 100 DAT. Unextracted residues (bound residues) increased slowly throughout the incubation, teaching maximum levels of 10.7% AR in Calwich Abbey at 100 DAT and 12.4% AR in Emperor Lake at 76 DAT.

D. Volatile Radioactivity

Significant radioactivity was detected in the PU bungs in both systems from 30 DAT, reaching maximum levels of 9.5% AR in Calwich Abbey at 30 DAT and 5.6% AR in Emperor Lake by 100 DAT. Subsequently, elected amples of PU bung extracts from both systems were analysed by HPLC and the volatile radioactivity was confirmed to be volatile ¹⁴C-spiroxatoine.

The level of applied radioactivity recovered in the volatile traps was 4.9% AR for both water/sediment systems over all sampling intervals and was detected in the KOP trap and was assumed to be carbon dioxide (not confirmed as 3% AR).

E. Degradation of Parent Compound

Following application of [cvolohexyf-1-14Q]-spiro amine, spiroxamine showed rapid dissipation in the water phase of both systems, declining from 79.9 - 83.9% AR (mean of duplicate samples) at 0 DAT to <1.0% by 76 DAT. In the Calwich Abbey system, the amount of spiroxamine in the sediment increased to 45.4% AR after 7 DAT and subsequently decreased to 30.0% AR after 100 DAT. In the Emperor Lake system, the amount of Spiroxamine in the sediment increased to 69.2% AR after 42 DAT and subsequently decreased to 58.6% AR after 100 DAT.

Degradation of feyclohexyl- 6⁴C]-spiroxamine was accompanied by the formation of one major degradation product M06 (piroxamine-acid: max 44.5% AR at 42 DAT) and several other minor metabolites M01 (spiroxamine-desetto): max 44.3% AR at 100 DAT), M02 (spiroxamine-despropyl: max 3.2% AR at 30 DAC), M05 (spiroxamine-N-oxide: max 2.3% AR at 7 DAT), M11 (spiroxamine-desethyl acid: max 3.3% AR at 76 DAT) and M12 (spiroxamine- despropyl acid: max 3.0% AR at 62 DAT). Some other minor unidentified metabolites were observed, none of which exceeded a total of 3.0% AR at any sampling interval.

F. Degradation Kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.2.2.3/08 (M-763141-01-1).



G. Isomers of Parent Compound

Additional work is being conducted on the chiral analysis of the samples for parent spiroxamine. This work will provide the quantified amounts of each individual isomer of spiroxamine in all samples.

III. Conclusions

Spiroxamine degraded in water/sediment systems under aerobic conditions (20°C) with (0.59,4% of applied radioactivity remaining as parent compound after 100 DAT in the Calwich Abbey and Emperer Lake systems, respectively. Some volatility of parent spiroxamine was diserved (max 9.5%) in addition to low amounts (<4.9% AR) of other volatiles (assumed to be carbon dioxide). The amounts of other z of tractable radioactivity were <12.4% AR (mainly human). The major metabolic pathways involved ox dation of a methyl group to form metabolite M06 (proxamine-acid, maximum 44.5% AR).

A re-evaluation of the degradation kinetics in accordance with POCUS guidance document on degradation kinetics (2014) is performed in the report of esenced under point KCA 2.2.3/98 (M-763141-01-1).

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/20

The study was conducted to study guideline(s) OECD 308 (required guideline). The study is considered valid to assess the aerobic degradation of [cyclonexy] - ⁴C] spiroxamine in aerobic water/sediment systems.

Existing studies, previously evaluated

	KCA22.2.3 0 ~ ~ ~ ~ ~
Report Author:	
Report Year:	
Report Title	Aerobi@metabolism@fKWG@168 in an aquatic model ecosystem
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Document No:	$\frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}}} = \frac{\mathbf{M}_{\mathbf{M}}^{\mathbf{M}}}{\mathbf{M}} = $
Guideline(s) followed in	BBA Ref .: Deg dability and Rate of Plant Protection Products in
study:	Water Himmen System 5.1 (Dec. 1000)
Deviations from current	Yestrefer bolow) and a second se
test guideline:	Some minor deviation(s) not relevant for the reliability of the study (described in
¥ -	Sudy stymmary & &
Previous evaluation:	yes, evaluated and accepted
	DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recoge	DAB (1997), RAB (2010), RAR (2017) Yes, conducted order GDP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Ves C Ves C

Executive Summary

The route and rate of degradation of [coclohexyl-1-¹⁴C]-spiroxamine was investigated in two different water/sediment of the milliger⁸, Germany and Stilwell, USA) under laboratory aerobic conditions in the dark at 0°C for up to 100 days. The sediments and the water were collected from an artificial damned poted (Hoerniger, silt loam, 4.4%OC, pH 5.7) and from a man made pond (Stilwell, silt clay loam, 1.6%OC, pH 6.8). [Cyclohexyl-1-¹⁴C]-spiroxamine (radiochemical purity 99.6%) was applied to

⁸ For consistence with other studies, spelling of Hoenniger may differ to that reported in the study.



the surface of the water overlying sediment at a target rate of 0.25 mg a.s./L, which was equivalent to a field application rate of 750 g/ha (assuming a water body depth of 30 cm). Test systems were filled with a layer of sediment to a depth of 2-2.5 cm (98 g dry weight Hoenniger and 166 g dry weigh Stilvell) and overlying water to a depth of 6 cm; giving a ratio of approximately 1:3 v/v.

Each test vessel was attached to volatile traps of i) oil-coated (2% parrafin oil in hexane) quartz glass wool for sorption of organic volatiles and, ii) soda lime to collect carbon dioxide. A control system containing no test substance was used for the determination of biological activity.

Duplicate treated samples of each water/sediment system were removed for analysis after 0.0 7, 14, 33, 56 and 100 days of incubation.

Overlying water was carefully decanted into a glass, vessel containing appropriate amounts of acetonic trile. Sediment samples were extracted three times at room temperature with aceton file, while later time points were refluxed with methanol for 6 hours. All samples were analysed by NLC methods with the identification of the metabolite M06 determined be GC/MS. The LOD for a single peak was $\geq 0.1\%$ of the applied radioactivity.

The overall mean material balance was 102.1% and 100.9% AR for the Hoenniger and Stilwelt water/sediment systems, respectively.

The mean proportion of total radioactivity extracted from sediment samples increased slowly over the duration of the study from 7.5% AR (mean) at 0 DAT to 49.3% AR (mean) at 00 DAT in the Hoenniger system. The Stilwell system increased strailarly, from 7.2% AR (mean) at 0 DAT to 79.5% AR (mean) at 100 DAT. The mean proportion of total radioactivity in the overbying water defined blowly over time from 87.0% AR (mean) at 0 DAT to 2.1% AR (mean) at 100 DAT in the Hoenniger system. The Stilwell system declined similarly, from 92.4% AR (mean) at 0 DAT to 6.9% AR (mean) at 100 DAT. Non-extracted residues (bound residues) increased slowly throughout the incubation, reaching maximum levels of 44.0% AR (mean) in Hypenniger at 100 DAT and 48.9% AR (mean) in Stilwell at 76 DAT.

Following application of [cyclohexyl-1, C]-spiroxamine, spiroxamine showed rapid dissipation in the water phase of both systems, declining from 83.7% AR (mean) at 0 DAT to 0.6% by 100 DAT in the Hoenniger systems. Similarly, in the Stilwell system spiroxamine showed rapid dissipation in the water phase of both systems, declining from 80.0% AR (mean) at 0 DAT to 20.1% by 100 DAT. In the Hoenniger system, the amount of spiroxamine in the sediment increased to a maximum of 52.0% AR (mean) after 14 DAT and subsequently decreased to 42.7% AR (mean) after 100 DAT. In the Stilwell system, the amount of spiroxamine in the sediment increased to a maximum of 23.6% AR (mean) after 100 DAT.

Degradation of [cycloboxyl-1, *C]-sproxamine in the total system was accompanied by the formation of one major degradation product M06 (spiroxamine-acid. max 7.7% AR (mean) at 56 DAT) which was determined to be >5% AR for more than the consecutive time points. Additionally, several other minor metabolities M01 (spiroxamine-desethy): max 1.9% AR (mean) at 33 DAT), M02 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-despropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-hydroxy max 2.3% AR (mean) at 4 DAJ). Some other minor unidentified metabolites were observed but none of which exceeded a total of 2.5% AF (mean) at any sampling interval.

 DT_{50} values for the degradation of spiroxymine were calculated in the report, however, a re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014²) was performed in the opport presented under point KCA 7.2.2.3/08 (M-763141-01-1).



I. **Materials and Methods**

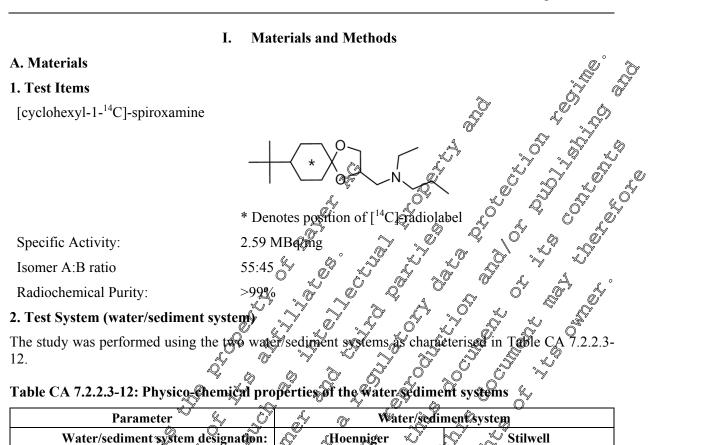


Table CA 7.2.2.3-12:	Physico-Chei	mičal p	roperties of	`the₩a	ter sedi	ment s	svstems	K.
	• ~C*	N I	_ · · · · · · · · · · · · · · · · · · ·	\sim	a^{\vee}	A.	•	\cap^{v}

Parameter & S	water/sedin	nentsystem							
Parameter Control Water/sediment system designation: Geographic Location	A Hoenniger	Stilwell							
Geographic Location		, <u>, , , , , , , , , , , , , , , , , , </u>							
City	S Wipperfürth O	Kansas							
Geographic Location	Germany A	USA USA							
Security Security Constructoristics									
Textural Classification (USDA)	Silt loan Q	Silty clay loam							
I extural Classification (USLAF) Sand [50 - 2000 μm] Silt [2 - 50 μm] Clay [< 2 μm]	32¢ 0°	4.3							
Silt [2 ² ⁵ ⁶ μm]	5¥.3 0 [×]	57.9							
Clay [< 2 μm]	16.4 ×	37.9							
pH in H ₂ O start/end in KCl start/end									
in H ₂ O start/end	6,2,76.0 5.6 / 5.7	7.8 / 7.8							
in KCl start/end	<u>م</u> جمع <u>5.6</u> / 5.7	6.8 / 6.8							
Organic Matter (%)* Or $\sqrt{2}$	6,2,9,6.0 5,6/5.7 7.6*	2.8*							
Organic Parbon (%)	× × 4.4	1.6							
$\frac{N_{\text{(total)}}(\text{mg/kg}) \text{ start/end}}{P_{\text{(total)}}(\text{mg/kg}) \text{ start/end}} \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad} \qquad \xrightarrow{\sim} \qquad} \qquad\xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad} \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad} \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad \xrightarrow{\sim} \qquad $	4000/4000	2000/3000							
P(total) (mg/kg) start/end	1030/1000	700/710							
Biological (responsion) activity (mg CO/h/kg) Sediment TS)									
Sediment TS									
Initial, 0 DAST & S &	21	12							
Final, 100 DAT $^{\circ}$ $^{\circ}$ $^{\circ}$	12	7							
Initial, 0 DAST	4 / 7	4 / 6							
Total organic or thor (h)g/L)	8.7	13.2							
- KA - CA									
3									



Parameter	Water/sediment system			
Water/sediment system designation:	Hoenniger		Stilwell	
Nitrate content (mg/L) start/end	77.3/2		80.9/2	
Phosphorus content (mg/L) start/end	<0.03/<1	~	0.20/<1	
Water	characteristics		4	
Total organic carbon (mg/L)	4 / 7	4	4/6 ~~	
Hardness (mg equiv CaCO ₃ /L) start/end	8.7	20°	13,2 , 2 *	
Nitrate content (mg/L) start/end	£.3/2	Ű	80.9/2 0	
Phosphorus content (mg/L) start/end	×0.03/<1	,Ô ^y	0.20/20	
Calculated by multiplying organic carbon content by 1.72	24 (not reported)	4		

The sediments and the overlying water were collected from an artificial dammed pond Hoemiger, Germany) and from a man made pond (Stilwell, US). No details provided on test system history. Prior to study initiation the aqueous sediment was passed through a 2 mm mesh sieve and thoroughly mixed before the dry weight was determined. The water samples were filtered through paper filters of the system has been appendix on the system has been appendix of the system has been appe

B. Study Design

1. Experimental Conditions

The behaviour of [cyclohexyl-1-¹⁴6]-spiroxamine was investigated in two contrasting sedurient water systems (Hoenniger and Stilwell) over aperiod of 100 days.

Each test vessel containing a sediment layer (2-2.5 cm depth; 98 g dry weight Hoenniger and 166 g dry weigh Stilwell) and an overlying water layer (6 cm) i.e. a water to sediment ratio of *ca.* 1:3 v/v. The water layer was gently agilated (25 rpm) by use of a magnetic stirrer. Each test vessel was attached to volatile traps of i) oil-coated (2% parafin oil in hexane) guartz glass wool for soption of organic volatiles and, ii) soda lime to collect carbon dioxide. Samples were incubated in the dark at a temperature of $20\pm2^{\circ}$ C.

Water/sediment system samples were pre-acclimatised to the incubation conditions (20°C, dark) for 47 days before application of the tensubstance. Measurements of oxygen content, pH and redox potential were recorded.

[Cyclohe χ]-1-¹⁴C]-spiro xamine was applied to the surface of the vater overlying sediment using a glass syringe at a target rate of 0.25 mg a.s./L, which was equivalent to a field application rate of 750 g/ha (assuming a water word depth of 20 cm) χ

A total of 20 batches (for each water-sediment system) were treated with the application solution. Two additional batches without addition of the spirox amine was used for the determination of biological activity.

2. Sampling

Duplicate treated samples of each water/sediment system were removed for analysis after 0, 0.25, 1, 2, 7, 14, 33, 56 and 100 days of incontation. Untreated samples were analysed for biomass at the beginning and end of the experiment.

3. Analytical Procedures

For supermitant water 50 mL was drained off into a Erlenmeyer flask containing 1N NaOH (1 mL) for later processing determination of CO_2 and/or carbonates). The remaining water was centrifuged and filtrated with any precipitate formed were combined together with the sediment sample to be extracted.

The volume and radioactivity content of the supernatant water was determined, before samples were analysed ising TLC methods.

Sediment sample were extracted three times with acetonitrile at room temperature. The combined acetonitrile extracts were analysed using TLC methods. Aliquots of the extracted sediment of the day 2-100 samples were further extracted with methanol under reflux for 6 hours. After centrifugation and



filtration, the supernatant was analysed by TLC methods.

Volatile radioactivity collected in volatile traps was quantified by LSC. Any radioactivity in the popyurethane foam bung was extracted using ethyl acetate and quantified by LSC. Carbon dioxide fr the calcium hydroxide traps determined using 18% hydrochloric acid and quantified by LSC

Following homogenisation, non-extractable residues (NER) in extracted sediments were determined combustion.

Characterisation of radioactivity was carried out using relevant reference compound by co-cliromators raphy. For identification of the metabolite M06 gas-chromatography was also conducted. The LOD ac a single peak was $\geq 0.1\%$ of the applied radioactivity.

4. Determination of degradation kinetics

The DT50 and DT90 of spiroxamine determined in the study was reported for each site. However, evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (FOCUS 2014²) was performed in the report presented under point KCA \emptyset 2.2.3(08 (M- \Im 631 01-1).

Results and Diseussior

A. Data

The distribution of radioactivity for each water/sediments system incubated at 30°C following application of [cyclohexyl-1-14C]-spiroxamore are summatised in Table CA 72.3-1 Dand Table CA 7.2.2.3-14.

The characterisation of radioactivity for each water/sediment are summarised that overall means) in Table CA 7.2.2.3-15 and Table CA 70.2.3-19. The characterisation of radioactivity for each separate layer for each water/sediment are summarised (as individual replicates) in Table CA 22.2.3-16 to Table CA 7.2.2.3-18 for the Hoeneriger system and in Table (7.2.2.3-20 K Table CA 7.2.2.3-22 for the Stilwell system.

Table CA 7.2.2.3-13: Recovery and distribution of radioactivity following treatment of Hoen-Riger system with Colohexyl-1&C]-speroxamine at 20°C under aerobic Ś conditions/mean % AR Ľ Ĩ

	A	A N		¥ V	$\mathcal{O}_{\mathcal{V}}$	(1)Y			
Compañad	E S Incubation time (DAT)								
Compound	~~~ 0~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.25	L L	<u></u>	ື 7 🔊	14	33	56	100
Supernatant water	Q \$7.0 🎸		\$29.4	≪15.2¢	3.9	2.4	2.3	3.2	2.1
Sediment extract	۶× 7	2 4.6	×44.7	[™] 52.9	\$.6	55.1	54.7	46.2	49.3
Non-extractable radioactivity	Ő.6	20.3 C			6 44.2	48.6	43.3	44.5	44.0
CO ₂ *	n.d.		Q.1	Q 1.4	1.8	2.0	3.3	6.6	6.8
Total	100,0		£101.0		102.4	108.0	103.5	100.4	102.2

n.d.: not defected, DAT: days after treatment

Oversell total recovery = 102.1% AR All values expressed as percentage mean of applied ranoactivity (% AR). Mean values determined outside the study report.



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Table CA 7.2.2.3-14: Recovery and distribution of radioactivity following treatment of Stilwell system with [cyclohexyl-1-14C]-spiroxamine at 20°C under aerobic condi- . tions [mean % AR]

Compound				Incuba	tion time	e (DAT)			<u>S</u>	O'
Compound	0	0.25	1	2	7	14	N	56 🦼	100	
Supernatant water	92.4	62.9	49.0	36.3	15.2	13.4	Ø .0	8.7 *	6.9	
Sediment extract	7.7	36.2	47.2	61.1	82.1	87.7	â 90.6	88.0	38.9	Ĉ)
Non-extractable radioactivity	6.5 ^A	22.8	29.7	42.0	Č52.9	60.7	65.2	×67.7 ~	48.9	(r -
CO ₂ *	n.d.	1.4	2.2	2.0	1.5	25	3.6	5.50	16.8	Ô
Total	100.0	100.4	98.3	99.2	98.8	₫03.6	103.	1022		×

n.a.: not analysed, n.d.: not detected, DAT: days after treatment

* Includes the CO₂-part of the supernatant water. Volatile organic compounds 0.1% AR, at any time. Α

Distribution of radioactivity of the membrane filter (M03 and non-extracted portion) \mathcal{O} Overall total recovery = 100.9% AR

All values expressed as percentage of applied radioactivity (% AR). Mean values determined outside the study report Ũ Ø

Table CA 7.2.2.3-15: Characterisation of radioactivity following treatment of Hoenniger system with [cyclohexx] 1-14 []*spire amine at 20 °C under aerobic conditions [mean % ARD Overview of means Ò

				407				<u>~</u> ~		
Compour	a		-Q'		🗞 Incuba	tion time		ð ô		
Compoun	a	0		x 1 0	2. 13.6	J.	∂ ⁷ 14 °C		\$ 56	100
Spirovonino	W	83.7	~ \$51.5 [*]		13.6	≫1.1 _0	° [™] 0.&	0.7	0.6	0.6
Spiroxamine	S	7.5	[∞] 24.¢	4\$ <i>.</i> 3	\$30.7 @	¥ 48.8	52%	s \$9.2 o	40.4	42.7
M01	W	n.d	n.d.	Sn.d.	n.d		⊀n.d. ≈	∑ 0.2√	n.d.	0.1
(desethyl)	S	n.d.	A.3	0.6	<u>1</u> ®"	n.d. N.1 (v	0.2 🏷	1.5	1.2	1.5
M02	W	9 .8	🖓 n.d. 🏑	n.d.	g.d.	°∕∕n.d. ()	n.d	` %)~3	0.1	0.1
(despropyl)	S	Øn.d.	02	A.3	NO.5 S	0.8,	6.9	×1.6	1.5	1.8
M03	WŚ	2.6	20,7	≪1.0 ∼	0.79	niga.	<i>√</i> n.d. √	03	0.1	0.1
(N-oxide)	S	N .	≫0.2 🐇	0.	Q.5	~0.5 _{(C}		0.2	0.4	0.9
M06	W	d. n.d() n.d.O	ńką.	0.7) 2.2 ×	1 1	0.3	2.2	0.7
(acid)	s	🕫 n.d. 🏁	næd.	_∢ n.d. 🔊	⊳ n.d.	n.d.	ר.4	1.3	1.9	1.0
M05	W	0,5	۳۲.d.	≈ ⁿ .d. [©]	n.d.	d . ∧	Øn.d.	n.d.	n.d.	n.d.
(hydrox)	S	m.d.	60.1	v	nd.	₩ ^{0.9} 0	1.5	0.7	0.8	0.7
Other	W		∕″0.2⊘	ØŽ.	°∕≫0.3 🤬	0.6	0.6	0.5	0.5	0.8
unknowns	S 🐔	n.d. 🔨	p.d.	×0.1 @	n.dO	0.5	n.d.	0.1	0.2	0.9
n d · not dataatad	DAT	dauchter	transant	V K.		Or				

n.d.: not detected, DAT: day after tranment and a province of the study report. All values expressed as percentage of mean applied radioaction (% Apr). Mean values determined outside the study report.

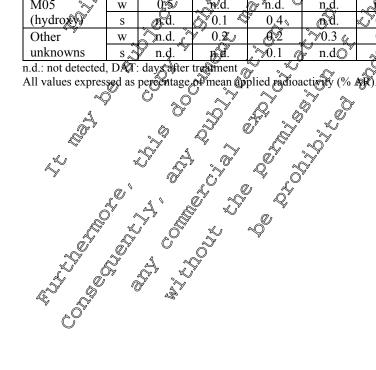




Table CA 7.2.2.3-16: Characterisation of radioactivity following treatment of Hoenniger system with [cyclohexyl-1-14C]-spiroxamine at 20°C under aerobic conditions -____^ Water laver [% AR]

			r layer [%	/I-1-14C]-8 ‰ AR1	spiroxami	ne at 20		raerobic	conditio	ons – 。
		•• atc								- S
Com-	Repli-				Incubation	· · · · ·		33		((//))
pound	cate	0	0.25	1	2	7	14		56	100
Spirox-	A	95.1	52.1	23.1	7.8	1.2	0.7	©0.9	0.7	0,7
mine	В	75.2	50.9	29.3	19.4	1.0	0.8	V	<u></u>	Ø.7
	Mean	85.2	51.5	26.2	13.6	1.1	0.8	0.7	\$9.6	y 0.6
M01	A	n.d.	n.d.	n.d.	n.d. 📎	n.d.	nd.	0.3	°n.d	0.7 0.6 n.d
de-	B	n.d.	n.d.	n.d.	n.d	n.d.	onzd.	0.1	n.C	1091
sethyl)	Mean	n.d.	n.d.	n.d.	næ.	n.d.	n.d.	0.2	n.e.	. (n.d. ,)
M02	A	1.1	n.d.	n.d.	Tr.d.	n.d.	n.¢	0.4	$\mathcal{O}_{0.1}^{\text{n.d.}}$	n.d.
despro-	В	0.4	n.d.		🖉 n.d.	n dy	s n.d.	0.2		
oyl)	Mean	0.8 2.1	n.d.	n.d. & 0.5 ♥	n.¢.°	nd.	Kn.d. 🔬	0.30 04	næd.	≪ov.d.
M03	A B		0.8		***	h.d.	≯ n.d.⊘ n.d.	0.2	n.d. 0 0.1 0 n.d.	<u>n.d.</u>
N-ox- de)		2.1 2.1	0.6 0.7	14 ×¥.0	0.7. V	n.d.Q		# ¥	0 0.1	<u>и</u> .е.
ue)	Mean				n.@	n .d.	n.d.	0.2 <u>/</u> 0.5	n.a. ~ ≰ 7	4 0.5
M06	A B	n.d.	n.d.	n.d. 📎	11.00 				6.7 @3.6	$\bigcirc \frac{0.3}{0.8}$
acid)	Mean	n.d.	n.d.	≮ <u>, 11.0</u> 4. ″ ⊸≪a	°≫0.7 ≪	y 0.1		0.3 á	2.2	
M05	A	n.d. 0.5	n.d.() n.d.()	നുട്രി. ്രn.d. ഗ്ര	n.đ		On.d.	n.d.Ö	n.dy	n.d.
hy-	B	0.5	n.ds @∡d `	© n.d. ⊘	n 9	n.d.	$\int^{1.d.}$	n d	4. %. %. %.	n.d.
droxy)	Mean	0.5	n.d.	n de	n d. _ n.d.		n <i>a</i> g.	n.d.	On.d.	n.d.
Other	A	n.d.	n.d.		n.d. 🕜	0.7	0.8	0.6	0.2	1.5
ın-	B	n.d	0.3	6 0.2	0,5	0.7 0.4	× 0.3 ~	0.0	0.2	0.1
nowns	Maan	nd	A.2	0.2 0.2			0.5	0.40 65 4	0.5	0.1
L D D			n.dy 0.3 19.2 Apattment e study tepo							
				~						



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Table CA 7.2.2.3-17: Characterisation of radioactivity following treatment of Hoenniger system with [cyclohexyl-1-14C]-spiroxamine at 20°C under aerobic conditions -Sediment laver [% AR]

	See	diment la	ayer [%	AKJ							AC I
C	Repli-				Incuba	tion time	(DAT)	~ .		O) I	d'
Compound	cate	0	0.25	1	2	7	14		56 🦿	1000	
Que incere	А	4.0	22.0	44.6	56.1	47.1	53.9	@49.4	49.4	42,6	
Spirox- amine	В	10.9	25.9	41.9	45.2	50.5	50.04	49.0	26.3	\$ 2.7	Ô
amme	Mean	7.5	24.0	43.3	50.7	48.8	52.0	49.2	^ 40.4 °≈	¥42.7	0
M01	А	n.d.	0.4	0.6	1.2	1.2	Ø .2	2.8 (0.8	1.0	
M01 (desetbyl)	В	n.d.	0.2	0.5	1.3	1.1	6 %0.2	0.5	1.0	Å,6	Ô
(desethyl)	Mean	n.d.	0.3	0.6	A. 3	1.2 🔬	0.2	10	1€2		
M02	А	n.d.	0.1	0.3	0.5	0.9	¢چ¢	A2.2	∛ 1.0	0 1.5	Í
	В	n.d.	0.1	0.3	0.4	0%	§.0.8	^{~~} 0.9 \ ⁽	1.9	18	
(despropyl)	Mean	n.d.	0.1	0,3	B .4	\$0.8 ×	J 0.9 (1,0	15	×1.8	
M02	А	n.d.	0.2	0 .1	Ø.6 ×	0.5 × 0.0	Q.D	1	. 0.2 <u></u>	1.4	
M03 (N-oxide)	В	n.d.	0.1	🐒 n.d. 🦓	0.4	0.0	0.2	_∞ ŏ.2 (0.5 Ö	0,3	
(IN-OXIGE)	Mean	n.d.	0.2 🕺	n,d. 🗡	Q.5	≈0.5	A.0.3	0.2	0.4	.0.9	
M06	А	n.d.	n.¢	înd.	@.d. 🔬	∛n.d. Ó	0.4	2.G	×0/3	×0.5	
(acid)	В	n.d.	pr.Q.	& M.d.	n.d	n.d	00	.3	ð 3.4	1.4	
(aciu)	Mean	n.d.		🔊 n.d. 🏷	n.ď.√	n.d.	A.4	Ĩ.3 ≲	1.2	1.0	
M05	А	n.d. *	₿ n.d	04	nd.	A.0	0 1.7 0	n.de	0.6	0.7	
(hydroxy)	В	n.d.Ø	0:2°	@4	Sn.d. (v 0.7	1.20	, 0.7	% 1.0	0.6	
(liyuloxy)	Mean	n.d.	0.1	₩0.4	n.d. 🐬	0,₽>	\$ 5	0.7	O [*] 0.8	0.7	
Other	А	n.d.	∽n.d. ~	0.2 ×	n.@	0.7	An.d. 🗞	2 0.2	n.d.	1.7	
unknowns	B 2	n.d.	n.dô	n Ø.	m.d.	_≈ ∿0.3 ≪)"n.d	n d.	0.3	0.1	
ulikilöwlis	Mean	n.d.	p_d.	ð 0 .1 🔬	Øn.d. Ő	× 0.5	n.d.	<u>Ø</u> 1	0.2	0.8	

 Image
 n.d.
 n.d.



Table CA 7.2.2.3-18: Characterisation of radioactivity following treatment of Hoenniger system with [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions – Total system [% AR]

		system	·	C]-spii	0xamm	c at 20 (Junuer		conuntio		
Common a	Repli-				Incuba	tion time	(DAT)	~		6	0°
Compound	cate	0	0.25	1	2	7	14	33	56 🦼	100	
Chinar	А	99.1	74.1	67.7	63.9	48.3	54.6	© 50.3	50.1 "	43,0	
Spirox- amine	В	83.1	76.8	71.2	64.6	51.5	50.8	49.5	£.7	3 3.4	ĈQ
amme	Mean	91.1	75.5	69.5	64.3 ₀₀	49.9	52.8	49.9	×41.0 ×	y 43.3	P
M01	А	n.d.	0.4	0.6	1.2	1.2	Ø.2	3.1 (0.8	1, W	
(desethyl)	В	n.d.	0.2	0.5	1.3	1.1	\$ ⁰ .2	0.60	1.0	Å7	Ó
(desetilyi)	Mean	n.d.	0.3	0.6	A. 3	1.2	0.2	10	1€2	O1.5	×
M02	А	1.1	0.1	0.3	⇒ 0.5	0.9	(the second s	2.6	Sy 1.0	1.75	
(despropyl)	В	0.4	0.1	0.3	0.4	0%6	s Ø.8	1.1	2.0	19	
(despropyr)	Mean	0.8	0.1	0,3	B .4	<i>.</i> ≫0.8 ≰	J 0.9	1,0	1,5	≪1.8	
M03	А	2.1	1.0	0 .6	×م 0.6®	0.5	Q.D	\$5	0.2	1.4	
(N-oxide)	В	2.1	0.7	s 1.4 🕷	1.80	0.Q	0.2	<u></u> , ŏ.4 (0.5 0 0.4	0,3	
(IN-OXICE)	Mean	2.1	0.9 🕺	/ [®] 1,0 [°] / [°]	1.2	⊘0.5	A0.3 C	0.4		.0.9	
M06	А	n.d.	n.¢	n.d.	@a.d. 🔬	≪y 3.7 Ó	1.7	2.8	_%_0	÷1.0	
(acid)	В	n.d.	r.d. 4	& M.d.	1.3~	0.7	10	.4	¢7.0	2.2	
(acid)	Mean	n.d.	"n.d. 4	🔊 n.d. 🏷	0.16	27	A.5	گ 1.6 <i>گ</i>	419	1.7	
M05	А	0.5 4		08	ðel.	21	01.70	2 1.6 00	0.6	0.7	
(hydroxy)	В	0.5	0.2	@ď	Sn.d. (0.7	1.20	مراجع 0.7	<u>ال</u>	0.6	
(liyuloxy)	Mean	Ø.5 [°]	0.1	0.4	n.d. 🐬	0,£	¢5	0. 7	O´ 0.8	0.7	
Other	А	n.d.	Syn.d.	0.4%	00	ĺ.4	_~°0.0 %	2 0.8		3.2	
unknowns	B s	n.d.	0.36	002	0.5	<u></u> ∿0.7 ≪) [*] 0.3	04	1.0	0.2	
d : not dotootod	Mean	n.d.	<u>9</u> ,2	ð i .3 👌	@ 0.2 Č	1.	0.6	8 6	0.7	1.6]

n.d.: not detected, DAT: days after atment

Table CA 7.2.2.3-19: Characterisation of radioactivity following treatment of Stilwell system with [cyclohexyl-14, C]-spiroxamine at 20°C under aerobic conditions [mean % AR] - Overview of means

Q				A Õ	, °°°	a.	1 and			
Compound	J	õ	S &	<u>°, </u>	Lacuba	tion time	(ĎAT)			
Compound	1	× 0 ×	0.25	Â,	<u></u>	♡ 7.≫	14	33	56	100
Spiroxamine	W 🖄		55.4	s ₽ 2.9 s	⊌″26.5%	9:\$	2.2	0.4	0.1	n.d.
Spiroxamme	Ŕ	1.2	2 .3	©14.9 0	16.2	2.9	21.8	20.8	16.5	23.6
M01	W	Q4	Šn.d. 🖉	0,2%	49 .5	\$0.4	0.4	n.d.	n.d.	n.d.
(desethyl)	s			AN d.	∞~0.7	1.0	n.d.	0.1	0.3	0.6
M02 🔏	W	0.7	~B3		0.7	0.2	n.d.	0.2	n.d.	n.d.
(despropy)	S	n₅d.	Åð.3 a	0.5~	_0K5	0.9	1.1	0.6	0.5	1.3
M03	W	°≯/1.3	∞6.7	5,9	8.7	2.7	2.9	0.9	0.3	0.5
(N-oxide)	S 🚽	N(Y . N	01		°≫ [°] 0.6	1.5	1.0	0.7	0.6	0.7
M06/	W	>> n.d. → n.¢	n.d.	Rn.d.	n.d.	1.7	6.7	4.8	6.0	4.0
(acid)	ا `	n.d.	√n.d@	n.d	n.d.	n.d.	1.0	1.6	1.8	2.3
M11 (de-	∽w .	🖂 II.U. 🥂	n.d	n.ď.	n.d.	n.d.	0.4	0.5	0.4	0.4
sethyl acid)		n.d	n.d.	An.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
M05	W	n.c.	,⇔µĭ.d.	∛n.d.	n.d.	n.d.	n.d.	0.2	n.d.	n.d.
(hydrox	S.	" n.d.	0 n.d.	1.3	0.7	1.5	2.3	1.4	0.5	1.2
	· · · · ·	🖓 n.d. 🔊	0.5	n.d.	n.d.	0.8	1.0	2.1	2.0	2.2
unknowns	s 🖉	n.d 🗡	n.d.	0.5	0.6	1.5	0.1	0.4	0.3	0.5

n.d. not detected, DAT: days after treatment

All values expressed as percentage of mean applied radioactivity (% AR). Mean values determined outside the study report.



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Table CA 7.2.2.3-20: Characterisation of radioactivity following treatment of Stilwell system with [cyclohexyl-1-14C]-spiroxamine at 20°C under aerobic conditions -َ © Water laver [% AR]

		wate	r layer [%	o AKJ							Â,
Com-	Repli-				Incubatio	on time (I	DAT)	~		5	0°
pound	cate	0	0.25	1	2	7	14	A 33	56 🦼	100	
Chiror	А	87.1	56.3	48.7	27.0	9.1	2.1	@0.4	n.d.	n.d.	
Spirox- amine	В	72.9	54.3	37.1	26.0	9.9	2.3	0.3	- OF	% .d.	ĈQ
amme	Mean	80.0	55.4	42.9	26.5	9.5	2.2	0.4	\$9.1	y n.d.	0
M01	Α	0.2	n.d.	n.d.	0.4	0.3	065	n.d. (n.d.	n.d	, e
(de-	В	0.5	n.d.	0.3	0.5	0.4	6 9.3	n.d. 🖉	n.D	nd.	Ő
sethyl)	Mean	0.4	n.d.	0.2	05	0.4	§ 0.4	n.Ø	n.el.	"On.d. 🎽	×
M02	Α	0.7	0.6	n.d.	6 .8	0.2 🖄	n.¢5°	A 2	√n.d.	n.d 🌾	
(despro-	В	0.7	n.d.	n.d.	0.8	021	s_n.d.	0.2	o _{n.d.} Q	ŋ d.	
pyl)	Mean	0.7	0.3	n.d. 🔬	0. Z °		🔊 n.d. 🔬	0.20	ned.	≪ov.d.	
M03	Α	10.8	8.2	6.4 Q [*]	. 802	2.4	y 2.70°	03	0.4	g 0.5	
(N-ox-	В	11.8	5.2	<u>54</u> 4	J.2 @	3.0Q	3.0	0.9	0 [°] 0.2	[»] 0.4	
ide)	Mean	11.3	6. 7	_≪ 5 .9 _∧	> 8.7, >	2.7	A.9	ر» 0.9 _{% را}	0.4 0 0.2 0 0.3	Q.5	
M06	А	n.d.	n.d.	Nn.d, N	n.@	<u>4.8</u>	°°∕3.8√?	4.Q	<u>4</u> .2	A.2	
(acid)	В	n.d.	n.d.	n.d.	d. ~	y 1.6 💥	9.5	A 9	07.7	3.4	
	Mean	n.d.	n.d.	ળ∂ર્લ.	`%n.d. %	1.6 1.7	×6.7	<u>Å</u> 4.8 á	§ 6.0 🦓	4.0	
M11	Α	n.d.	n.d	🔊 n.d. 👌	n.¢	R.C.	On.d.	0.3	0:3/	0.3	
(de-	В	n.d.	@v.d. 🔉	🖉 n.d. 🗭	n a.	On.d.	¥ 0.7℃	66	& 0.5	0.4	
sethyl acid)	Mean	n.d.	n.d.		, n.d.	n.d	~0 , 4	<u>ک</u> 0.5	© [°] 0.4	0.4	
M05	А	n.d	n.H.	Sn.d.	n.d.	_n⊾d.	n.d. ~	0.2	n.d.	n.d.	
(hy-	В	n.d. 🏾	And.	n.d.	Rd.	n.d.	n.d.		n.d.	n.d.	
droxy)	Mean	n,d.	n.d.	n.d.	n.d	o [©] n.d.∡ ∕ n.d ⊙	nkd.	<u>م</u> بر مربع	n.d.	n.d.	
Other	Α	ýn.d.		₽ .0. ∧	🔊 n.d 🕉	Q .7	Q.2	≈ 1.9	1.5	1.8	
un-	B	n.do	×Q,3	≪ ^y n.d∧	n.Q.	Ø0.8	§ 0.7_©	2.3	2.4	2.5	
knowns	Mean	n.d.	~0.5 (n.đ.y	n.d.	[∞] 0.8 €		2.1	2.0	2.2	

Production of the state reported to the stat



Table CA 7.2.2.3-21: Characterisation of radioactivity following treatment of Stilwell system with [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions -Sediment layer [% AR]

	See	diment la	ayer [%	ARJ							Š
G	Repli-				Incuba	tion time	(DAT)	~ .		0)	0°
Compound	cate	0	0.25	1	2	7	14	33	56 🦿	100	
Sminor	А	0.7	17.3	12.3	15.8	22.3	22.7	© [®] 22.7	17.5 "	26,3	
Spirox- amine	В	1.7	7.2	17.4	16.5	23.5	20.8	18.8	6.4	20 .9	ĈQ
annie	Mean	1.2	12.3	14.9	16.2	22.9	21.8	20.8	<u>`</u> `16.5 `>	23.6	1
M01	А	n.d.	1.1	n.d.	0.6	1.0	Ø/d.	0.1	0.2	0.	
(desethyl)	В	n.d.	0.4	n.d.	0.7 [°]	0.9	Sn.d.	0.1	0.3	<u>Å</u> .7	Ő
(desetilyi)	Mean	n.d.	0.8	n.d.	0.7	1.0 🔬	n.d.	<u></u>	°8.3		
M02	Α	n.d.	0.4	0.5	0.5	0.8	<u>b</u> j°	Ø.6	ا √0.5 €	0 0.6	
(despropyl)	В	n.d.	0.2	0.4	0.4	1)0	~¶.0	^{~~} 0.6 \	0.5	14	
(despropyr)	Mean	n.d.	0.3	0,5	B .5	<i>≫</i> 0.9 ≰	ົ 1.1		8,5	≪1 [×] .3	
M03	Α	n.d.	0.2	0.4	Ø0.4 ×	1.4		\$ 56	0.5	0.6	
(N-oxide)	В	n.d.	n.d.	s_0.4 🥡		1.Q	0.9	_∞ ŏ.7 () ^v 0.6 Ø	[™] 0.7 .0.7	
(it oxide)	Mean	n.d.	0.1 🕺	0,4%	Q.6	≈1.5	A1.0 C	» 0.7 _{% /}	0.6	0 7	
M06	Α	n.d.	n.d	în.d.	@r.d. 🔪	√n.d. Ó	× 0.6 ×	1.5	% ₽.4	<u>4</u> 2.6	
(acid)	В	n.d.	II.C.	6 M.d.	n.d	n.d	10	J.6	¢¥2.1	1.9	
(acid)	Mean	n.d.		🔊 n.d. 🥎		n.d.	A.O	A 1.6 S	1.8	2.3	
M11 (de-	Α	n.d. *	₿ n.d	n.d	ðel.	An.d.	0 n.d. 0	n.de	n?¢.	n.d.	
sethyl acid)	В	n.d.Ø	₽.€	fØð.	Sn.d.	0 n.d.	n.d	72.d. 	& n.d.	n.d.	
settiyi deld)	Mean	n.d.	n.d.	An.d.	🖱 n.d. 🗡	n de 🗸	ngd.		O [°] n.d.	n.d.	
M05	А	n.d.	∽n.d	1.2%	0.0	ĺ.4	2.4 %	2 1.4 ₀	0.5	1.1	
(hydroxy)	B 🦻	n.d.	n.do	104	<u>0.7</u>	_≈ ∿1.5 ≪) [*] 2.2	14	0.5	1.3	
(liyuloxy)	Mean	n.d.	p.d.	ð f. 3 🔬	Ø 0.7 Č	1.5	2.3	<u>65</u> 4	0.5	1.2	
Other	A	ngel.	Kn.d.	1.0	0,7~>>	10"	Ø.1	°≫0.3	0.2	0.5	
unknowns	Ľ,	n.d.	n.d	1.0 n.d.	QC)4	@1.7	n.d.	[≫] 0.4	0.4	0.4	
unkilowils	Mean (<u>) n.d. y</u>	n.ð	_^ €,5	• ~0.6	2 1.5 S	0,1	0.4	0.3	0.5	

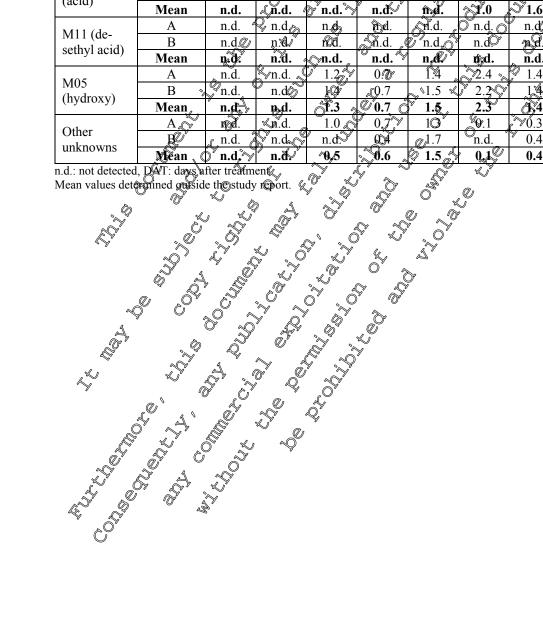




Table CA 7.2.2.3-22: Characterisation of radioactivity following treatment of Stilwell system with [cyclohexyl-1-¹⁴C]-spiroxamine at 20°C under aerobic conditions – 7 tal system [% AR]

	tal	system	[% AR]							<u> </u>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
G	Repli-				Incuba	tion time	(DAT)	~ .		\mathcal{O}	0°
Compound	cate	0	0.25	1	2	7	14	33	56 🦿		
Quince	Α	87.8	73.6	61.0	42.8	31.4	24.8	@23.1	17.5 "	26,3	
Spirox- amine	В	74.6	61.7	54.5	42.5	33.4	23.14	19.1	13.6	20.9	Ô
annne	Mean	81.2	67.7	57.8	42.7	32.4	24	21.2	°∕¶6.6 °≈	23.6	
M01	А	0.2	1.1	n.d.	1.6	1.3	Ø.5	0.1	0.2	0.	Ô
(desethyl)	В	0.5	0.4	0.3	1.2	1.3	6 %0.3	0.1 0	0.3	Å.7	Ő
(desetilyi)	Mean	0.4	0.8	0.2	A. 2	1.4	0.4	00	6.3	.O0.6 🏅	×
M02	А	0.7	1.0	0.5	1.0	1.0	b)°	69.8	√y 0.5 [°]	1.14	
(despropyl)	В	0.7	0.2	0.4	1.2	12	°. 4.0	0.8	0.5%		
(despropyr)	Mean	0.7	0.6	0,5	& .1		$\int 1.1_{\text{K}}$	0,80	8,5	≪1.3	
M03	Α	10.8	8.4	<u>6.8</u>	Ø8.6	9 3.8	3.0° 3.9	£3	0.9	1.1	
(N-oxide)	В	11.8	5.2	1 5.8 n	<u>10.</u>	4.0		<u> </u>	0.8°		
(IN-OXICE)	Mean	11.3	6.8 🕺		Q.3	% 4.2́	A.3.9 (¥ 1.6	0.9	<u>A</u> 2	
M06	А	n.d.	n.¢	ñ.d.	@1.d. 、	≪1.8 Ć	4.47	6. Q	\$.6	4 7.1	
(acid)	В	n.d.	n.c.	& M.d.	n.d	1.6	108	6 .5	¢9.8	5.3	
(aciu)	Mean	n.d.	"n.d. 4	🔊 n.d. 🏷		1.7	A.7	ð 6.4 Ś	7.8	6.3	
M11 (de-	А	n.d. *	₿ [`] n.d _⊘	n.d	ðel.	An.d.	0 n.d. 0	0.3	0,3	0.3	
sethyl acid)	В	n.d.Ø	n.€/ຶ	fØð.	Sn.d.	n.d.	0.70	0.5	% _0.5	0.4	
settiyi acid)	Mean	n.d.	n.d.	⊘n.d .	n.d. 🐬	nd	Ø 54		O″ 0.4	0.4	
M05	Α	n.d.	∛n.d. ~		0.0	1.4	2.4 🗞	2 1.6	0.5	1.1	
(hydroxy)	B 🦻	n.d.	n.dô	1,QF	0.7	_≈ ∿1.5 ≪	r . // /	150	0.5	1.3	
(liyuloxy)	Mean	n.d.	p.d.	Å1.3	Ø 0.7 Ć	1.5	2.3	B 6	0.5	1.2	
Other	A	nod.	ר.6	1.0	0,7~>>	200 "	₩.3	Ž2.2	1.7	2.3	
unknowns	₿¢°	n.d.	0.3		QC4	@2.5	0.7	∛ 2.7	2.8	2.9	
	Mean (ð n.d. 🔊	0.5	~ 0,5	× \$0.6	§ 2.3	1,1	2.5	2.3	2.7	

n.d.: not detected, DWT: days after treatment Mean values determined gaiside the study oport.

B. Material Balance

The material balance (mean) at each sampling interval sanged from 98.3 to 108.0% AR for the two test systems. The overall mean material balance was 102.1 and 00.9% AR for the Hoenniger and Stilwell water/sediment systems respectively.

C. Extractable and Non-Extractable Residues

The mean proportion of total radioactivity extracted from sediment samples increased slowly over time from 7.5% AR (mean) at 0 DAT to 49.3% AR (mean) at 100 DAT in the Hoenniger system. The Stilwell system increased similarly, from 0.2% AR (mean) at 0 DAT to 79.5% AR (mean) at 100 DAT. The mean proportion of total radioactivity in the overlying water declined slowly over time from 87.0% AR (mean) at 0 DAT to 2.1% AR (mean) at 100 DAT in the Hoenniger system. The Stilwell system declined similarly, from 92.4% AR (mean) at 0 DAT to 6.9% AR (mean) at 100 DAT. Non-extracted residues (bound residues) increased slowly throughout the incubation, reaching maximum levels of 44.0% AR (mean) in Property at 400 DAT and 48.9% AR (mean) in Stilwell at 76 DAT.

D. Volatile Radioactivity

Significant adioactivity carbon dioxide was in both systems from 30 DAT, reaching maximum levels of 6.8% AR in Hoenniger at 100 DAT and 16.8% AR in Stilwell by 100 DAT. Subsequently, selected samples of PU bung extracts from both systems were analysed by HPLC and the volatile radioactivity was confirmed to be volatile ¹⁴C-spiroxamine.



The level of applied radioactivity recovered as volatile organic material ≤0.1% AR for all systems measured.

E. Degradation of Parent Compound

Following application of [cyclohexyl-1-¹⁴C]-spiroxamine, spiroxamine showed apid dissipation in the water phase of both systems, declining from 83.7% AR (mean) at 0 DAT to \$6% by 100 DAT in the Hoenniger systems. Similarly, in the Stilwell system spiroxamine showed rapid dissipation in the water phase of both systems, declining from 80.0% AR (mean) at 0 DAT to ≥0. K by 100 DAT. In the Hoene niger system, the amount of spiroxamine in the sediment jureased to a maximum of \$2.0% AR (mean) after 14 DAT and subsequently decreased to 42.7% AR (mean) after 400 DAT. In the Stillwell system, the amount of spiroxamine in the sediment increased to a maximum of 23,6% ARQ means after 100 DAT. Q

Degradation of [cyclohexyl-1-14C]-spiroxamine in the total system was accompanied by the formation of one major degradation product M06 (spiroxamine-acid: max 7.7% AR (mean) at 36 DAY) which was determined to be >5% AR for more than two consecutive time points. Additionally, several other minor metabolites M01 (spiroxamine-desethyl: max 1.9% AR (mean) at 33 DAT), M02 (spiroxamine-despiropyl: max 1.9% AR (mean) at 33 DAT), M03 (spiroxamine-Noxide max 9.3% AR (mean) at 2 DAT), M11 (spiroxamine-desethyl acid: max 0.5% AR (mean) at 33 DAP) and M05 (spiroxamine- bydroxy max 2.3% AR (mean) at 14 DAT). Some other minor undentified metabolites were observed but none of which exceeded a total of 2.5% AR (mean) at any sampling interval.

F. Degradation Kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.2.2.3/08 (M-763141-01-Q).

Conclusions

[Cyclohexyl-1-14C]- Firoxamine derade (In water/sediment systems ander aerobic conditions (20°C, dark) with 0.6-20\$% of applied radioactivity remaining as parent compound after 100 DAT in the Hoenniger and Stilwell systems, respectively. Carbon dioxide was a major degradation project (max 16.8% at 100 BAT), while no volatile organic compound were observed. The amounts of non-extractable radioactivity were 44.0% and 48.9% AR (mean) at the end of the study for Hoenniger and Stilwell systems, respectively. The major metabolic pathways involved oxidation of a methyl group to form M06 (spiroxamine-acid, maximumo).7% AR (mean)). C

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) is performed in the report presented under point KCA 7.2.2.3/08 (M-763141-01-1). Ŵ

 \bigcirc

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study was conducted in accordance with study guideline(s) BBA Ref .: Degradability and Fate of Plant Protection Products in Water sediment System 5-1 (Dec. 1990) (similar to required guideline, minor differences). The study is considered valid to assess fate and behaviour of [cyclohexyl-1-14C]-spiroxamine in aerobic water

the state of the s



Data Point:	KCA 7.2.2.3/02
Report Author:	
Report Year:	1996
Report Title:	Aerobic metabolism of KWG 4168-N-Oxide in an aquatic model ecosystem
Report No:	PF4180
Document No:	<u>M-006094-01-1</u>
Guideline(s) followed in	BBA Ref.: Degradability and Fate of Plant Protection Products in
study:	Water sediment System 5-1 (Dec. 1990)
Deviations from current test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the reliability of the study (described, for study summary)
Previous evaluation:	yes, evaluated and accepted DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GQP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Supportive only O [*] O [*] Supportive only O [*]
Evenutive Summary	

Executive Summary

The route and rate of degradation of [cyclohexyl-1-10]-spirbxamine N-oxide (M03) way investigated in one water/sediment systems (Hoendiger⁸, silt loan, 4.4% OC, pH 5.7) under aboratory aerobic conditions in the dark at 20°C for up to 6 days. The purpose of this study was to investigate the metabolite M03 which was detected in a previous water sediment crudy at low concentrations (see KCA 7.2.2.3/01 (<u>M-006015-01-1</u>)) and was not intended to be a full standalone study. The study was intended to simulate a use rate of 750 a.s./ha_therefore considering a transformation of 30% of the parent spiroxamine into spiroxamine N-oxide (M03) and a water depth of 30 cm the application rate corresponds to 0.066 mg/500 mL water. Test systems were failed with a layer of sediment to a depth of 1.7 cm (31.7 g dry weight) and overlying water (500 mL)

Two vessels were treated with application solution, closed with an oxygen permeable trap attachment and kept in the dark at $20\pm2^{\circ}$ At the first sampling dates (day 4 and 3), only water samples were taken, whilst from day 6 onwards complete patches were analysed

After decantation the sediment was extracted with accionitrile at room temperature three times. The combined fiftered extracts were investigated by TLC. The radioactivity still present in the material of the filter was determined by combined combustion and LSC of trapped combustion gases. The stability of [cyclohexyl-1-¹⁴CI spiroxamine N-oxide (M03) under the condition of processing was demonstrated by adding the test spostance to an aliquet of most sediment and by processing as described above.

All liquid extracts were radioassayed Radioactive residues bound in the sediment were determined by combined combustion and LSC of trapped combustion gases. Aliquots of the sediments extracts or supernatant water were investigated by TQC on alica gel with one solvent systems. Components were visualised by autoradiography adioactivity scanning and in the case of unlabelled reference substances by reaction in an iodime chamber.

The overall mean material palance was 109.2% AR for the Hoenniger water/sediment systems.

A total amount of 22% of the test substance [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) was detected in the supernation water after 6 days. 40.9% AR was extracted in the form of the transformation product spiroxamine, with 7.2% AR found in the sediment and 3.7% AR from the aqueous phase. Another portion of 20.3% AR constituted non-extractable sediment residues.



I. **Materials and Methods**

A. Materials

1. Test Items

[cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03)

* Denotes po 3.4

Specific Activity:

Radiochemical Purity:

2. Test System (water/sediment system)

haracterised in Table The study was performed using the water/sediment so m`aş L.

Table CA 7.2.2.3-23: Physico-chemical properties of the water sedement systems

Parameter & & & Water/sediment system &
Water/sediment system designation
Geographic Location
City WipperPurth
Country
Geographic Location City Country Textural Classification (USDA) Sand [50 - 2000um] Silt [2 - 50 µm] Clay [< 24µm] Clay
Textural Classification (USDA)
Sand $[50 - 2000 \text{µm}]$ Silt $[2 - 50 \text{µm}]$ (%) $(%)$
Silt [2 – 50 µm] 🖓 🖏 🖉 (%)
Silt $[2 - 50 \mu m]$ $(2 - 50 \mu m]$ $(3 - 51.3)$ Clay $[< 2 \mu m]$ $(3 - 50 \mu m]$ $(3 - 51.3)$ pH $(3 - 50 \mu m)$ $(3 - 50 \mu m)$ $(3 - 50 \mu m)$ $(4 - 50 \mu m)$ $(5 - 50 \mu m$
in H ₂ O start/end $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $6.2 / 6.0$
in KCl start/end A A S S S.6 / 5.7
pH \swarrow m H ₂ O start/end \swarrow \checkmark \checkmark \checkmark \checkmark \checkmark \checkmark \checkmark \checkmark \sim
P _(total) (mg/kg) start/end 1030/1000
P(total) (mg/kg) start/end 3 4000/4000 P(total) (mg/kg) start/end 3 1030/1000 Biological (respiration) activity (mg/CO2/h/kg 3 3 Sediment TS) 3 3
Sediment IS)
Initial, DAT 0 21
Final, 100 Dopt 120
Total organite carbon (mg/ \mathbb{O}) $4/7$
P(total) (mg/kg) start/end 4000/4000 Pi(total) (mg/kg) start/end 1030/1000 Biological (respiration) activity (mg/CO ₂ /h/kg 21 Sediment TS) 12 Final, 100 D/OT 120 4/7 Hardness (mg equiv CaCO ₃ /L) Oart/end 8.7



Parameter	W	Vater/sediment sy	stem
Water/sediment system designation:		Hoenniger	01°
Nitrate content (mg/L) start/end		77.3/2	
Phosphorus content (mg/L) start/end		<0.03/<1	
Wa	ter characteristics	-G	4 . 9
Total organic carbon (mg/L)		4 / 7	
Hardness (mg equiv CaCO ₃ /L) start/end	\$	85) ×	
Nitrate content (mg/L) start/end	- T	ØJ.3/2	
Phosphorus content (mg/L) start/end	d,	0.03/<1	

⁴ Calculated by multiplying organic carbon content by 1.724 (not exported)

Although location not specified, the report does state that the source of the test system was from the same location as Α used for study KCA 7.2.2.3/01 (M-006015-01-1) \$

The sediments and the water were collected from an artificial damined poind (Hoenniger). No details provided on test system history. Prior to study initiation, the aqueous settiment was passed through a 2 mm mesh sieve and thoroughly mixed before the dry weight was determined. The water samples were filtered through paper filters.

B. Study Design

1. Experimental Conditions

The behaviour of [cyclohexyl-1 d^4 C]-spiroxamine N oxide (\$103) was investigated in one sediment/water systems (Hoenniger) over a period of 6 days. The purpose of this study was to investigate the metabolite M03 which was detected in a previous water sediment study of low concentrations, see KCA 7.2.2.3/01 (M-006015-01-).

Test systems were filled with a layer of sediment to a depth of 1. Tem (31.7 g dry weight) and overlying water (500 mL). The water layer was genery agit and (30 rpm) by use of a magnetic stirrer. Each test vessel was attached to a calcium bydroxide volatile trap with quarts wool plugs and polyurethane foam bungs to collect carbon dioxide. Samples were incubated in the dark at a temperature of 20±2°C. The study was intended to simulate a userate of 750 fs./ha, therefore considering a transformation of 50% of the parent spiroxamine into spiroxamine N_zoxide (M03) and a water depth of 30 cm the application rate corresponds to 0.066 mg/500 mL water.

2. Sampling

A C Ľ Duplicate treated samples of each water sediment system were removed for analysis after 1, 3 and 6 days of incubation. At the first sampling dates (days) and s, only water samples were taken, whilst on day 6 complet@batches wer@analysed.

3. Analytical Procedure

After decantation, the sediment was extracted with acetonitrile at room temperature three times. The combined filtered expracts were investigated by FLC. The radioactivity still present in the material of the fister was determined by confisient combustion and LSC of trapped combustion gases. The stability of [cyclohexyl-]⁴C]-spiroxatione N@xide (M03) under the condition of processing was demonstrated by adding the test substance of an aliquot of moist sediment and by processing as described above.

All liquid extracts were radioas sayed. Radioactive residues bound in the sediment were determined by combined combastion and LSG of trapped combustion gases. Aliquots of the sediments extracts or supernated water were investigated by TLC on silica gel with one solvent systems. The limit of detection (LOD) for a \mathfrak{G} ingle peak was $\geq 0.1\%$ of the applied radioactivity. Components were visualised by autoractography, radioactivity scanning and in the case of unlabelled reference substances by reaction in an iodine shamber.



II. **Results and Discussion**

A. Data

The distribution and characterisation of radioactivity for the water/sediment system incubated $\frac{1}{200}$ following application of [cyclohexyl-1-14C]-spiroxamine N-oxide (M03) are summarised in Table 7.2.2.3-24 and Table CA 7.2.2.3-25. ñ

Table CA 7.2.2.3-24: Recovery and distribution of radioactivity following treatment of Hoen Ś

7.2.2.3-24 and Table CA 7.2.2.	3-25. ry and distribution of radioactivity following treatment of Hoen- stem with [cyclohexyl-1- ¹ ©]-spiroxamire N-oxide (\$403) order of conditions [mean % AR]
T.I.I. (14 7 4 4 4 4 B	ry and distribution of radioactivity following treatment of Hoen- stem with [cyclohexyl-1-10]-spiroxamine N-oxide (1403) under conditions [mean % AR]
Table CA 7.2.2.3-24: Recover	'y and distribution of radioactivity following treatment of Hoen- $\sqrt{2}$
niger sys	conditions [mean % AR *
	conditions [mean % AR]
Compound	Incubation time (DAT) Image: Constraint of the constraint of t
Supernatant water	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
Sediment	
Non-extractable radioactivity	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Total	$\begin{array}{c c c c c c c c c c c c c c c c c c c $
n.a.: not analysed, DAT: days after tre	
Overall mean radioactive from the wh	iole system was $108,2\%$ ARat 6 DAA, $0^{\prime\prime}$ $3^{\prime\prime}$ $2^{\prime\prime}$ $3^{\prime\prime}$ $3^{\prime\prime}$
The values expressed as mean percenta	
S' 4	
ĝ A d	
Ó A S	
	x ~~
õ	n.a. 2 n.a. 2 76.0 n.a. 2 n.a. 2 2 1.1 2 atment nole systemy as 109.2% AR36 0 DAt age of antijed ramactivit (% AR3) 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	1 3 6 n.a. 0 na 76.0 n.a. 0 na 76.0 n.a. 0 60 action 0 0 action 0 action



Table CA 7.2.2.3-25: Characterisation of radioactivity following treatment of Hoenniger system with [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) under aerobic conditions [% AR]

	tions [% .	AKJ						Â,
				Incubation	time (DAT)	^ .	5	Ø
	Commonwel		1		3		í D	
	Compound	Repli-	Replicate	Replicate	Replicate	Replicate	Replicate	
		cate A	В	Α	BA	A Ô	₿ [°]	ĝ
	Spiroxamine	0.3	0.3	2.3	3.0	1.9 >>	\$.4	1
	M01 (desethyl)	0.5	0.8	1.9	Ø .4	22	3.8	
ater	M02 (despropyl)	0.6	0.8	2.1	€2.3	Ø.9 🐔	3,3	Ő
W2	M03 (N-oxide)	76.3	80.3	52.4	52.6	23.5 🖓	D .5	, M
ant	M06 (acid)	n.d.	n.d	0.8	6,9	0.85		1
nat	M11 (desethyl acid)	n.d.	19RQ).	n.d	∘ ¶n.d.	Ø.9	0,5	
Supernatant water	M12 (despropyl acid)	n.d.	n.d.		n.d	n.d.	<0.1	
	M15 (ketone)	n.d.	n.d	@ 0.5 Q	0.9	n.Ø	@ n.d. 😽	1
	Total	77.7 🔊	82.2	× 60 A	62.7	31.7 '	∞ n.d. √ 34	
	Spiroxamine	n.a	_°~√n.a Ø	_ 17: 3 .	0 [×] n.a. ×	\$37.4 🖉	37.0	
	M01 (desethyl)	n Q (n.a	"An.a. 🖉	nca.	7.5	7.0	
	M02 (despropyl)	"n.a. V	r∛n.âx∛	[∞] n.a.	An.a.		2 4.7	
Sediment	M03 (N-oxide)	^Q n.a.⊘	a. 🎓	r n∡?	0 n.a.	<u> </u>	× 1.8	
dim	M15 (ketone)		Øn.a. S	Øa.	n.a	≫ ^O 3.6‰	3.1	
Se	Unknown 🔊	n.a. 🔬	🗇 n.a.	n.a.	dha.	0. © ′	3.1	
	Unextracted por- tion*	n.a. S	nga.	⊘ n.a. ×	h.a.	19.8	21.1	
	Total 🖉	, n.a.	n.a. O'	j Or.a. 🔬	n.a.	76.8	75.2	
	Total 🔊 🔗	≾ ŋ.̃a.	n,av	√∽ n.a. O [®]	yr.a.	108.5	109.9	
	Spireamine	Å ^v n.a _€	n A.	∑ n.æ,	n.a.	39.3	42.4	
	M05 (deseto) 1	y n.a.√	_~	riza.	y na	9.7	10.8	
	MO2 (despropyl) 🚿	n.a.	≯ n.a.√	n.a.	na.	8.0	8.0	
u u	M03 (Noxide)	Gnia. 🖏	nca.	Ö n.a	_@ n.a.	26.5	22.3	
/ste	M00 (acid)	ۇ n.a	🔊 🕅 .a. 🕥	🕅 n.a.	🖉 n.a.	0.8	1.2	
l sy	M11 (desethy acid)	n 🐨	n.a.	~ a. ~	n.a.	0.4	0.5	
Total system	M12 (degpropylő)	nr.a.	n.a		n.a.	n.d.	<0.1	
	M15 (ketone)	n.a. 🏏	n.a. O	An.a.	n.a.	3.6	3.1	
	Onknown 🔊	naar.	n.a 🖉	"Cn.a.	n.a.	0.8	0.5	
	U Total	- ∽ n.a.	້ ກ.ຄ.ັ	[™] n.a.	n.a.	89.1	88.9	

n.a.: not analysed, n.d.: not detected, DAT, days after treatment Overall mean radioactive from the who system was 1002% APCat 6 DAT.

B. Material Balance

The material balance was 109.2% AR at the one sampling interval where measured (6 day). ٥

C. Degradation of Parent Compound

A total amount of 22% of the test substance [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) was detected in the supermatant water of days. 37.2% AR were extracted in the form of the transformation product sproxamine from the sediment and a further 3.7% AR from the aqueous phase. Another portion of 20.3% constituted non-extractable sediment residues. The authors of the study concluded that the outcome of the experiment cannot be explained by degradation of the test compound during processing of the sediment, as it had been proved by recovery experiments with [cyclohexyl-1-14C]-spiroxamine Noxide (MO3) that it remains intact under the processing conditions.



III. Conclusions

The behaviour of [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) was investigated in one sediment water systems (Hoenniger) over a period of 6 days in a small scale investigation. The purpose of this study was to investigate the fate of the metabolite M03 which was detected in a previous water sediment study at low concentrations (KCA 7.2.2.3/01 (<u>M-006015-01-1</u>)). A total amount of 22% of the test substance [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) was detected in the supernatant water after 6 days. 37.2% was extracted in the form of the transformation product spiroxamine from the sediment and 3.7% from the aqueous phase. Another portion of 20.3% constituted non-extractable sediment/residues.

Assessment and conclusion by applicant: Study meets the current guidance and the requirements in 283/2013 The study was not conducted to study guideline(s) QPCD 398 (regulared guideline) in entirety. However, the study is considered supplementary information to assess fate and behaviour of [cyclohexyl-1-¹⁴C]-spiroxamine N-oxide (M03) in aerobic water sediment systems Data Point: Report Author: Report Year: 1996 MetaGolism & KWCA168 and its Koxide in a quatic model ecosystem and the Report Title: ecotoxicological relevance of the Noxide O Report No: M9937 🖉 M-032874-01& Document No: Guideline(s) followed in None study: Deviations from current None test guideline: Previous evaluation: yes, evaluated and accepted DAR (1907), RAR (2010), RAR 201 Ĩ GLP/Officially reco not applicable. nised testing facilities: 1 Acceptate fity/Reliabilit Supportive only K. Executive Summary O

This study was previously considered during the evaluation of spiroxamine (DAR (1997), RAR (2010), RAR (2017)) and is therefore included again for completeness. The study reviews the fate and behaviour of the metabolite M03 (spiroxamine-N-oxide) observed in the studies KCA 7.2.2.3/01 (M-006015-01-1) and KCA 7.2.2.3/02 (M-00604-01-1) and contains no primary data. Full summaries of the referenced studies are provided under their respectively locations.

Assessment and conclusion by applicant:

The study and its data are considered as supplementary data with no use in risk assessment.



Data Point:	KCA 7.2.2.3/04
Report Author:	;
Report Year:	2008
Report Title:	[1,3-Dioxolane-4-14C]spiroxamine: Aerobic aquatic metabolism
Report No:	MEF-07/483
Document No:	<u>M-303324-01-1</u>
Guideline(s) followed in	OECD 308; 95/36/EC amending 91/414/EEC, Annexes II and III; SETAC Prove-
study:	dures, March 1995
Deviations from current	None Co L L L
test guideline:	None G A A A A A A A A A A A A A A A A A A
Previous evaluation:	yes, evaluated and accepted
	RAR (2010), RAR (2017) 🖉 👋 🖉 🌾
GLP/Officially recog-	Yes, conducted under GLP Officially recognised (asting facilities)
nised testing facilities:	
Acceptability/Reliability:	Yes $(\begin{array}{cccccccccccccccccccccccccccccccccccc$

Executive Summary

The route and rate of degradation of [1,3⁺ Hoxolare-4⁻¹⁴C]-spiroxamine was investigated in two different water/sediment systems (Hoenniger and Anglerveiher, Germany) under laboratory perobic conditions in the dark at 20°C for up to 118 days (

The sediments and the water samples were collected from an application of Hoeninger, sandy loam, 3.8% OC, pH 5.2) and from a man made lake (Anglerweither, sand, 0.8% OC, pH 6.6). [1,3dioxolane-4-¹⁴C]-spiroxamine radiochemical purity 98% was applied to the surface of the water overlying sediment at a target rate of 0.25 mc a.s./L which was equivalent to a field application rate of 750 g/ha (assuming a water body depth of 30 cm). The water to sediment ratio was 3:1 (v/v). Sediment volumes of 175 mL (height ca, 2 cm) were transferred to the incubation vessels and water volumes of 520 mL (height ca, 6 cm) were added.

Prior to application of the test item, the systems were maintained under test conditions for the purpose of equilibration of 7 days. The flasks were incubated in the dark at 20°C. Aerobic conditions were maintained by the flow of air through an inflet. The laboratory phicrocosm flasks were connected with traps to collect CO₀ (using calcium hydroxide) and votatile organic compounds (using polyurethane foam). The redox potential as well as the pH and the dissolved oxygen content were determined before processing of water and sediment samples. Duplicate treated samples of each water/sediment system were removed for analysis after 0, 0, 25, 1, 2, 7, 14, 30, 61 and 178 days of incubation.

The water samples were analysed without any processing. The sediment samples were extracted with acetonitrile at ambient emperature, followed by a ket extraction for an hour using acetonitrile and by a hot extraction for 6 hours with methanol spiroxamine residues were analysed by HPLC. Identification of the test item was achieved by co-chromatography with reference item as well as by HPLC-MS/MS and HPLC. H-NMR.

The total material balance of the two water/sedupent systems was 94.0% of the applied radioactivity (AR) calculated as mean value of both systems and two parallel experiments for each system.

The radioactivity in the Anglerweiher water decreased steadily from 64.6% AR (mean) at 0 DAT to 10.9% AR (mean) at study end. The radioactivity in the Hoenniger water decreased from 62.5% of the AR (mean) at 0 DAT to 7.9% AR (mean) at study termination. Extractable ¹⁴C residues in the Anglerweiher sediment increased from 25.5% AR (mean) at 0 DAT, to a maximum of 63.4% AR (mean) at 2 DAT before decreasing to 18.9% AR (mean) at study termination. Extractable ¹⁴C residues in the Hoenniger sediment increased from 20.7% (mean) at 0 DAT, to a maximum of 46.6% (mean) at 2 DAT before decreasing to 32.8% AR (mean) at study end. The maximum of non-extractable ¹⁴C residues in the two sediments was 33.2% AR and 40.7% AR in Anglerweiher and Hoenniger, respectively (mean values).

At the end of the study, 27.1% (mean, Anglerweiher) and 7.6% (mean, Hoenniger) of the AR was present as CO₂. Organic volatile compounds amounted to less than 0.1% of the AR in both systems.



Following application of [1,3-dioxolane-4-¹⁴C]-spiroxamine, spiroxamine showed rapid dissipation in the water phase of both systems, declining from 62.5% AR (mean) at 0 DAT to below the LOD by 118 DAT in the Hoenniger systems. Similarly, in the Anglerweiher system spiroxamine showed rapid desipation in the water phase, declining from 64.6% AR (mean) at 0 DAT to below the LOD by 11 DAT.

In the Hoenniger system, the amount of spiroxamine in the sediment increased to a maximum of 54.2% AR (mean) after 2 DAT and subsequently decreased to 29.3% AR (mean) after 118 DAT. In the Anglerweiher system, the amount of spiroxamine in the sediment increased to a maximum of 60 % AR (mean) after 2 DAT, and subsequently decreased to 14.9% AR (mean) after 118 DAT

Degradation of [1,3-dioxolane-4-14C]-spiroxamine in the total system was accompanied by the for mation of one major degradation product M06 (spiroxamine-acid). In the water phase it amounted to a maximum of 25.6% of the AR (Anglerweiher) and 13.6% of the RR (Hoenniger Weiher). In the sect ment extracts M06 accounted for only 7.9% and 8.9% of the AR, respectively. Additionally several other minor unknown metabolites were observed but not identified in the report, with the sum of minor metabolites reached a maximum of 13.5% AR(61 D&T) and 4.2% AR (61 DAT) in the total system for the Anglerweiher and Hoenniger system respectively. Nevertheless, each unknown metabolito peak did not exceed 3% (mean) of the AR.

DT₅₀ values for the degradation of spire xamine were calculated in the report, however, are-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014), was performed in the report presented under point KCA 7.2.2 9/08 (10-763) 1-01-19. Materials and Methods

A. Materials

1. Test Items

[1,3-dioxolane-4-

ne-4-¹⁴CK spirox mine ?

The study was performed using the two water/ediment systems as characterised in Table CA 7.2.2.3-26.



Parameter	Water/sedin	ment system 🖉 🏷
Water/sediment system designation:	Anglerweiher	Hoenniger Weiher
Geographic Location		
	Leverkusen,	Wasserfuhr, close to Wips
City	North Rhine-Westphalia	s perfueth,
-		North Rhine-Westphalia,
Country	Gernany	Germany 25
	ment characteristics	
Textural Classification (USDA)	Sand A	Sandy Ivam
Sand [50 - 2000 μm] (%)	95.7 95.7	
Silt $[2 - 50 \mu\text{m}]$ (%)	· · · · · · · · · · · · · · · · · · ·	39.20
Clay [< 2 μ m] (%)	95.7 95.7 3.5 9 0.8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	§ 10.7
pH		5 - 5.2
in H ₂ O	\sim \sim 7.2 \sim \sim	5.2 × 5.2
in CaCl ₂	~ 0 6,6 0 J	
Organic Matter (%)		. . 6 .5
Organic Carbon (%)	0.8 5	0 5 3.8 V
N _(total) (%)	0 ² 5 ² 0.00 5 ⁴	Q <u>2</u> 6
P _(total) (mg P/kg)		Q493
Mierobiel Activity	O O A A	27 .Q
[mg CO_2 /hr/kg sediment (dry wt)]		
Initial, DAT 0 🔬 🔊 🖉 🤇		s 32.9
Final, 118 DAT	5 396 × 4 5 × 3.8 °	13.1
Cation Exchange Capacity (meq./100 g)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Ø 13.9
	ter characteristics	
Temperature 🖉 🖉 🖉	8.5 0	6.0
pH Q X X	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	7.2
	DAT 118*0	Initial: <2
Total ofganic carbon (10g/L)	DAT 118 %	DAT 118: 18
Hardness (°dH) "Deutsche Härte" German scale for hardnes of water, indicating [mg/L		
scale for hardness of water indicating [mg/L		9.8
<u>CaCO3</u>		070/
Oxygen Concentration (saturation)	6 ⁷ 6 81%	87%
Total Nitrogen (mg/L)	5.1	3.8
Redox Rotential E _h (my) at sampling	282 ×	300

Table CA 7.2.2.3-26: Physico-chemical properties of the water sediment systems

The sediments and the water were collected from an artificial dammed pond (Hoenniger) and from a small lake from a reclaimed gravel pit (Anglerweiher). Samples were taken for both the Hoenniger and Anglerweiher are on the 27th over the 2007. The pesticide history of the two sites shows no pesticides have been used. The sediment was collected from the top 20-50 cm and was passed through a 2 mm mesh sieve prior to use.

B. Study Design

1. Experimental Conditions

The behaviour of [1,3-dioxolane-4-¹⁴C]-spiroxamine was investigated in two contrasting sediment water systems (Hoenniger and Anglerweiher) over a period of 118 days.

The water to sediment ratio was 3:1 (v/v). Sediment volumes of 175 mL (height *ca*. 2 cm) were transferred to the incubation vessels, and water volumes of 520 mL (height *ca*. 6 cm) was added. Prior to



application the systems were maintained under the test conditions for an equilibration period of 7 days. The laboratory microcosm flasks were connected with traps to collect CO_2 (using soda lime) and volatile organic compounds (using polyurethane foam).

The test item [1,3-dioxolane-4-¹⁴C]-spiroxamine was applied onto the water surface at a rate of about 175 μ g/batch, corresponding to about 250 μ g/L water. The flasks were incubated in the dark at 2000 with the water layer gently agitated using a magnetic stirrer. Aerobic conditions were maintained by passive exchange of air through the solid traps.

2. Sampling

The redox potential as well as the pH and the dissolved oxygen coment were determined before processing of water and sediment samples. Duplicate treated samples of each water sediment system as well as volatile traps were removed for analysis after 0, 0.25, 1, 2, 7, 14, 30, 61 and 118 days of incubation.

3. Analytical Procedures

The supernatant water was decanted from the sediment and centrifuged. Aliquots of water were investigated by HPLC without concentration. Representative aliquots were also investigated by HP-TEC at optional sampling dates to confirm the EPLC esults. An aliquot of 59 mL se the centrifuged supernatant water was adjusted to alkaline pH app used for the determination of dissolved $CO_{2.5}$

The moist sediment was extracted svice with acctonitible for 60 min using a haker. Then, the sediment was extracted with acctonitrile ander terllux for 60 min. After each extraction step the samples were centrifuged and the supernatants were decayed. All extracts were combined for analysis.

Finally, the sediment was extracted once under frarsh conditions (methanol, 6 hour under reflux). The amount of radioactivity was determined by liquid sontillation counting (LSC) of appropriate aliquots. Aliquots of the sediment extracts were concentrated and analysed by HPLC. The extracted sediment residue was air-dried, weighed and homogenised in a planet mill. The amount of radioactivity in the non-extractable residue (NER) was detected by combistion/LSC.

The non-extractable (bound) residue remaining after this extraction procedure was representatively characterised for both sediments at day 118. The portion of humic humic acid and fulvic acid was determined using a sequence of treatments with NaOH, HCP, centrifugation, and washing.

Spiroxamine and the M06 web identified by co-chomatograph with reference compounds as well as by HPLC-MS/MS and HPLC-H-NMR. The LOO for a single peak in the sediment extracts and in water was 2.3% AR and 2.8% AR, respectively.

The radioactivity absorbed by the social lime 1^{4} CO₂ was liberated by 18% aqueous HCl and purged with nitrogen into cooled 0SC cocktails. The absorbed radioactivity in the scintillation cocktails was measured by LSC. The amount of 1^{4} CO₂ in the sediment was determined at the last sampling interval for both systems. 0^{4} CO₂ was quantified in the same manner as described for the calcium hydroxide.

The chemical identity of 14 CO₂ trapped in the calcium hydroxide was shown for a water/sediment sample of the Anglerweiher system at day 118. The carbon dioxide was re-liberated from the LSC cocktail by slow addition of glacial acetic acid and the RA was absorbed in a series of three connected trap vessels filled with aqueous MaOH. After RA determination of aliquots by LSC, aqueous Na₂CO₃ solution and aqueous BaC₂ solution were added to the solution of the first trap. After centrifugation, aliquots of the supernatative solution were radioassayed by LSC. The observed inclusion of 99.2% of the radioactivity of the NaOH solution into the 4 C]BaCO₃ precipitate was considered as a chemical proof for the identity of 14 Cccarbon dioxide.

Votatile organic compounds possibly contained in the PU foam plugs were extracted with ethyl acetate and alignots were radio-assayed by LSC. Due to the low amount (<0.1% AR) they were not further analysed.



4. Determination of degradation kinetics

II.

The DT₅₀ and DT₉₀ of spiroxamine determined in the study was reported for each site. However, a ϖ^2 evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) and the EFSA guidance on deriving DegT_{50} values from laboratory and field dispation studies (EFSA 2014), was performed in the report presented under point KCA 7.2.2.3/08 M-763141-01-1).

Results and Discussion

- O

A. Data

The redox potential in the supernatant water of both test systems after acclimation remained of high positive mV-values (225 to 272 mV). The redox potential in the second was between 140 mV and 279 mV. Some variations between different vessels were observed In general, sufficient avget (approximately 72 - 98% of saturation) was available in the individual vessels at each sampling time. The data showed that the supernatant water was aerobic during the entire incubation period

The microbial activity indicated that the systems were biologically active during the entire period of the test. In the Anglerweiher system as well as in the Hoenniger system, are duction of the microbial activity was observed during the course of the experiment. This is often observed for laboratory experiments due to the gradual depletion of nutricots in the sediment and the lack of further sable organic matter as a source of energy. The total organic carbon content (TOČ) of the water phase was in a range of <2 to 18 mg/L in both systems.

The extraction efficiency of the method was tested for sediment samples of day 0 (approximately 2 h post-application). A total of 91.1% and 86.4% AR was extracted from sediment of Anglerweiher and Hoenniger Weiher, respectively, using three times acetonitrile (two extractions at ambient temperature and one extraction under reflux, and one extraction under aggravated conditions with methanol (Table B.8.4-7 and Table B.8.4-8). This proceedure, left a non-extractable residue of only 3.3% and 7.7% of the AR for the two sedements. The ossults indicated that [1,3-dioxolane-4-14C] spiroxamine was rapidly bound to the sediment and that the extraction method was suitable to extract the applied test item from the sediment matrix.

The distribution each water sediment system incubated at 20°C following application of [1,3-dioxolane-4-14C]-spiroxamine are summarized in Fable CA 7.2,2.3-27 and Table CA 7.2.2.3-28. The characterisation of radioactivity for each water/sediment are summarised (as overall means) in Table CA 7.2.2.3-29 and Table CA 7.2,2,3-33. The characterisation of radioactivity for each separate layer for each water/sediment are summarised (agridividual repricates) in Table CA 7.2.2.3-30 to Table CA 7.2.2.3-32 for the Anglerweither system and in Table CA 7.2.2.3-34 to Table CA 7.2.2.3-36 for the Hoenniger Weiher system?

glerweiber system with [1,32dioxolane-4-14C]-spiroxamine under aerobic

Table CA 7.2.2.3-27: Recovery and distribution of radioactivity following treatment of An-

	ons ane	ang A	K						
	Ô,	2. d.) [*]	Incuba	tion time	e (DAT)			
Compound		0.25	1	2	7	14	30	61	118
Overlying water	61.8	48 .0	46.8	23.1	28.0	33.7	27.4	25.7	11.4
Sediment extract C	26.5	20.2	41.1	64.3	52.9	45.6	43.3	29.4	20.2
(Sub-wildi)	91.1	95.7	87.7	88.2	80.9	76.5	70.0	51.9	31.0
Non-extractable radioactivity	3.3	2.1	6.0	7.2	11.7	16.4	17.0	25.8	33.2
CQ37 & CQ37	n.a.	< 0.1	0.2	0.3	0.9	1.5	6.6	13.4	27.1
Volatile organic	n.a.	< 0.1	< 0.1	< 0.1	0.1	0.1	<0.1	< 0.1	< 0.1
Total 💭	94.5	97.9	93.9	95.8	93.5	94.4	93.6	91.2	91.3

nditions Inhoon (A D

n.a.: not analysed, DAT: days after treatment

Overall total recovery = 94.0% AR

All values expressed as mean percentage of applied radioactivity (% AR)



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Table CA 7.2.2.3-28: Recovery and distribution of radioactivity following treatment of Hoenniger Weiher system with [1,3-dioxolane-4-14C]-spiroxamine under aerobic conditions [mean % AR]

				Incuba	tion time	e (DAT)	~		<u>,</u>
Compound	0	0.25	1	2	7	14	30	614	118
Overlying water	62.5	64.7	38.2	21.5	16.0	16.0	6.9	402	A.9
Sediment extract	23.9	22.8	40.9	54.4	45.4	39,0	48.4	× 44.4 v	Q38.1 K
(sub-total)	86.4	87.5	79.1	<u>7</u> \$9	58.5	\$5.0	55.3	J 48.5	43
Non-extractable radioactivity	7.2	8.5	15.2	20.3	34.4	38.0	38.2	409	40,7
CO_2^*	n.a.	< 0.1	0.1	∮ 0.1	0.20	0.4	Ø.8	Q.8	A.6 &
Volatile organic	n.a.	< 0.1	<0.1	< 0.1	<q1< td=""><td><i>≤</i>0.1</td><td><i>i</i>\$0.1</td><td>0.1 (گ> _</td><td>€<0.1.®</td></q1<>	<i>≤</i> 0.1	<i>i</i> \$0.1	0.1 (گ> _	€<0.1.®
Total	94.1	96.1	940°	96.2	<u>~</u> 93.1	93.4	₽94.40	ຶ 92. 5	91

n.a.: not analysed, DAT: days after treatment

Overall total recovery = 94.0% AR

All values expressed as mean percentage of applied radeactivity A AR

Ø Table CA 7.2.2.3-29: Characterisation of radioactivity following treatment of Anglerweiher system in the total water-sediment system with [1,3-dioxolane-4-14]-spiroxamine under gerobic conditions mean & AR Over few of means

			Ô ^y	<u>0r · y</u>	Incuba	tiød time		ĩ " ĩ		
Compound		0 @	0.25	A.			14	30	61	118
Carino manino	W	64.0	75%.5	40.7	©15.5 🖇	14	19	n.d.	n.d.	n.d.
Spiroxamine	S	25.5) 19.8 🔇	39.84	60,1	43:19	°≈¥5.2 °	Q31.3	17.1	14.9
M06	W s	Øn.d. (D n.d	2	4.7°	9.4	\$25.6~	234	15.1	3.3
(acid)	s	n.d.	n.d.	SY.	A.8 É	3.0	4.69	29	6.3	4.0
Min on motok olitoo*	Ŵ	n d.	_≪ n.d.	3.8	3.7~	4,3	Q,5	°~2.8	7.5	7.5
Minor metabolites*	S	fo a	Qn.d.	1.3	23	6.0	©6.3 4	∮ 4.1	6.0	1.3

n.d.: not detected, DAT days after treatment

All values expressed as mean percentage of applied radioactivity & ARD

Each individual metabolite $\leq 3\%$ of the AR. Due to an application error a DAT, only one replicate was used for calculation of the values for 7 DAT.

0 Table CA7.2.2.3-30: Recovery and distribution of radioactivity following treatment of An-@lerwether system with [19-dioxolane-494C]-spiroxamine under aerobic conditions of the Water byer [% AR]

	<u> </u>	<i>()</i> ,	<u> </u>	(0)?	<u> </u>					
Compound	🚯 🖗 🖉		(0752)	, K	Incuba	tion time	(DAT)			
Compound	🖉 cateo 🕅	A	0.25	$0^{9}1.0$	2 💞	7	14	30	61	118
- A	ĭ _A O	© 01.8 ∧	78.0	41 47 4000	19,6	14.3	2.2	n.d.	n.d.	n.d.
Spiroxamine	В	©*67.49	73.	<u>4000</u>	@ 0.4	7.2^{**}	1.6	n.d.	n.d.	n.d.
	Mean 🖗	643	7 5 .5	20. 7 %	×15.5	14.3	1.9	n.d.	n.d.	n.d.
	A	n.d.	∽n.d^	\$1.7 \$	7.5	9.4	28.9	23.9	18.0	4.1
M06 (acid)	A B	, in a	n.d. n.d		1.8	4.3**	22.4	22.8	12.1	2.5
(aciu)	Mean "	ິ n.d.Û	n.d.	<u>"</u> Qľ	4.7	9.4	25.6	23.4	15.1	3.3
Minormo		n d.	~n₂.d.	Q 3.7	5.0	4.3	2.7	3.1	7.7	7.3
Minor me- tabolites*	₿ B	Jar.d.	≪n.d.	[∞] 4.0	2.4	0.9^{**}	4.2	2.5	7.2	7.8
tabolites*	Mean	∱ [®] n.d.∢	n.dQ	3.8	3.7	4.3	3.5	2.8	7.5	7.5

n.d.: not detected, DAAT: day Cafter treatment

All values expressed as percentage of applied radioactivity (% AR)

Each metabolite 3% of the AR

due to an application of ror, of sample A was used for calculation



ð

Table CA 7.2.2.3-31: Recovery and distribution of radioactivity following treatment of Anglerweiher system with [1,3-dioxolane-4-¹⁴C]-spiroxamine under aerobic conditions in the sediment layer [% AR]

									<u></u>	¥.
Repli-				Incuba	tion time	(DAT)		,	<u> </u>	ÿ
cate	0	0.25	1	2	7	14	2 30	61	118	
А	27.6	18.5	37.7	51.3	43.9	35.6	@28.8	18,9 ″	16,3	
В	23.5	21.1	41.8	68.9	15.8**	34.8	33.8	15.3	A3.1 Ø)
Mean	25.5	19.8	39.8	60.1 _{@s}	43.9	35.2	31.3	`17.1 `2	14.9	
А	n.d.	n.d.	n.d.	1.0	3.0	Ø.5	9.4 (6.2	4, V	J.
В	n.d.	n.d.	n.d.	2 .6 [®]	2.0^{**}	A.6	6.5 0	5.D		ĴV .
Mean	n.d.	n.d.	n.d.	1.8	3.0	4.0	70	63	Q 4.0	
А	1.0	n.d.	1.6	0.0	6.0 🔗	56)°	<i>6</i> % .5	L 5.1	1.2	
В	1.0	n.d.	1.0	4.6	2.3**	s.¶.5	1.7 \	7,99	J.S.	
Mean	1.0	n.d.	k .3	2,3		ر 6.3 ا	4.1 0	6.9	×1.3	
	cate A B Mean A B Mean A B Mean	cate 0 A 27.6 B 23.5 Mean 25.5 A n.d. B n.d. Mean n.d. Mean n.d. Mean 1.0 B 1.0 Mean 1.0	cate 0 0.25 A 27.6 18.5 B 23.5 21.1 Mean 25.5 19.8 A n.d. n.d. B n.d. n.d. B n.d. n.d. B 1.0 n.d. B 1.0 n.d. B 1.0 n.d.	cate 0 0.25 1 A 27.6 18.5 37.7 B 23.5 21.1 41.8 Mean 25.5 19.8 39.8 A n.d. n.d. n.d. B n.d. n.d. n.d. B n.d. n.d. 1.6 B 1.0 n.d. 1.0 Mean 1.0 n.d. 1.0	cate 0 0.25 1 2 A 27.6 18.5 37.7 51.3 B 23.5 21.1 41.8 68.9 Mean 25.5 19.8 39.8 60.1 A n.d. n.d. n.d. 1.0 B n.d. n.d. n.d. 2.6 Mean n.d. n.d. n.d. 2.6 Mean n.d. n.d. n.d. 2.6 Mean n.d. n.d. 1.6 0.0 B 1.0 n.d. 1.6 0.0 B 1.0 n.d. 1.0 4.6 Mean 1.0 n.d. 1.0 3.3	cate 0 0.25 1 2 7 A 27.6 18.5 37.7 51.3 43.9 B 23.5 21.1 41.8 68.9 15.8** Mean 25.5 19.8 39.8 60.1 43.9 A n.d. n.d. n.d. 1.0 3.0 B n.d. n.d. n.d. 2.6 2.0** Mean n.d. n.d. n.d. 2.6 2.0** Mean n.d. n.d. n.d. 2.6 2.0** Mean n.d. n.d. 1.6 0.0 6.0 B 1.0 n.d. 1.0 4.6 2.3** Mean 1.0 n.d. 1.3 2.3 0.0 5.0	cate 0 0.25 1 2 7 14 A 27.6 18.5 37.7 51.3 43.9 35.6 B 23.5 21.1 41.8 68.9 15.8** 34.8 Mean 25.5 19.8 39.8 60.1 43.9 35.2 A n.d. n.d. n.d. 1.0 3.0 25.5 A n.d. n.d. n.d. 2.6 2.0** 44.6 Mean n.d. n.d. n.d. 2.6 2.0** 44.6 Mean n.d. n.d. 1.6 0.0 6.0 54 B 1.0 n.d. 1.6 0.0 6.0 54 5 Mean 1.0 n.d. 1.0 4.6 2.3** 5.5 Mean 1.0 n.d. 1.0 4.6 2.3** 5.5	cate 0 0.25 1 2 7 14 30 A 27.6 18.5 37.7 51.3 43.9 35.6 28.8 B 23.5 21.1 41.8 68.9 15.8** 34.8 33.8 Mean 25.5 19.8 39.8 60.1 43.9 35.2 31.3 A n.d. n.d. n.d. 1.0 3.0 62.5 9.4 B n.d. n.d. n.d. 2.6 2.0** 44.6 65.5 Mean n.d. n.d. n.d. 2.6 2.0** 4.6 6.5 Mean n.d. n.d. 1.6 0.0 6.0 53 6.5 B 1.0 n.d. 1.0 4.6 2.3** 7.5 1.7 Mean 1.0 n.d. 1.0 4.6 2.3** 7.5 1.7	cate 0 0.25 1 2 7 14 30 61 A 27.6 18.5 37.7 51.3 43.9 35.6 28.8 18.9 B 23.5 21.1 41.8 68.9 15.8** 34.8 33.8 53 Mean 25.5 19.8 39.8 60.1 43.9 35.2 31.3 17.1 A n.d. n.d. n.d. 1.0 3.0 3.5 9.4 6.9 B n.d. n.d. n.d. 1.0 3.0 3.5 9.4 6.9 Mean n.d. n.d. n.d. 2.6 2.0** 4.6 6.5 5.2 Mean n.d. n.d. n.d. 2.6 2.0** 4.6 6.5 5.2 5.1 B n.d. n.d. 1.6 0.0 6.0 51 6.5 5.1 B 1.0 n.d. 1.6 0.0 6.0 51 5.1 7.7 7.9 Mean 1.0 n.d.	cate 0 0.25 1 2 7 14 30 61 118 A 27.6 18.5 37.7 51.3 43.9 35.6 28.8 18.9 h6.5 B 23.5 21.1 41.8 68.9 15.8** 34.8 33.8 5.3 43.1 Mean 25.5 19.8 39.8 60.1 43.9 35.2 31.3 17.1 14.9 A n.d. n.d. n.d. 1.0 3.0 2.5 9.4 6.9 4.0 B n.d. n.d. n.d. 2.6 2.0^{**} 4.6 6.5 5.7 3.3 Mean n.d. n.d. 2.6 2.0^{**} 4.6 6.5 5.7 3.3 Mean n.d. n.d. 2.6 2.0^{**} 4.6 6.5 5.7 3.3 Mean n.d. n.d. 2.6 2.0^{**} 4.0 7.9 6.3 4.0 A 1.0 n.d. 1.6 9.0 6.0^{*}

n.d.: not detected, DAT: days after treatment

All values expressed as percentage of applied radioactivity (%)

* Each metabolite $\leq 3\%$ of the AR.

** due to an application error, only sample A was used for calculation

Table CA 7.2.2.3-32: Recovery and instribution of radioactivity following freatment of Anglerweiher system with [1,3-dioxolane 4-14C] spiro camine under aerobic conditions in the total stater-sediment system [% R]

			\sim	-0			0	<u> </u>	×.	
Compound	Repli-		, "Y		Incuba	tion time	(D&T)	۵. ۵.	0	
Compound	cate	Ŏ	0.25) 1 /	20	7	<u>`</u> 14 %	🦻 30 🖏	61	118
	A 2	89.4	96. S	7808	61.9	⊳ \$8.2 ≪	Ĵ∛37.§Ş	288	18.9	16.5
Spiroxamine	В	90 2	94 ,1	81.8	Ø89.3 C	Š [*] - ≪,	36.4	8	15.3	13.3
	Mean	90.1	\$95.3	80.5	75,6	58Q ²	37.1	31.3	17.1	14.9
M06	JB (n.d.	n.d	1.7	85	d.2.4	32.4	[¥] 33.3	24.9	8.8
(acid)	, ŠBઁ, (D ^v n.d	n.ð.	25	×¥.4 /		27,0%	29.3	17.8	5.8
(aciu)	Mean	n.d. [×]	A.d.	2.1	≫ 6. <u>२</u>	12,4	29.6	31.3	21.4	7.3
Minormo	A A A B	\$0.0	Q _{n.d.} %	5.3	5.0	10.3	©7.8	9.6	12.8	5.5
Minor me-	BO	~1.0 ¢) n.d <u>.</u>	5.0 5.1	Ē.Ŏ	<u> </u>	¥11.7	4.2	14.2	9.1
tabolites 🗟	Mean 🕺	1,0	n Ø.	5.1	_∞ 6.0 _≪	10.3	9.8	6.9	13.5	8.5

n.d.: not detected, DAT: dags after matment

- due to an application error, only sample A was used for cateulation

All values expressed as percentage of applied radioactivity, (% AR

* Each metabolite $\leq 36^{\circ}$ of the AR.

Table CA 7.2.3-33 Characterisation of radioactivity following treatment of Hoenniger Weiher system in the total water-sediment system with [1,3-dioxolane-4-¹⁴C]-spiroxamine under aeropic conditions [mean % AR] – overview of means

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Confinitional	Ş	A			Incuba	tion time	(DAT)			
Compound 🛛		$\mathcal{S}'0$	0.2\$		2	7**	14	30	61	118
Spiroxamine _	W	62£5	64.7	\$5.5	16.3	3.6	1.5	n.d.	n.d.	n.d.
	9 S	23 .7	\$2 .8	Q40.5	54.2	45.2	37.8	48.4	35.1	29.3
M06	W	"În.d.	∼n.d.Ø	n.d.	2.0	7.9	13.6	6.3	3.8	4.7
(acid)	S) n.d 💭	n.d	n.d.	n.d.	n.d.	0.7	n.d.	5.0	8.9
Minor metabolities*	W		n.d.	2.0	3.3	1.7	0.9	n.d.	n.d.	0.2
Millor netadolines	s	ĵħ.d.	n.d.	n.d.	n.d.	n.d.	0.5	n.d.	4.2	n.d.

n.d.: not detected, DAT days after treatment

All values expressed as mean percentage of applied radioactivity (% AR)

* Each individual metabolite $\leq 3\%$ of the AR.

** Die to an application error at 7 DAT, only one replicate was used for calculation of the values for 7 DAT.



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Table CA 7.2.2.3-34: Recovery and distribution of radioactivity following treatment of Hoenniger system with [1,3-dioxolane-4-14C]-spiroxamine under aerobic conditions in the water laver [% AR]

10	ns m un	, water i		ΜŊ					
Repli-				Incuba	tion time	e (DAT)	~		S. O
cate	0	0.25	1	2	7	14	3 0	61	118
А	61.9	64.4	34.1	20.0	1.9	1.8	Øn.d.	n.d.	nd.
В	63.2	65.1	36.9	12.5	5.3	1.1	n.d.	pod.	Sn.d.
Mean	62.5	64.7	35.5	16.3 _A	3.6	1,5	n.d.	`` M.d. ``	n.d.
А	n.d.	n.d.	n.d.	1.7	11.1	Ø.9	6.5 (y 4.2	3,20
В	n.d.	n.d.	n.d.	2.2 [*]	4.8	<i>6</i> ¥5.3	6.1	3,3	é lé
Mean	n.d.	n.d.	n.d.	2.0	7.9	13.6	63	38	Q 4. 7
А	n.d.	n.d.	2.8	3.3	n.d. 🖇	næd.°	۵۷.d.	≪n.d.	n.d.
В	n.d.	n.d.	1.2	3.2	3.8	<u>`</u> ¶.8	n.d. \	n.d. 🦃	_9⊈°
Mean	n.d.	n.d.	2,0	3,3	31.7 3	<u> </u>	n.dÔ`	n.d.	40 .2
	Repli- cate A B Mean A B Mean A B	Repli- cate 0 A 61.9 B 63.2 Mean 62.5 A n.d. B n.d. Mean n.d. B n.d. B n.d. B n.d. B n.d. Mean n.d.	Repli- cate 0 0.25 A 61.9 64.4 B 63.2 65.1 Mean 62.5 64.7 A n.d. n.d. B n.d. n.d. A n.d. n.d. B n.d. n.d. Mean n.d. n.d. A n.d. n.d.	Repli- cate 0 0.25 1 A 61.9 64.4 34.1 B 63.2 65.1 36.9 Mean 62.5 64.7 35.5 A n.d. n.d. n.d. B n.d. n.d. n.d. A n.d. n.d. n.d. B n.d. n.d. n.d. B n.d. n.d. n.d. B n.d. n.d. n.d. B n.d. n.d. n.d. A n.d. n.d. 1.24	cate 0 0.25 1 2 A 61.9 64.4 34.1 20.0 B 63.2 65.1 36.9 12.5 Mean 62.5 64.7 35.5 16.3 A n.d. n.d. n.d. 1.7 B n.d. n.d. n.d. 2.2 Mean n.d. n.d. n.d. 2.2 Mean n.d. n.d. n.d. 2.2 Mean n.d. n.d. 1.2 3.3 B n.d. n.d. 1.2 3.2	Repli- cate Incubation time A 61.9 64.4 34.1 20.0 1.9 B 63.2 65.1 36.9 12.5 5.3 Mean 62.5 64.7 35.5 16.3 3.6 A n.d. n.d. n.d. 1.7 11.1 B n.d. n.d. n.d. 2.2 4.8 Mean n.d. n.d. n.d. 2.0 7.9 A n.d. n.d. n.d. 2.8 3.3 n.d.	Replicate Incubation time (DAT) cate 0 0.25 1 2 7 14 A 61.9 64.4 34.1 20.0 1.9 1.8 B 63.2 65.1 36.9 12.5 5.3 1.1.4 Mean 62.5 64.7 35.5 16.3 3.6 15 A n.d. n.d. n.d. 1.7 11.1 0.9 9 B n.d. n.d. n.d. 1.6 7.9 13.6 A n.d. n.d. n.d. 7.9 13.6	Incubation time (DAT) cate 0 0.25 1 2 7 14 30 A 61.9 64.4 34.1 20.0 1.9 1.8 n.d. B 63.2 65.1 36.9 12.5 5.3 1.1.4 n.d. Mean 62.5 64.7 35.5 16.3 3.6 1.5 n.d. B n.d. n.d. n.d. 1.7 11.1 0.9 6.5 B n.d. n.d. n.d. 2.2 4.8 5.3 6.1 Mean n.d. n.d. n.d. 2.2 4.8 5.3 6.1 Mean n.d. n.d. 2.2 4.8 5.3 6.1 0.1 Mean n.d. n.d. n.d. 2.2 4.8 5.3 6.1 0.1 Mean n.d. n.d. 2.8 3.3 n.d. n.d. 0.4 0.4 B n.d.	Incubation time (DAT) Cate 0 0.25 1 2 7 14 30 61 A 61.9 64.4 34.1 20.0 1.9 1.8 n.d. n.d. n.d. B 63.2 65.1 36.9 12.5 5.3 1.1 n.d. n.d. n.d. Mean 62.5 64.7 35.5 16.3 3.6 1.5 n.d. n.

n.d.: not detected, DAT: days after treatment

All values expressed as percentage of applied radioactivity (%)

* Each metabolite $\leq 3\%$ of the AR.

Table CA 7.2.2.3-35: Recovery and distribution of radioactivity following treatment of Hoenniger system with [13-diexplane 214C]-spiroxamine prider aerobic conditions in the sediment layer [%AR] \sim Ò

			V Ø	- Q		h CÔ	. <u> </u>		**	
Compound	Repli-			0	mcuba	tion time	(DAT)	ð	8	
Compound	cate	зÛ,	0.25	S 1	2	7	¢4	õ 30	© 61	118
	А	25.4	°∑22.9 €	41.5	50.2	44.1	<u>3</u> 8.4 °≈	45.80	29.5	24.3
Spiroxamine	B °	22.0	22.10	385	\$8.2	∞46.2 🐇	J ^v 37,∫Ş	50.9	40.8	34.3
	Mean ₄ ,	23	22,8	ðð.5 🖇	\$54.2 C	ັ 45.2	37.8	. 48.4	35.1	29.3
M06	A	rtQd.	And.	n.d. n.d.	n.¢.	n.Q.	1∕. 4	n.d.	7.1	11.4
(acid)	B	"n.d. (՝Տ՝ n d⊲⊘	n.d.		@1.d.			2.9	6.4
(aciu)	Mean 🔪	D´n.d 🌂	n.d.	n.d.	<u>`</u> n.d	Ø1.d.	n.d. 0.7	n.d.	5.0	8.9
Minorma	A D	n.d.	ħ∕d.	@n.d. 🖌	y n.d	n.¢	1 <u>6</u>	n.d.	6.7	n.d.
Minor me-	A B	_≪ ŋ.d.	n.d. 🖇	🖌 n.d.🖉	n d	n.¢ Md.	@n.d.	n.d.	1.7	n.d.
	Meăn	n.d.) n.d.	n⊳đ.	fūď.	, n.d. 👌	[⊘] 0.5	n.d.	4.2	n.d.

n.d.: not detexted, DAT: days after treatment All values expressed as percentage of applied radioactivity (% AR)

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* Each metabolite $\leq 3\%$ of the AR.

0 Table CA 7.2.2.336: Recovery and distribution of radioactivity following treatment of Hoen-Diger System with [6,3-dioSolane 4-14C]-spiroxamine under aerobic condi-tion Sin the total water-sediment system [% AR]

	n	<u> </u>								
Composed	Repli-	No.	Ŵ,	× .	Incuba	tion time	(DAT)			
Compound	cate	, 0 %	0.25	مہ 1 🖏	[≫] 2	7	14	30	61	118
<i>"</i> ¢	A Y	3 7.3 (& 87.3 ©	75.67	70.2	46.0	40.2	45.8	29.5	24.3
Spiroxamine	B a	85.2	87.8∛	76.4	70.7	51.5	38.2	50.9	40.8	34.3
	. Mean	86.2	84.5	76.0	70.5	48.8	39.3	48.4	35.1	29.3
M04	A A	n.d.	Nn.d.	[™] n.d.	1.7	11.1	13.3	6.5	11.3	14.7
M06 (acid)		Sn.d.	n.d	n.d.	2.2	4.8	15.3	6.1	6.2	12.5
(aciu) (*	Marean ô	n.dS	n.d.	n.d.	2.0	7.9	14.3	6.3	8.8	13.6
Miner me-	Aftean &	p.Q.	n.d.	2.8	3.3	n.d.	1.0	n.d.	6.7	n.d.
		≪n.d.	n.d.	1.2	3.2	3.3	1.8	n.d.	1.7	0.4
tabolites*	Mean	💙 n.d.	n.d.	2.0	3.3	1.7	1.4	n.d.	4.2	0.2

n.d. not detected, DAT: days after treatment

All values expressed as percentage of applied radioactivity (% AR)

* Each metabolite $\leq 3\%$ of the AR.



B. Material Balance

The total material balance of the two water/sediment systems was 94.0% of the applied radioactivity (AR) calculated as mean value of both systems and two parallel experiments for each system. The complete material balance found at all sampling intervals demonstrated that no significant portion of radioactivity dissipated from the vessels or was lost during processing.

C. Extractable and Non-Extractable Residues

The radioactivity in the Anglerweiher water decreased steadily from 64.6% AR (mean) at 0 DAT to 10.9% AR (mean) at study end. The radioactivity in the Kreenniger Weiker water decreased from 62.9% of the AR (mean) at 0 DAT to 4.9% AR (mean) at study termination. Extractable ^AC residues in the O Anglerweiher sediment increased from 25.5% AR (mean) at 0 DAT to a maximum of 63.4% AR (mean) at 2 DAT before decreasing to 18.9% AR (mean) at study termination. Extractable ¹⁴C residues in the Hoenniger sediment increased from 20.7% (mean) at 0 DAT, to a maximum of 46.6% (mean) at 2 DAT before decreasing to 32.8% AR (mean) at study end. The maximum of non-extractable ¹⁴C residues in the two sediments was 33.2% AR and 40.7% AR in Anglerweiher and Hoenniger, respectively (mean values).

The non-extractable (bound) residue remaining after the general extraction procedure was characterised at the end of the study (118 DAT) for both sediments. The results indicated that *ca* 15% AR could be assigned to the humic acid fraction, S_2 -55% AR to the futivic acid fraction and a 37% AR to the humin fraction.

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D. Volatile Radioactivity

The radioactivity found in the PU traps amount of to <0.0% of the AR for both systems. Therefore, only a negligible amount of radioactivity was assigned to velatile organic compounds. At the end of the study, 27.1% AR (mean, Anglerweiher) and 7.6% δR (mean, Hochniget) was present as CO₂.

E. Degradation of Parent Compound

Following application of Q1,3-dioxolane-4-¹⁴CF-spiroxamine, spiroxamine, showed rapid dissipation in the water phase of both systems, declining from 62,5% AR (mean) at 0 DAT to below the LOD by 118 DAT in the Hoenniger Weiher system. Similarly in the Anglerweiher system spiroxamine showed rapid dissipation in the water phase, declining from 64.6% AR (mean) at 0 DAT to below the LOD by 118 DAT.

In the Hoenniger Weiher system, the amount of piroxamine in the sediment increased to a maximum of 54.2% AR (mean) after 2 DAP and subsequently decreased to 29.3% AR (mean) after 118 DAT. In the Anglerweiher system, the amount of spiroxamine in the sediment increased to a maximum of 60.1% AR (mean) after 2 DAP, and subsequently decreased to 14.9% AR (mean) after 118 DAT.

Degradation of [1,3-dioxolane O^{4} C]-sproxamine in the total system was accompanied by the formation of one major degradation product M06 (spiroxamine-acid). In the water phase, it amounted to a maximum of 25.6% of the AR (Anglerweicher) and 13.6% of the AR (Hoenniger Weiher). In the sediment extracts, M06 accounted for only 5.9% and 8.9% of the AR, respectively. Additionally, several other minor unknown metabolites were observed but not identified in the report, with the sum of minor metabolites reached a maximum of 15.5% AR (61 DAT) and 4.2% AR (61 DAT) in the total system for the Anglerweiter and Hoenniger Weiher system respectively. Nevertheless, each zone did not exceed 3% (mean) of the AR.

F. Degradation Kinetics

Degradation rates determined in the report are superseded by the report presented under point KCA 7.22.3/08 (M-763141-01-1).



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III. Conclusions

The distribution of radioactivity following application of [1,3-dioxolane-4-¹⁴C]-spiroxamine showed that spiroxamine was rapidly translocated from the water phase to the sediment in both systems. Spirox-amine was degraded under the test conditions. The main metabolite in water and sediment was M06 (maximum formation: 31.3%). The sum of minor metabolites (not defined in the report) reached a maximum of 13.5%. ¹⁴CO₂ was formed indicating mineralisation of the parent compound and its intermediate degradation products.

A re-evaluation of the degradation kinetics in accordance with FOCUS guidance document on degradation kinetics (2014) was performed and is presented in the report under point KCA 7.22.3/08 (M-763141-01-1).

Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013. The study was conducted to study guideline(s) OPCD 308 (required guideline). The study is considered valid to assess the aerobic degradation of [1,3-dioxolane $\Phi^{14}C$]-spiroxanine in aerobic water sediment systems.

Data Point:	$V C \Lambda 7^{2} \mathcal{H} O 2 / \mathcal{H} \mathcal{H}$
Report Author:	
Report Year:	
Report Title:	Rinetic modelling evaluations of data from water sediment studies to derive mod-
	Vellinglendpoints
Report No:	VC\$\$\$8/029
Document No:	<u>M-304009-01-1</u>
Guideline(s) followed in	91/414 PEC, 97/36/EC of Julo 1995 Section 5, Subsection 7.2.1.3
study: 🏷 🔊	
Deviations from Current	None of the state
test guideline:	
Previous evaluation: 🦼	yes, evaluated accepted 0 0
	RAR (2010) RAR (2017) 2 2
GLP/Officially recog	No, not conducted under GLP/Officially recognised testing facilities
nised testing facilities.	
Acceptability/Religibility:	Yes C C C C

Executive Summary

This study was previous considered during the evaluation of spiroxamine (RAR (2010), RAR (2017)) and is therefore included again for completeness. The study performs a kinetic evaluation according to FOCUS 2006⁵ of water/sediment-systems reported in studies KCA 7.2.2.3/04 (M-303324-01-1) and KCA 7.2.2.3/06 (M-060(D-02-1)). The function evaluation reported in this study is superseded by the new kinetic evaluation performed in study KCA 7.2.2.3/08 (M-763141-01-1) on all water/sediment systems from relevant studies.

Assessment and conclusion by applicant:

The study and its data are considered as supplementary data with no use in risk assessment.

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Data Point:	KCA 7.2.2.3/06	
Report Author:		
Report Year:	1998	ð
Report Title:	Anaerobic aquatic metabolism of the active ingredient KWG 4168	A A A A A A A A A A A A A A A A A A A
Report No:	PF4288	,
Document No:	<u>M-006010-02-1</u>	
Guideline(s) followed in study:	US EPA Pesticide Assessment Guidelines, Subdivision N, Chemistry Environmental Fate, § 162-3: Anaerobic Aquatic Metholism Studio	Ş
Deviations from current test guideline:	Yes (refer below) Some minor deviation(s) not relevant for the reliability of the study (described by study summary)	ó
Previous evaluation:	yes, evaluated and accepted Q^{γ} RAR (2010), RAR (2017)	1
GLP/Officially recog- nised testing facilities:	Yes, conducted under GOP/Officially recognised lesting facilities	
Acceptability/Reliability:	$\frac{ \operatorname{Yes}}{\sqrt{2}} = \frac{\sqrt{2}}{\sqrt{2}} + \frac{\sqrt{2}}{\sqrt$	

Executive Summary

The route and rate of degradation of [coclohexyl-1-1] [0]-spiroxamine was investigated in a water sediment systems (Stilwell, USA, silty claploam, Y.22% OC, pH 7.4) inder laboratory anagrobic conditions at 20°C in the dark over a period of 360 days. As such, the study is not relevant under the data requirements in EC Regulation 283/2013. However, the study as proviously considered during the evaluation of spiroxamine (RAR (2010), RAR (2017)) and is therefore included again for completeness but as supplemental information only.

Incubation vessels were filled with 200 mL of the sediment (285 g proist weight = 130 g dry weight) and filled up to a total volume of 500 mL with water giving a ratio of approximately 1:2.5 (v/v).

[Cyclohexyl-1-¹⁴C]-spiroxamine (ratiochemical pairity $\frac{299\%}{100}$) was applied to the surface of the water overlying sediment at a target rate of 38 pg of a.s/500 mP, which was equivalent to an annual application of three applications of $\sqrt{.5}$ kg a.s./ ha; on a point of 2 m depth.

Before application of the active substance, the system was pre-incubated under anaerobic conditions $(N_2, 200 \text{ mL/min})$ and additives were supplied in order to get a negative redox potential. The incubation vessels were first closed with a bubble counter attachment in order to led CO₂ escape developed from the added sucrose. When the system became anaerobic, this attachment was replaced by an 'air sample bag' which fed into two calcium bydroxide volatile trap to callect carbon dioxide and other volatile compounds. Each vessel was incubated in the dark at 20°C while being gently agitated by mechanical shaker.

To determine influence of the biomass of the degradation of [cyclohexyl-1-¹⁴C]-spiroxamine during incubation four samples were spirilised. The samples were autoclaves three times for 20 minutes at 121°C. Under sterile condition 5.8 g of mercuric chloride was applied to the supernatant along with the test substance. The application solution was sterilised by filtration through a sterile filter.

Overlying water was carefully decanted into reglass vessel containing appropriate amounts of acetonitrile. Sediment camples were extracted three times at room temperature with acetonitrile, while later time points were refluxed with methanol for 6 hours. All samples were analysed by TLC methods.

The material balance (main) at each sampling interval ranged from 92.4 to 102.8% AR. The overall mean material balance was 985% AR for the Stilwell water/sediment system.

The mean proportion of total radioactivity extracted from sediment samples and in the supernatant water remained consistent over the 360 day incubation; starting from 89.5% AR at 0 DAT and remaining at 72.0% AR at 360 DAT. Non-extracted residues (bound residues) increased slowly throughout the incubation, reaching maximum levels of 20.4% AR at 250 DAT.

During the incubation period of 360 days an amount equivalent to $\leq 2.8\%$ of the applied radioactivity



adiolabel

was degraded to carbon dioxide. Only trace amounts of organic volatile compounds were detected during the incubation time (< 0.1% AR).

[Cyclohexyl-1-¹⁴C]-spiroxamine showed rapid dissipation in the water phase, declining from 47.9 ĂR (mean of duplicate samples) at 0 DAT to 0.2% by 360 DAT. The amounts of non-extractable adioactivity increased slowly throughout the incubation, reaching maximum levels of 20.4% AR at 250 DAP. The major metabolic pathways involved the formation of M01 (spiroxamine-desethyl: max 8.8% AR at 14 DAT, total system) which was observed at two consecutive time-points at greater than the A eral other minor metabolites were also observed.

The whole system DT₅₀ value for spiroxamine under anaerobic conditions was 27

Materials and Methods I.

A. Materials

1. Test Items

[cyclohexyl-1-¹⁴C]-spiroxamine

63 MBalmg

Specific Activity:

Radiochemical Purity:

2. Test System (water sediment system)

systems as characterised in Table CA 7.2.2.3-The study was performed using the one water/sediment -3% Physico-chemical properties of the water sediment systems 37.

enotes position of

Table CA 7.2.2.3

Parameter D	Water/sediment system
Water/sediment system designation; Geographic Location City Output Country Sedat	Stillwell
Geographic Location	
	MRP Pond
	Stilwell,
	Kansas
Country A	MRP Pond Stilwell, Kansas USA
Sede	nent characteristics
Lextural Classification (USIAA)	Silty clay loam
Sand [50 - 2000 μm]	6.8
Silt $[2 - 50 \ \mu\text{m}]$	56.5
Clay [$< 2 \mu m$] \sim \sim \sim \sim \sim \sim \sim \sim	36.7
pH in H ₂ O ($(1,1)$) in 0.0 TM Ca O_{7} (1:1)	
in H ₂ O ₍₁ ,1)	8.0
in 0.011 Ca@y(1:1)	7.4
Organic Matter (%)	2.1*
Organic@arbon (%)	1.22
Cation Exchange Capacity (meq/100 g)	23



Parameter	Water/sediment system	1
Water/sediment system designation:	Stillwell Q ₁ °	~
Biological (respiration) activity [mg CO ₂ /h/kg sediment (dry weight)]		S.
Initial, DAT 0		
Final, DAT 360 (average)	10	
Wa	iter characteristics	Ş,
Dissolved oxygen concentration, at the time of treatment (mg/L)		Å
Total organic carbon (mg/L)		×
Hardness (degree DH)	A 45°.8 A 44	2
N(total) (mg/kg dry weight)		
P(total) (mg/kg dry weight)	2 07 2 2 706 S 7	
* Calculated by multiplying organic carbon content by		•

Water and sediment were freshly sampled from a pond in Stilwell on the 23rd of March 1994. The equeous sediment was passed through a 2 mm mesh sieve and was thoroughly mixed before use. No pesticide history was given for previous years before the trial for either site.

B. Study Design

1. Experimental Conditions

The behaviour of [cyclohexy]¹-¹⁴@]-spirocomine was investigated in one sediment water systems (Stilwell) over a period of 360 days.

Incubation vessels were filled with 200 mL of the ediment (28% g moist weigh) = 130 g dry weight) and filled up to a total volume of 500 mL with water giving a ratio of approximately 1:2.5 (v/v). Before application of the active substance, the system was pre-incubated under anaerobic conditions (N₂, 200 mL/min) and additives (sucrose) were supplied in order to get a negative redox potential. The incubation vessels were first closed with a bubble counter attachment in order to led CO₂ escape developed from the added sucrose. When the system became anaerobic chis attachment was replaced by an 'air sample bag'.

The test application rate was intended to simulated use tate will three applications of 1.5 kg a.s./ha. This rate corresponded to a concentration of 38 µg a.s./500 mL considering a water layer of 200 cm. The application solution was applied to the surface of the water overlying sediment and the system. After application of the est solution each vessel was purged with nitrogen below the air sample bag was connect to a calcium by droxide trap for the collection of carbon dioxide and other volatile compounds. Each vessel was incubated in the dark of 20°C while being gently agitated by mechanical shaker (30 rpm).

The biological activity was determined in the sectment before application. To check the influence of the biomass on the degradation of [cyclohexyl-1-4C]-spiroxamine during incubation four samples were sterilised. The samples were autoclayes three times for 20 minutes at 121°C. Under sterile condition, 5.8 g of mercure chloride was applied to the supernatant along with the test substance. The application solution was derilised by furation through a sterile filter.

The biological activity was determined in the sediment before application. Two vessels were incubated with and without spiraxamine to determine the influence of the incubation and the test substance on the biological system. The redox potential was negative throughout the entire study; therefore, no further procedures were necessary to keep the systems anaerobic.

2. Sampling

Duplicate samples for each water/sediment system were removed for analysis after 0 (2 hour), 3, 7, 14, 31, 61, 122, 250 and 360 DAT (days after treatment). Sterile samples were sample taken in duplicate



from the sterile water/sediment system at 61 and 360 DAT.

3. Analytical Procedures

Before opening of the vessels, volatiles possibly present in the head-space of the flasks were purged into the trap attachment by means of a stream of nitrogen. The radioactivity in the calcium hydroxide was determined by LSC after having added hydrochloric acid in a closed apparatus and after having trapped the released carbon dioxide. The pH-value and oxygen content of the solution, and the redox potential of water and sediment were determined. An aliquot of the supernatant water was added with sodium hydroxide in order to keep possibly dissolved carbon dioxide in solution. After centrifugation the water phase was radio-assayed. In order to measure dissolved carbon dioxide, the water was then transferred into a closed apparatus, amended with hydrochloric acid and the released carbon dioxid@was mapped and measured by LSC. The precipitate was added to the remainder of the sediment.

The main amount of the aqueous phase was centrifuged and then filtered. The precipitates resulting from the centrifugation steps were extracted three times with acetonitrile at room temperature. The fiftered extracts were combined after each centrifugation. An alignot of the second was mixed with quartz sand and extracted once with methanol under reflex (2 hours). All extracts were investigated by bSC and TLC. The remaining non-extractable radio activity was determined by combustion and LSC analysis of trapped combustion gases.

Water samples and sediment extracts were investigated by TLC with four solvent systems of silica gel and RP-silica gel plates. Components were visualised by autoradiography, radioactivity scanning and in the case of unlabelled reference substances by feacting in an addine chamber or by spraying with cobalt-II-thiocyanate. Identification of the metabolites was performed by mass spectroscopy after isolation of radioactive zones obtained by TLV. The detection limit for a single peak was >021% of the applied radioactivity.

4. Determination of degradation kinetics

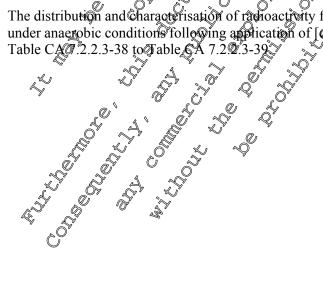
Degradation kinetics were determined in the report using first order kinetics. The degradation rates presented in the report have not been re-calculated to current guidance (i & FOCUS 2014²) as the study is supplied as supporting information only.

Results and Discussion &

A. Data

It was confirmed that the water sediment system was biologically active during the entire test period and that it was an aerobic. The oxygen saturation was measured to be < 3% and the redox potential between -120 and -296 mV confirming that the test systems were anaerobic during the study.

The distribution and characterisation of ratioactivity for each water/sediment system incubated at 20°C under anaerobic conditions following application of [cyclohexyl-1-¹⁴C]-spiroxamine are summarised in





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Table CA 7.2.2.3-38: Recovery and distribution of radioactivity following treatment of Stilwell system with [cyclohexyl-1-14C]-spiroxamine at 20°C under anaerobic conditions [mean % AR] Ľ

	CI CI	ons find	an 701	III]							, Q
					Incubat	tion time	e (DAT)		~	S.	0°
Compound	0*	3	7	14	31	61	122	250	360	Sterile	
Supernatant water	51.1	42.1	25.8	15.6	9.5	8.4	9.5		5.2 <	2.3 ° 1.9 ~	ŝ,
Sediment ex- tract	38.4	37.6	62.5	68.0	73.1	₩3.0	68.7	0 64.1	66	889 85,3	Ĩ
(sub-total)	89.5	79.7	88.3	83.6	82.	81.4	782	70.8	<u>B</u> 2.0	\$0.4 \$7.2	×
CO_2	0.1	0.1	0.1	0.3	0 .1	0.5	6.6	چ2.8 ر	م 1.9 م		
Non-extracta- ble radioactiv- ity	8.0	21.1	11.4	13.7	16.6	° 15.3	~	20:9 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	183	×17.2 ×14.2	
Folded filter	2.5	0.4	0.2	0,2	đ3	0.3	Q0.7	© _{0.2}	0.4		
Total AR	100.0	101.2	99.9	\$97.7	°م	≫97.4 _≫	, 96. <u>8</u> -1	94.5	92.4	1028 102.1	
DAT [.] days after trea	atment			× .	Y al	yO	Š,	°~/			•

DAT: days after treatment

* Sample taken at 2 hours is representative of zero time point. Overall total recovery = 98.5% AR All values expressed as mean percentage of applied radioactivity (% AR

Ô Ò Table CA 7.2.2.3-39: Characterisation of radioactivity following treatment of Stilwell system with [syclohexyl-1-4°C]-spiroxamine at 20°C under anaerobic conditions [mean % AR]

				al a		K)	\sim	K,		
	A	Ča ,	No.	Leeubat	ion time	e (DAT)				
Compound			14.0			122	250	2(0	ste	rile
-			~	31%	61	1 42	289	360	61	100
Total	510 42	26.0	45.7	\$ 9 6	Ø.7	Å9.6	C6 .9	5.4	2.4	2.0
Ôs	38.5 31.3	£48.9	1 \$2.0	\$9.7	\$3.8 C	\$ 56.2%	¥47.3	52.6	81.9	71.8
Spirox-	47.9 037.1	\$18.7k	9.6	3.90	1.3	0.3	0.2	0.2	1.6	0.6
amine	d [™] 32.7 [™] 31 <i>¿</i>	48,9	9.6× 52.9	590 597	53.8	\$6.2	47.3	52.6	81.9	71.8
M01 w	KI X2	\$5.9	P.9	0 1	Ø.4 »	@0.4	0.3	0.1	n.d.	0.2
(desether) s	2.4 2.5	\$5.9	√6.9	\$ ⁷ 5.7 🔬	8.0 C	y [≫] 4.7	6.7	7.1	2.5	5.2
M02 W	0.3 7 0.9	1.3	0.7%	069	0.3	0.1	0.1	0.1	0.2	0.2
(despropyl)	0.3 > 0.9 0.8 > 1.6	2:54	373	2	3.9	3.2	3.2	2.0	2.4	4.5
M03	12 08	~¶4	×1.0	0.5	0.6 1.2	0.2	0.4	n.d.	0.2	0.9
(N-oxide) 🖉 s	<u>6</u> 0.4 <u>0.6</u>	ູ ບິ 0.6 ($0.3 \\ 0.7 \\ 0.7 \\ 0$	1.2	0.5	2.2	0.5	0.7	0.8
M06 ~ w	⊈ n.d.⊙ 0.ð	0.6	1.4× 0,6	2>9,	3.7	5.0	1.1	3.2	0.1	n.d.
(acid) <u>s</u>			0,0	. @19	1.3	2.5	1.5	1.9	n.d.	n.d.
M11 (des w	¢od. 2.2	@.2	20.3 ∘	0.4	0.9	1.4	1.5	0.6	<0.1	n.d.
ethyl acrd) s	n.d. " n.d.	n.d. 🗸	'l∾ n.d∾O	0.2	0.5	n.d.	0.2	0.2	n.d.	n.d.
M12 (des- w	n.d n.d	n.d n.d.	nd	0.1	0.9	1.8	1.6	0.4	n.d.	n.d.
Propyl acid) s	n.o. n.d.	n.ď.	_@d.	n.d.	0.3	n.d.	0.3	n.d.	n.d.	n.d.
M15 Øw	n.d. n.d.	~0.4 j	n.d.	0.1	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
(Ketone) S	A 1.3 1.6	2.8	∛ 2.5	1.9	2.8	1.1	2.4	2.1	0.7	0.9
Other 🖉 🐙	0.78 0.6 69 08	28	0.8	0.4	0.6	0.4	1.7	0.8	0.2	0.1
unknown	67 08	1.6	1.9	1.0	1.5	0.7	0.5	0.5	0.1	0.3

n.d.: not dejected, DAT: days after treatment

* Sample taken of hours is representative of zero time point. Overal total recovery #98.5% AR

All values expressed as mean percentage of applied radioactivity (% AR)

B. Material Balance

The material balance (mean) at each sampling interval ranged from 92.4 to 102.8% AR. The overall mean material balance was 98.5% AR for the Stilwell water/sediment system.



C. Extractable and Non-Extractable Residues

The mean proportion of total radioactivity extracted from sediment samples and in the supernatant water remained consistent over the 360 day incubation; starting from 89.5% AR at 0 DAT and remaining at 72.0% AR at 360 DAT. Non-extracted residues (bound residues) increased slowly throughout the incubation, reaching maximum levels of 20.4% AR at 250 DAT.

D. Volatile Radioactivity

During the incubation period of 360 days, an amount equivalent to $\leq 2.8\%$ of the applied radioactivity was degraded to carbon dioxide. Only trace amounts of organic volatile compounds were detected, during the incubation time (< 0.1% e.g. methane).

E. Degradation of Parent Compound

Following application of [cyclohexyl-1-¹⁴C]-spirokamine, spirokamine, showed rapid dissipation in the water phase, declining from 47.9 AR (mean of duplicate samples) at 0 DAU to 0.2% by 360 DAP. The amount of spirokamine in the sediment increased 59.7% AR after 21 DAP and subsequently decreased to 52.6% AR after 360 DAT.

Degradation of [cyclohexyl-1-¹⁴C]-spiro amine was accompanied by the formation of one major degradation product M01 (spiroxamine-desethyl: max 8.8% AR at 14 DAT, total system) which was observed at two consecutive time-points at greater than 5% AR. In addition, several other minor metabolites M06 (spiroxamine-acid: max 5.0% AR at 122 DAT), M02 (spiroxamine-despropyl: max 3.9% AR at 61 DAT), M03 (spiroxamine-N-oxide: max 2.2% AR at 50 DAT), M01 (spiroxamine-desethyl acid: max 1.5% AR at 250 DAT), M12 (spiroxamine-despropyl acid? max 4.8% AR at 122 DAT) and M15 (spiroxamine-ketone: max 2.8% AR at 7 DAT). Some other minor unidentified metabolites were observed but none of which exceeded a total of 2.8% AR at any sampling interval.

F. Degradation Kineties

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The whole system Df 50 value for piroxumine was 279 days

III. 🗡 Conclusions

Spiroxamine degraded in water/sediment systems under maerobic conditions (20°C) with 52.8% of AR (mean) remaining as parent compound after 360 DAT in the Stilwell system. Low amounts of carbon dioxide accumulation was observed max 2.8% AR mean in addition to low amounts (0.1% AR) of other volatiles. The amounts of non-extractable radioactivity increased slowly throughout the incubation, reaching maximum levels of 20.4% AR at 250 DAT. The major metabolic pathways involved the formation of M01 (spiroxamine desettivit: max 8.8% AR at 04 DAT, total system) which was observed at two consecutive time points at greater than 5% AR. Several other minor metabolites were also observed.

The whole system DT₅₀ value for spirovamine under anaerobic conditions was 279 days.

Assessment and conclusion by applicant:

The study was conducted to study guideline(s) USEPA (=EPA): N, 162-3 (<u>not</u> equivalent to required guideline). The study is not considered valid to assess the aerobic degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in aerobic water/sediment/systems.

The study and its data are considered as supplementary data with no use in risk assessment.

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Executive Summary

The degradation/dissipation behaviour of either [cyclonexy] P^{-14} Cl spiroxamine or [1,3-dioxolane-4-¹⁴C]-spiroxamine was investigated in three laboratory studies (KCA 7.2.2.3/01 ($\frac{0.006005-01-0}{0.000005-01-0}$), KCA 7.2.2.3/04 ($\underline{M-303324-01-1}$) and KCA 7.2.2.3/07 ($\underline{M-762}$ 28-01 $\underline{0}$)) involving six water/sedament systems.

The data from these studies have been used to determine the degradation dissipation DE 50's of spiroxamine in water/sediment. The data were considered appropriate for calculation of both persistence and modelling endpoints. In the KCA 3.2.2.3/01 (M@0601501-1) study the metabolite M06 was detected at >5% applied radioactivity (AR) in the Stilwell total system only. In the CA 7.2.2.3/04 (M-303324-01-1) study the metabolite M06 was detected at >5% applied radioactivity (AR) with e supernatant water and in the sediment extracts of both water sediment systems. Where not abolites were detected at >5% AR and showed a chear decline in the total system, a kinetics assessment were performed. In the KCA 7.2.2.3/07 (M-763128-01-1) study the metabolite M06 was detected at >3% applied radioactivity (AR) in the supernatant water and in the sediment extracts of both water sediment systems. Where metabolites were detected at >5% AR and showed a clear decline in the fotal system, a kinetics assessment were performed. The data from these studies were malysed using the CAKE v3.4 (2020) software package according to guidance provided by FOCUS (2014) Based on Level P-1 and M-1 kinetics (single compartment kinetics). DT50 and DT96 values were exculated for comparison with relevant study triggers and persistence criteria and separate DF₅₀ values were calculated for use as modelling endpoints. The FOCUS (2014) How charts for calculating persistence and modelling endpoints have been followed. Each compartment of the water/sediment systems has been considered following the steps in the flowcharts. \sim

The persistence and modelling indpoints for spiroxamine and metabolite M06 are summarised in Table CA 7.2.2.3-40 and Table CA 7.2.2.3-41, respectively.

⁹ I. Materials and Methods

The degradation dissipation behaviour of other [cyclohexyl-1-¹⁴C]-spiroxamine or [1,3-dioxolane-4-¹⁴C]-spiroxamine was investigated in three laboratory studies (KCA 7.2.2.3/01 (<u>M-006015-01-1</u>), KCA 7.2.2.3/04 (<u>M-303274-01</u>) and KCA 72.2.3/07 (<u>M-763128-01-1</u>)) involving six water/sediment systems.

For the KCA (2.2.34) (<u>M-006015-01-1</u>) study the data were sufficient to allow for the calculation of kinetic endpoints for spiroramine. However, for the Stilwell test system kinetics could not be fitted for the sediment phase as no decline was determined. The limit of detection (LOD) for thin layer chromatography (TLC) was reported as 0.1% of the applied radioactivity. The limit of quantification (LOQ) was not reported, therefore for the purposes of data generation, it was assumed that the LOD is nominally 1/3 LOQ (LOQ assumed as 0.3% AR).



For the KCA 7.2.2.3/04 (M-303324-01-1) study the data were sufficient to allow for the calculation of kinetic endpoints for spiroxamine. For the metabolite M06, data was not sufficient to determine kinetics for the sediment phase for the Hoenninger system. The LOQ for the HP-TLC methods was determined for a single peak in the water and sediment extracts to be in the range of 0.1% AR. The LOD was determined to be 0.77% AR.

For the KCA 7.2.2.3/07 (<u>M-763128-01-1</u>) study the data were sufficient to allow for the calculation of kinetic endpoints for spiroxamine. For the metabolite M06, data was not sufficient to determine kinetics for either the Calwich Abbey or Emperor Lake systems. The LOQ for the HPLC methods was determined for a single peak in the water and sediment extracts to be in the range of 0.9% AR. The LOD was determined to be 0.3% AR.

Full details of the water/sediment systems are provided in the study report.

A. Data handling

Input data were generated according to the data handling recommendations made in the FOCUS guidance for degradation kinetics (FOCUS, 2014). True duplicate samples were analysed in all three studies, so these individual values were used in the kinetic assessment. The handling of values below the limit of detection (LOD) and limit of quantification (LOQ) was performed according to the procedure recommended by (FOCUS, 2014) as follows

- All values between LOD and LOQ were set to the actual measured value. If the actual measured concentration was not reported 9.5 × 600 ± LOD was used.
- Set sample < LOD just after detection amount to 0.5×10^{10}
- All samples after the first non-detect (LOD) were omitted unless positive detections above LOQ were made later in the experiment. In that case samples were included up to the first non-detect (<LOD) which is NQU followed by later positive samples above LOQ.

The initial percent acovery of sphoxample, M_0 , in the total system and the water phase was set equivalent to the initial mass balance value for the total system. The initial percent recovery for spiroxamine in the sediment was selected based of the individual maximum values that provided the average maximum value in sediment.

In all three studies, M_0 , in the total system and the water phase were corrected for radiochemical purity. Where metabolites were detected at >5% and showed a clear decline in the total system, a kinetic assessment was performed. Where the concentrations of a metabolite in the total system were still increasing at the end of the study a kinetics assessment could be performed. The initial amounts of the metabolites were set to 9%.

B. Input data

The data input to the kinetic models for each water sediment system is provided in detail in the study report (see Table 3-4 to Table 3-9 pages 16-21).

C. Kinetic modelling

The kinetic modelling was conducted using CAKE version 3.4 (2020). In the first instance, the data were directly fitted, with the complete usable data set and unconstrained initial concentration (M_0) .

The acceptability of kinetic fits was judged both visually and according to the χ^2 error and the t-test functions as recommended by FOCUS (2014). The visual assessment is recommended as the main tool for assessing goodness of it. However, it is also recommended that a χ^2 error of less than 15% and a t-test probability of greater than 95% (p < 0.05) / 90% (p < 0.1) for estimated degradation rate constants indicate an acceptable fit. The χ^2 error was not considered as an absolute cut-off criterion as FOCUS guidance indicates that there will be cases where the error is higher than 15%, but the fit still represents



a reasonable description of the degradation behaviour. This particularly the case for field data and metabolites. In such situations examination of plots of residuals for systematic error is considered important. The t-test assesses whether degradation rate constants differs significantly from zero (i.e. no degradation). Alternatively, confidence intervals can be examined. In this assessment, the t-test was chosen for assessing confidence in rate constants. [The t-test was also not considered as an absolute catoff criterion as FOCUS guidance indicates that where p is between 0.05 and 0.5 the parameter may still be considered acceptable. In such situations the visual quality of the fit was considered important.]

When fitting the FOMC model, FOCUS guidance indicates that the t-test is not appropriate as a measure of confidence for the gamma-distribution parameters α and β (smaller values of β indicate more radii degradation, and α only indicates the shape of the curve and has nothing to do with the rate of degradat. O tion). Therefore, if a FOMC fit indicated slow degradation, confidence intervals for β were examined to determine if they were high compared to the parameter estimate, which would indicate that the parameter estimate was not reliable.

When calculating modelling endpoints for a metabolite, it was considered important to derive a formation fraction wherever possible. In the FOCUS powsheets, if the SFO it for a metholite is not considered acceptable, a case-by-case decision is required. The first option given is to assess the decline of the metabolite after its maximum ('top-down' method However, the method dogs not allow formation fraction assessment. The second option given is to fix the formation fraction to a worst was value (usually 1) and use this in combination with a porst-case DT% (usually 1000 days). However, this method almost always results in a clear overestimation of observed metabolic resides. The final option given is to use alternative - but conservative estimates that describe the observed patterns. In this assessment, alternative - but conservative estimates were chosen. These were implemented by fixing the formation fraction to the fitted value and using this in combination with a conservative DT₅₀ for vice versa. The parameter to amend and its value were chosen based on expert judgement and iterative amendments to give a conservative description of the observed metabolite esidue pattern. In general, however, if residues throughout the study were underestimated, the formation fraction was conservatively amended, and if only residues fate in the study were underestinated, the DT₅₀ was conservatively amended. On rare occasions adjusting both parameters is necessary to obtain a conservative estimate that describes the observed pattern.

The FOCUS (2014) Level P-I flowcharts for carculating persistence and modelling endpoints for spiroxamine and Level M-F flowcharts carculating persistence and modelling endpoints based on metabolite formation and degradation have been followed Each water/sediment compartment has been considered following the steps in the flowchart and the considerations are discussed in detail on the following pages. The full CAKE outputs from all kinetic fits (including the initial settings) are presented in the study report (see Appendix 2 for persistence fits and Appendix 3 for modelling fits.

Results and Discussion

A. Persistence/trigger endpoints

The kinetic evaluation was conducted using CARE version 3.4 (2020) following the FOCUS (2014) Level P-I decision flowchart for persistence endpoints for spiroxamine. A summary of the fits achieved and decisions taken is provided for each test system in Appendix 5.1: and for each system in Appendix 5.1.1 to Appendix 5.1.6.

The resulting persistence of best-fit endpoints are presented in Table CA 7.2.2.3-40.

The spirovamin persistence DT_{50} values in the total system ranged from 1.4-118 days and DT_{90} values ranged from 85,7-628 days.

The spiroxamine persistence DT_{50} values in the surface water ranged from 0.27 - 7.69 days and DT_{90} values ranged from 2.5-36.4 days.

Dissipation of spiroxamine in sediment could not be accurately fit to a kinetic model in three of the six test systems resulting in a number of presented FOCUS default endpoints. The spiroxamine persistence DT_{50} values in the sediment phase ranged from 24.3-1,000 days and DT_{90} values ranged from 191-3,320



days.

For the M06 persistence values in the total system, an acceptable fit could only be determined for the form of the test systems resulting in a number of presented FOCUS default endpoints. The total system gave persistence DT_{50} values of 47 - 1,000 days and DT_{90} values ranged from 156 - 2,320 days.

For M06 persistence in surface water DT₅₀ values could only be established in two of four trials, resulting in a number of presented FOCUS default endpoints, and ranged from 8.31-1,000 days and DT90% values ranged from 156-3,320 days.

For M06 persistence values in the sediment phase, an acceptable fit could only be determined for one of the four test systems resulting in a number of presented FOCUS default endpoints. The sequence of the sequence gave a range of DT_{50} values of 89.2 – 1,000 days and a range of DT_{50} value of 290 - 3,320 days

B. Modelling endpoints

The kinetic evaluation was conducted using CAKE (2020) following the FOCUS (2014) decision flowchart for modelling endpoints. A summary of the fit achieved and decisions taken is provided for each test system in Appendix 5.2, and for each system in Appendix 5.2.1 to Appendix 5.26.

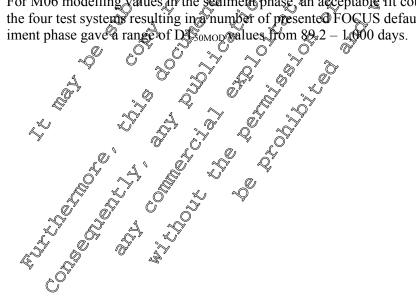
The resulting modelling endpoints are presented in Table (

The spiroxamine modelling (DT₅₀, b) values in the total system ranged from 42.8 1,000 days, with a geometric mean of 157.9 days in the total system. The spire aming mode Ming (DT 50M6D) values in the surface water ranged from 0.47-8.35 days with a geometric mean of \$52 days in the surface water. Dissipation of spiroxamine in sediment could not be accurately fit to a kinetic model in three of the six test systems resulting in a number of presented FOCUS default endpoints, The spiroxamine modelling (DT_{50MOD}) values in the sediment phase ranged from 72.0-0,000 days, with a geometric mean of 269.9 days in the sediment. \bigcap

For the M06 persistence values in the total system, an acceptable fit could only be determined for one of the test systems resulting in a number of presented FOCUS default endpoints. M06 modelling total system gave a geomean DT_{5010D} value of 293.6 days (f.f. 0.453).

For M06 modelling water phase gave two established DT_{50MpD} values from the four soils, resulting in a number of presented FQCUS default endpoints, ranging from 32.84,000 days.

For M06 modelling values in the sediment phase, an acceptable fit could only be determined for one of the four test systems resulting in a number of presented FOGUS default endpoints. M06 modelling sed-





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Water/sedi	ment sys	tem		Spiroxamine							M06à Obh with						
	pH (1	H2O)	Total s	system	Wa	Water		ment	Kinetics	Total system		Water C				Kinet	
System name	water	sed.	DT50/ DT90 (days)	χ2 er- ror (%)	DT50/ DT90 (days)	χ2 er- ror (%)	DT50/ DT90 (days)	χ2 er- ror↓	(TS / War ter Sed)	DT 507	72 er- FOC	o DT 50/ DT 96 (days)	ror (%)		ror (%)	ics (TS / Wate / Sed)	
CA 7.2.2.3/01 (<u>M-006015</u>	5 <u>-01-1</u>) te	mp 20°C		· · ·				<u>}</u>				0"	Č ^e	£0*		
Hoenniger water	ND	5.6	51.4/ 628 ¹	6.8	0.274/ 2.51	1.96 K	282 ¹ / 871 ¹ ¢	â	DFØP/ DFOP/ SF@?	~ O ·	1 1 1	A BERN	lot observ	ed Der	<u></u>		
Stilwell	ND	6.8	1.37/ 83.7	10.3	0.401/5	6.03 C	\$1,000 / 3,320 C	NA NA	DFOP/ DFOP/ Dcf.	/3,330	NA NA	S.D.t.	Not obser	ved \$5%		Def./ NA/ N	
CA 7.2.2.3/04 (M-303324	<u>1-01-1</u>) te	mp 20°C	<u>Itor</u>		<u> </u>	<u>ġ</u>	ATC -	ð de	all' i	<u>}</u> 00	TOTAL STATES	, Ĝ				
Anglerweiher	7.1	7.2	9.47/ 237	04.44 04.44	0\894/ 7.08	£ 3.84	24.3/ 24.3/ 24.3/	UL OL	FOMC(HS/	**************************************	26.9 ⁰	46.9/> 01556	9.26	89.2/ 296	0.393	SFO/ SFO* SFO*	
Hoenniger water	7.2	5.5	9.82/ 429 ¹	4.79	0.596/ 3.6	چ 3.77	1171/ 53881		DFO FOMC/ SFO*	4,000 / © 3,320	JAA S	8.31/ >1,000	9.07	1,000 / 3,320	NA	Def/ FOMC Def	
CA 7.2.2.3/07 (M-763128	<u>8-01-1</u>) te	mp 20°C	1.0		-0 ⁻⁰	972	and de	CC -	ne							
Calwich Ab- bey	8.2	7.2	220/ 453 ¹	0 ⁰²¹	5.610 JIN 6	12 <i>8</i> 5	1,000 ¹ 3.320	OPE	FOMC SFQ Def.	1,000 / 3,320	NA	1,000 / 3,320	NA	1,000 / 3,320	NA	Def/ Def/ Def	
Emperor Lake	6.9 _S *	¢ 5.2	118 ¹ / 474 ¹	5.68	7.69. ^C 3036.4			NA	O HS/	1,000 / 3,320	NA	1,000 / 3,320	NA	1,000 / 3,320	NA	Def/ Def/ Def	
S total system. NE		st-case :	11№/ 1628** -	TA .	7.6%	169	1,000/ 3,320	Offic		1,000/ 3,320		1,000/ 3,320		1,000/ 3,320			

TS total system. ND not determined NA Not applicable. * Decline after that [top-down]. ** Worst-cases from different systems. Def. default ¹ Interpret with care – extrapolated beyond experimentationer of the provide the providet th



Page 324 of 654 2021-03-31 Document MCA – Section 7: Fate and behaviour in the environment Spiroxamine

Water/sed	iment sys	stem				Spiroxa	mine					1	N V	106	áQ.	Ś	
	pH (Total s	system	Wa		Sedi	nent	Kinetics	Total system					Sedia	pent	Kinetics
System name	wa- ter	sed.	DT50/ DT90 (days)	χ2 error (%)	DT50/ DT90 (days)	χ2 error (%)	DT50/ DT90 (days)	χ2 error (%)	(TS/ Was ter/ Sed)	DT 50/ DT 900	f. f .	2 er- ror (%)	DT50/ 。DT90 (davg)	error (%)	DT\$0/\$ ~DP90 (days)~	error	(TS/ Wa- ter/ Sed)
CA 7.2.2.3/01	(<u>M-006</u>	015-01-1) temp 20	°C			• • • /		2 × 2		A			a C	(unjs)»		Ċ
Hoenniger water	ND	5.6	249	6.8	0.468	21.5	262	5.98	DFOP/ SEO/SFO*	e ^{11e} a	r Byr	3.0. ^t	Nød	bserved)) _~(,e ^{for}	
Stilwell	ND	6.8	42.8	10.3	0.965	24.1	NO.00	NAG	DFOP SEO/ Def	hede	0.15	° 69.2%	»	° Not ob	served		SFO/ ND ND
CA 7.2.2.3/04	(<u>M-303</u>	<u>324-01-1</u>) temp 20	°C		19	F	<i>></i>	00			8.1	A ^E	THOU OU	, 		
An- glerweiher	7.1	7.2	72.6	5.37	0.81	د 12.4	0* 172.0	\$.91	DFOR SFO/ DFOP*&	\$43.1 _0	0.9412		4699.24	9.26	89.2	0.393	SFO/ SFO*/ SFO*
Hoenniger water	7.2	5.5	184	4.00	0.728	0 [%] 8 18 %	9117 .	0 ⁴ 1 ⁰ 5.9	DE OP/		103	38.4	32.8 ¹	25.4	1,000	ND	Def/ SFO*/ Def
CA 7.2.2.3/07	(<u>M-763</u>)	28-01-1) temp 20	°C	*		0 ^{fr}	12	. 10 ¹⁰	01/2	C. Lar	nt ^ĝ					
Calwich Ab- bey	8.2	7.2	1,000	NA	S.61	NR \$	175	10.7	Def/SFQC SFO	1,000	0.65	20.1	1,000	NA	1,000	NA	SFO/ Def Def
Emperor Lake	6.9	5.2	109	\$39	8.35 ^{°)}	18.3	1,000	Ô'nA	SFO/ SFO/ Def of	48.4 D	0.4251	34.7	1,000	NA	1,000	NA	SFO/ Def Def
A	eometric rithmetic	mean : mean :	1570° 1		2 21.52 20CULG	er Lo ^{di}	2009.9	JOIL	the 10	2 9 2.6	- 0.453	[198.0		546.5		
~	E UIT TH	Jerroo Lerroo	re' ntly ntly		pull' cial the pe	Perce Perce		ed a	SFO/ SFO Def/ SFO SFO/ SFO/ Def N								



III. Conclusions

Persistence/trigger and modelling endpoints (DT₅₀ and DT₉₀) representing the degradation rate of piroxamine in water/sediment studies were calculated in accordance with FOCUS (2014) guidance

The spiroxamine persistence DT_{50} values in the total system ranged from 1.4-148 days and Df_{50} values ranged from 83.7-628 days. Modelling (DT_{50MOD}) values for spiroxamine ranged from 42.8-1,000 days, with a geometric mean of 157.9 days in the total system. The spiroxamine persistence DT_{50} values in the surface water ranged from 0.27 – 7.69 days and DT_{90} values ranged from 2.5-36.4 days. Modelling (DT_{50MOD}) values ranged from 0.47-8.35 days, with a geometric mean of 1.52 days in the surface water. Dissipation of spiroxamine in sediment could not be accurately fit too kinetic model in three of the six. The spiroxamine persistence DT_{50} values in the sediment phase ranged from 24.26 from 24.26 from 24.26 from 191-3.320 days. Modelling (DT_{50MOD}) values ranged from 72.0-1,000 days, with a geometric mean of 269.9 days in the sediment.

For the M06 persistence values in the total system an acceptable fit could only be determined for one of the test systems resulting in a number of presented FOCUS default endpoints. The total system gave persistence DT_{50} values of 47 - 1,000 days and DT_{90} values ranged from 1.56 - 3.520 days. M06 Modelling total system gave a geomean DQ_{50M00} value of 293.6 days (f.f = 0.453), for M06 persistence in surface water DT_{50} values could only be established in two of four trials, resulting in a number of presented FOCUS default endpoints, and ranged from 8.39-1,000 days and DT_{0} values ranged from 156-3,320 days. M06 modelling water phase also gave two established DT_{50M00} values from the four soils, resulting in a number of presented FOCUS default endpoints, ranging from 32.8-1,000 days. For M06 persistence values in the sediment phase, an acceptable fit could only be determined for one of the four test systems resulting in a number of presented FOCUS default endpoints. The sediment phase gave a range of DT_{50} values of 89.2 - 4.000 days and DT_{0} values of 296 - 3.320 days. M06 modelling sediment phase gave a from 8.92 - 1,000 days.

Assessment and condusion by applicant?

Study meets the cuffent guidance and the requirements in 283/2013

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The study was conducted to guideline (s) FOCUS 2006, 2014 (required guideline). The study is considered valid to assess best th and modelling DT₃₀ values for spiroxamine and associated metabolites in water/sediment studies.

CA 7.2.2.4 Irradiated water/sediment study

A study investigating the degradation of the active substance in water/sediment systems under artificial light has not been performed (higher tier option).

CA 7.2.3 Degradation in the saturated zone

Based on the information described under Point CP 9.2.4, following use of the formulated product, the active substance and any of the major degradation product as defined under Point CA 7.4.1, is not expected to Jeach through the soll profile to the saturated zone in significant quantities. Therefore, no further sudies have been carried out.

C& 9.3 Fate and behaviour in air

CA 7.9.1 Route and rate of degradation in air

The fate and behaviour of spiroxamine in air was assessed in the previous EU evaluation and no new data or assessment is provided here. The studies considered are one study calculating the expected half-



life of the active substance in the atmosphere (KCA 7.3.1/01 ($\underline{M-006025-02-1}$) and two studies investigating volatility of the active substance under simulated usage conditions:

Substance	Report reference	Document no.	Comment
Spiroxamine	KCA 7.3.1/01	<u>M-006025-02-1</u>	Submitted for first approval of spriox- amine, 1999. Reviewed under UK Consider
Spiroxamine	KCA 7.3.1/02	M-006029-01-1	amine, 1999. Reviewed under UR Consid
-			ered valid and acceptable.
Spiroxamine	KCA 7.3.1/03	<u>M-006028-01-1</u>	Submitted for first renewa Dof spirox-
			amine, 2010, Reviewed under UP. Considered valid and accentable
		- V	effed valid and acceptable.
•		L.	

Overview:

Based on an overall vapour pressure value for the whole active substance (i.e. combined A and B jobmers) of 4.7 x 10⁻³ Pa (20°) and individual vapour pressure values of 3.0 x 10⁻³ and 6.0 x 10⁻⁷ Pa (20°C) for the A and B diastereoisomers (see Point CA 2.2), respectively and calculated Henry's law constant for the whole active substance of 4 x 10⁻³ Pa m³/mcl (pH7 20°C) and individual Henry's law constants of 2.5 x 10⁻³ and 5.0 x 10⁻³ Pa m³/mol (pH7, 20°C) for the A and B diastereoisomers (see Point CA 2.2), respectively, spiroxamine is semi-volatile and may have a potential to volatilise from plant, soil and water surfaces. However, experimentally in studies investigating the amount of active substance volatilised under field conditions, it was shown that the amount volatilised was co. 2% after 24 hrs. Any volatilisation of the active substance from the laboratory soil studies under Surfaces in the water/sediment study (under Point CA 7, 2.2.3). However, the estimated photochemical oxidative degradation halflife (using the Atkinson equation) is air of the active substance spiroxamine is <3 hours and therefore, if present, spiroxamine will not persist in the amount photochemical oxidative degradation halflife (using the Atkinson equation) is air of the active substance spiroxamine is <3 hours and therefore, if present, spiroxamine will not persist in the amount photochemical oxidative degradation halflife (using the Atkinson equation) is air of the active substance spiroxamine is <3 hours and therefore, if present, spiroxamine will not persist in the amount photochemical oxidative degradation halfin the atmosphere.

\$	
Data Point:	KCA 7.2.301 @ 25 20 0 4
Data Point:	
Report Year:	
Report Year:	Caculation of the chemical lifetone of KWG 4168 in the troposphere
Report No:	PF4002 1 27 27 27
Documents No:	<u>M-006025-02-1</u>
Guideline(s) followed in	Federal Biological Institute for Agriculture and Forestry, Braunschweig,
study:	FTXG, Party IV, 6-7 (July 1990)
Deviations from current	None of the of the
test guideline: 🖗 🖉	
Previous evaluation:	yes evaluated and acceptor of
~~ Ŭ	DAR (4997), RAR (2010), RAR (2017)
GLP/Officially recog-	No, no conducted under GLE Officially recognised testing facilities
nised testong facilities: 🤣	
Acceptability/Reliability:	$Y es^{\gamma} \sim \sqrt{\gamma} \sqrt{\gamma}$
E	

Executive Summary

The decomposition rate constant of spiroxamine in the atmosphere is estimated according to the Atkinson's method using the Atmospheric Oxidation Program (version 1.51, US EPA).

The reaction rate constant of spucxamine with hydroxyl radical was calculated to be 162.4455 x 10^{-12} cm³ molecules cm³. Assuming that a 12-hour daytime hydroxyl radical concentration is 1.5 x 10^6 molecules cm⁻³, the corresponding DT₅₀ rate was calculated to be 0.790 hours (0.066 days). Such a short degradation rate indicates spiroxamine is not persistent in the atmosphere.

I. Material and Methods

The rate constant of spiroxamine, in the reaction with hydroxyl radical or ozone in air was calculated



based on the Atkinson's method by using the Atmospheric Oxidation Program (version 1.51, US EPA). The calculation is based on an annual and global averaged 12-hour daytime hydroxyl radical concentration of 1.5×10^6 molecules cm⁻³ and 24-hour daytime ozone concentration of 7×10^{11} molecules cm⁻³.

II. Results

The reaction rate constant of spiroxamine with hydroxyl radical was calculated to be 162.4485×10^{-22} cm³ molecules cm³.

III. Conclusions

The reaction rate constant of spiroxamine with hydroxyl radical was calculated to be 162 4455 x 10^{-12} cm³ molecules cm³ according to the Atkinson's method, using the Atmospheric Oxidation Programs (version 1.51, US EPA). Assuming that a 12-hour daytime hydroxyl radical concentration is 15×10^{-10} molecules cm⁻³, the corresponding DT₅₀ rate was calculated to be 0.790 bours (0.066 days). Such a short degradation rate indicates spiroxamine is not persistent in the atmosphere.

Assessment and conclusion by applicant.

Study meets the current guidance and the requirements in 283/2019. The study is an existing study that was proviously assessed in the DAR (1997) and the RAR (2010), RAR (2017) and accepted by the RMS.

Data Point:	KČÁ 7.3,1/02 2 4 a 4 a 4 a 4 a 4 a 4 a 4 a 4 a 4 a
Report Author:	
Report Year:	1994 Depermination of the volume field with the volume of the work of of th
Report Title:	Depermination of the volutization behavoour of KWG 4168 EC 500 in a field
	trial a a a a a
Report No:	ĎPF4023 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Document No:	M-006029(01-1)
Guideline(s) followed(in	BOA-Guidelinestor the string of Plant Products in Registration Procedures,
study:	Part IV 6-1 (July 1990) 7 7 4
Deviations from current	
test guideline:	
Previous evaluation:	yes, evaluated and accepted
	DAR (1997), RAR (2010), RAR (2017)
GLP/Officially recog-	DAR (1997), RAR (2010), RAR (2017) Yes conducted under GLP/Officially recognised testing facilities
nised testing facilities:	
Acceptability Reliability:	No and a second s
A	

Executive Summary

The volatilization behaviour of the active ingredient spiroxamine formulated as EC 500 was investigated in a registration study in accordance with the BBA-Guideline IV, 6-1. Three experiments were carried out under field conditions in containers, with a surface area of 1 m², sown with winter wheat (variety Orestis) at a sowing density 0.500 seeds pecm². Applications occurred a growth stages BBCH 37 – 39.

The applications using formulated [Cyclonexyl-1-¹⁴C] spiroxamine were made in May 1994. The application equipment consisted of a mobile steel frame to which a vertically adjustable platform with the arrangement of spay nozzles was attached. The space between the plant container and nozzle platform could be sealed in order to avoid contamination of the environment during application. Practice-relevant application was simulated by spraying with a set of 3 individual nozzles at a distance of 50 cm each. The spray boom was driven by an electronically pulsed motor at a speed of 6 km/h over a distance of 100 cm (total container). During the entire test period of 24 hours, the following climatic data were recorded. The total amount of formulated active ingredient reaching the target area (initial deposit) was 83-94% on plants and 17-6% on soil (including the rim of the vessels).



The 5 vessels in the center were used for sampling. Within 2 min of the application, one of these vessels was harvested for determination of the initial spray deposit. Further vessels were taken after 1, 3, 6 and 24 hours for processing. The sequence of removing plant vessels was (1) 2, 3, 4 and 5:

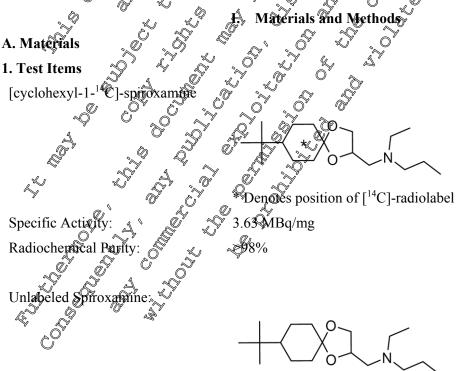
At sampling, the plants were cut off above the ground and transferred into acetonitrile. Subsequently the roots were removed from the soil, rinsed with acetonitrile and added to the plants. This acetonitrile solution and the rinsed soil were added to the first soil extraction. The plants were extracted three times with acetonitrile, the acetonitrile phases combined and investigated by two TLC methods

For soil, the top 2 cm was scraped off with a spoon and extracted three times with acetonitrile. Subsequently, the radioactivity and the content of active ingredient and metabolites were determined. The first extraction steps were carried out immediately in order to minimize volatilization effects during processing. The measured values immediately after application (vesseld) were defined as the applied radioactivity or applied amount of active ingredient for the further discussion.

The quantification of spiroxamine and relevant metabolites was made by evaluation of the thin-layer chromatograms developed with system I. System II was used to confirm the qualitative tesults obtained. The isomers A and B of spiroxamine were nominally separated by TLC but determined together. Plants and soil were extracted immediately after sampling. Extracts that were not analyzed directly were deep frozen and stored up to 2 months at approximately -20°C until analysis.

A total of 83-94% of radioactivity applied onto the simulated field segurent was detected on the plants and 17-6% on the ground (soil and rim of the vessels) Normalising the radioactivity measured on the plants immediately after application to 100% allowed the calculation of losses due to votatilization from the plant surfaces during the course of the total in percent of the initial deposit. After the maximum test duration of 24 hours, 74% (mean of three experiments) of the radioactivity having reached the plant stand was recovered.

On average, 26% of the radioactivity applied to the plants had volatilized (disappeared) from the plant surfaces after 24 hours. The analysis of the plant extracts indicated that the recovered radioactivity was predominantly unchanged parent compound. The volatilization rate from the simulated winter wheat field, including soil, with different weather scenarios was on average 24% within the measuring period of 24 hours.





Batch Number:	920522 ELB01
Radiochemical Purity:	99%

For the trial, radioactively labelled and non-labelled KWG 4168 were formulated as EC 500. [Cyclo-hexyl-1-14C]-spiroxamine and unlabelled spiroxamine were combined in acetonitrile. After evaporating the solvent, spiroxamine was thoroughly mixed with the blank formulation (formulation without active substance) and emulsified in 160 ml water by ultrasonication. Purity and content (radioactivity) of active ingredient were checked in the formulation before and after application (see Table CA 7.3.21).

Table CA 7.3.1-1: Com	position of sp	oray application	solution
-----------------------	----------------	------------------	----------

	*	· · · · @	× ×		
Formulation without A.S.	¹⁴ C-A		¹² C-A.S	Water	Newspecific ra-
300 mg	6.2 mg; 22	2.6 MBq		> ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	√75 KBe√mg°
				A A	

2. Test Soil

Fresh soil was collected from a single field ite and placed into containers for the conduct of the volatilisation experiment. The soil characterisation details car be found in Pable OA 7.30-2.

Table CA 7.3.1-2:	Physico-che	mical mon	erties of t	test soile	ØŸ
1 abic CA 7.5.1-2.	I hysico-chę	innear hissh			1

Parameter S S S S	Soil
Geographic Location	
City Q Q Q Q Q Q Q	Largenfield (Rhineland)
Country As A D A C	Germany
Textural Classification (NSDA) $\sqrt{(\%)}$	Loamy sand
Sand [50 - 2000 µm] 5 0 0 (%) 5 5	77.2
Sand [50 - 2000 µm] Silt [2 - 50 µm]	↓ 17.5 ↓ 17.5
$ \operatorname{Clay} \leq 4\mu \operatorname{III} $ $\mathcal{O}_{1} \ll \mathcal{O}_{2} \ll (70)$ $\mathcal{O}_{2} \ll \mathcal{O}_{2} \ll \mathcal{O}_{2} \ll \mathcal{O}_{2}$	5.2
$\begin{array}{c} c_{H}(y) = \frac{1}{2} \frac{1}$	
pH in CaCl ₂	5.9
$\frac{\text{In CaCl}_2}{\text{Organic Matter }} \xrightarrow{\sqrt{2}} $	2.41
	1.4
Water Holding Capacity (g F2O/100g soil Ory weight)	
Water Holding Capacity (gr20/100g soil 0ry weight) 40%	10.6
* Calculated by multiply organic arbon contact by 1.72	

* Calculated by multiplying organic carbon content by 1.72

B. Study Design

The objective of the present stridy was to determine the volatilization behaviour of the active ingredient in a practice-relevant trial, i.e. under field conditions, in compliance with the valid guideline. The study was carried out in the experimental station and laboratories of Bayer AG, Monheim in accordance with GLP regulations

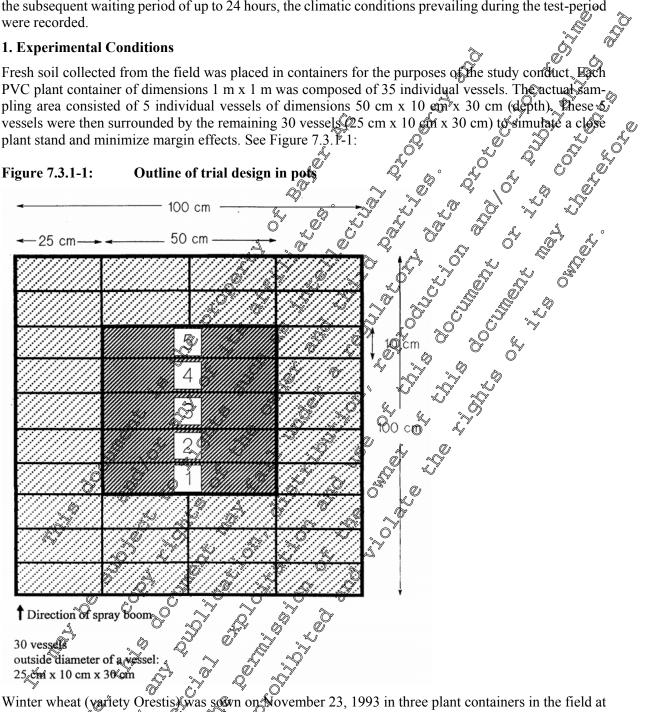
The use of radioactive labeled spiroxamine allowed the quantitative determination of both non-volatile degradation produces as well as metabolites and parts of parent compound bound to plant and soil matrices. These would not be detectable without the use of a tracer and hence would otherwise be included in the overall balance as seemingly volatilized spiroxamine. Since the use of radioactive isotopes in the free field is not permitted in Germany, for radiation protection and health reasons, the trials were carried out in plant containers under simulated field conditions in a controlled area. The crop was sprayed with



the formulated spiroxamine in a manner reflecting common practice i.e. using a set of nozzles. During the subsequent waiting period of up to 24 hours, the climatic conditions prevailing during the test-period were recorded.

1. Experimental Conditions

Fresh soil collected from the field was placed in containers for the purposes of the study conduct. Each PVC plant container of dimensions 1 m x 1 m was composed of 35 individual vessels. The actual campling area consisted of 5 individual vessels of dimensions 50 cm x 10 cm³x 30 cm (depth), these S vessels were then surrounded by the remaining 30 vessels \$25 cm x 10 cm x 30 cm) to simulate a close plant stand and minimize margin effects. See Figure 7.3. 1-1:



a sowing density of 500 seeds per m². Applications were made during May 16-24. The development stages of winter wheat were.

- BBCH39. flag@eaf just visible, but still rolled.

- BBGH39: Ligule of flag leaf just visible, flag leaf fully unrolled.

The application equipment consisted of a mobile steel frame to which a vertically adjustable platform with the arrangement of spay nozzles was attached. The space between the plant container and nozzle platform could be sealed in order to avoid contamination of the environment during application. Practice-relevant application was simulated by spraying with a set of 3 individual nozzles at a distance of 50



cm each. The spray boom was driven by an electronically pulsed motor at a speed of 6 km/h, the acceleration and the stopping distances were 10 cm each. The spray boom was moved at a constant speed over a distance of 100 cm. Nozzles, hoses, valves and the supply vessel with the application solution were attached to the spray boom. For the spraying process the supply vessel was put under pressure by means of pressurized air. Before and during application the solution was kept in means of a magnetic stirrer in order to prevent inhomogeneity of spray solution in the supply vessel. The spraying process was started by putting the supply vessel under pressure and turning on the magnetic stirrer. This was followed by opening magnetic valves fixed in front of the nozzles Only once a uniform sprage pattern was achieved was the spray boom moved over the plant stand at the predetermined speed. plication details are provided in Table CA 7.3.1-3:

Table CA /.3.1-3: Application details	Table CA 7.3.1-3:	Application details
---------------------------------------	-------------------	---------------------

Number of sprays	Spray boom height	Number of nozzles	Distance be- tween toz- zles	Nozzletype	Pressione at -	Travel speed
1	50 cm	3	*50 cm/	Leshler LU 20-94	3.6 bar	©6 km/k

Two min after application a lift truck was used to move the plant container from the application equipment without vibration. n

The spray pattern was checked in pre-tests (i.e. distribution of the spray solution and reproducibility). This was done using a radioactive compound with very low volatoration which was sprayed with the application equipment on filter paper. Five pieces corresponding to the area of the vessels, were cut out and the amount of the radioactivity of these filter paper pleces was determined.

The study was composed of 3 Andividual experiments. The applications were made in the morning in each case. Each trial lasted for 24 hours. See Table CA 7.3.1-4:

Table CA 7.3.1-Application date

Experiment 🔊 🕻		Start (hour 4)	Trial dates
1 0*		16200 and 0	May 16-17
2 🔊		A, 99:08 and a	May 18-19
3	ð s		May 24-25
- A			

hours the following climatic data were recorded: During the entire eriod o

- a) At the level of the
 - temperatur

 - -rainfal

b) At 2 m above ground

- ailing wind direction
- vine velocit
- duration of sunshine
- mtensity of sunshine.

The listed weather data were recorded with a weather station of Lambrecht Co. The data for wind, temperature and humidity were measured at one second intervals and averaged over periods of 10 min each.



2. Sampling

The 5 vessels in the center were used for sampling. Within 2 min of the application, one of these vessels was harvested for determination of the initial spray deposit. Further vessels were taken after 1, 3, and 24 hours for processing. The sequence of removing plant vessels was (1) 2, 3, 4 and 5:

3. Analytical Procedures

The plants were cut off above the ground and transferred into acetonitrile. Subsequently the roots were removed from the soil, rinsed with acetonitrile and added to the plants. This acetonitrile solution and the rinsed soil were added to the first soil extraction. The plants were extracted three times with acetonitrile, the acetonitrile phases combined and investigated by two TLC methods:

System I: Silica F-254 Merck 60 gel plates. Solvent system of acetonitrile water: Ammonia (25%) 80:18:2 composition.

System II: Silica RP-18 F-254 S Metek plates. First solvent system of n-hexane: dictiloromethane: 2-propyl alcohol: ammonia (25%) of 30:70:10:20/v). The second solvent system was chloroform:ethyl alcohol 50:50 (v/ $\sqrt{2}$).

The top 2 cm of the soil was scraped off with a spoor and extracted three times with acetonitrife. The first extraction steps were carried out immediately in order to minimize volatilization effects during processing. Subsequently, the radioactivity and the content of active ingredient and metabolites were determined The measured values immediately after application (vessel 1) were defined as applied radioactivity or applied amount of active ingredient for the further discussion.

The quantification of spiroxamine and relevant metabolites was made by evaluation of the thin-layer chromatograms developed with system I. System II was used to confirm the qualitative results obtained. The isomers A and B of spiroxamine were nominally separated by TLC but determined together. Plants and soil were extracted immediately after sampling Extracts that were not analyzed directly were deep frozen and stored up to 2 months at approximately -20°C until analysis. Parent compound and relevant metabolites were stable under these storage conditions. This was proven by analysis of a sample that had been stored for 6 months at -20°C. The detection limit for a single metabolite was >0.5% of the applied radioactivity.

A. Results and Discussion

A. Data

The results of the reasurement of the radioactivity distribution between soil and plants immediately after application to the target area are given in Table CA 7 OI-5.

Table CA 7 3 1-5: Distribution of radioactivity post-application

Experiment	Plants	Soil and rim
1: May 55,1994	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	6%
2: May 18, 1994		11%
3: May 24, 1994	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	17%

A total of 83-94% of radioactivity applied onto the simulated field was detected on the plants and 17-6% on the ground (soil) and can of the vessels).

Normalising the radioactivity measured on the plants immediately after application to 100% allowed the calculation of losses due to votatilization from the plant surfaces during the course of the trial in percent of the initial deposit. After the maximum test duration of 24 hours, 74% (mean of three experiments) of the radioactivity having reached the plant stand was recovered (Table CA 7.3.1-6).



Eunovimont	Initial danasit on plants]	ذ 7		
Experiment	Initial deposit on plants	1 hr	3h	6h	24 4
1	100%	61.1	67.9 🔊	63.6	Ð9.4 Ö
2	100%	93.3	78.0	88.1	64.9 0
3	100%	93.5	1080	84.7	87.6
Mean	100%	82.6	<u>&</u> 4.7	78.8	<u>74</u> 33

Analyses of the plant extracts indicated degradation of the parent compound during the incubation period of 24 hours. After 24 hours, 48% of the radioactivity applied on the plants was parent compound (mean value). See Table CA 7.3.1-7:

Table CA 7.3.1-7:	Composition of plant	extracts by TLC	(% applied	radioactivity)

			\mathbb{V}		~ ~ \	1,4 20
Eunoviment	1	& ,	ŝ,	¥ 🔊 🐇	0° Q 2	
Experiment	3 h	24 h⊜ [∞]	3 h 💭	2⁄4 h 🔊	∭ð h	2 4 h
Extracted portion	59.8	591	or 67.2	Q 55.6 O	96.6	J72.8 4
Spiroxamine	47.1	4 4.2	× 58,4 %	¥7 . 4	°° 73₂0	51.8
M01 (spiroxamine-de- sethyl)	4.5	0 ⁷ 5.6 ² ³	2.7	2.9 ×	9 .5 S	
M02 (spiroxamine- despropyl)	4.4	593 a. A.	2.8	° 0 (8.15	L 6.9
M03(spiroxamine-N-oxide)	2,0	2.7	\$2.6 J	Q1.8	~ 3 .8 &	4.8
Unknown (≥1)	¥.7 🐇	CB 4	ζ, 1 _ρ Ω,	× 0.8	Q 3.2	2.3
Unextracted portion:	<u>\$</u> \$ 8.1 °	A1.3	، 10.8	23 ~	× 14,3	14.8
Total	67	70.4	78.0	64.9 🔊	298 .1	87.6
, second s					~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	

Only 6 to 17% of the total radioactivity applied, reached the soil (including the rim of the vessels) due to the high coverage of the soil by the target plants. Recovery rates of this radioactivity showed a relatively high variation during the test period. During experiment of the radioactivity increased in the soil presumably due to rainfall. See Table CA 7.3 188.

Table CA 7.3.1-8: Jolatiosation of spiroxamine from soil surfaces

Experi	mont	ý, 4	The field	posit on soil O		Recovery in	% after:	
Experi		A.			🔊 1 hr	3h	6h	24 h
1	Q.	Q,	N 6 10	00%	\$ 113.6	151.2	151.7	192.5
2	~	ů O	0 <u></u> ~ 14	90%	97.7	71.4	93.4	42.8
3	4	Š		0% ~~ 0°	95.1	149.5	68.2	93.5
Mean	<u></u>	Č)	N OI	00% 🔬	102.1	124.0	104.4	109.6

The analyses of the soil extracts demonstrated that degradation of spiroxamine had occurred from TLC analysis. After 24 hours, 28% of the radioactivity applied on soil was parent compound (see Table CA 7.3.1-9).



E	1	[2	3	B Q° 7
Experiment	3 h	24 h	3 h	24 h	3 h	24 1
Extracted portion	50.2	31.1	38.7	16.3	<u>128.1</u>	55,6 0
Spiroxamine	44.2	24.5	35.5	12.9	A05.7	46.3
M01 (spiroxamine-de- sethyl)	1.2	1.0	0.5	0.5	5.1	
M02 (spiroxamine- despropyl)	1.0	0.8	0.8	0.5	4.7	2.0 §
M03(spiroxamine-N- oxide)	3.8	1.8	<u>4</u> .9	2014		
Unknown (≥1)	< 0.1	3.0	<0.1	~~0.1 ~ °	£2.8 £	Q.6 Q
Unextracted portion:	101.0	161.4	32.7	26.5°	~ <u>21.40</u> *	چ 35.9
Total	151.2	192.5	71.4	¢ 42.8	× 148,5	≪ 93 <i>,</i> 5

Table CA 7.3.1-9:	Composition of soil extracts by TLC (% applied radioactivity)

Despite different weather scenarios, the active ingredient showed a relatively uniform volatilization behaviour in the complete field segment consisting of target plants and accompanying soil. The fact that the radioactivity contents did not uniformly decline as the total progressed can be explained by the heterogeneity of the plant stands in the individual vessels. Processing of ability target areas carried out after 24 hours yielded recovery rates of 63-89%. The total rate of volatilization from the field segment plants and soil as parent compound or metabolite averaged 24%. See Orble QN 7.3, 510:

Table CA 7.3.1-10: Volatilisation of spiroxamine from the total system

Evenoviment		Trestor	dobacit ordenil	Ø		ecovery in	%after:	
Experiment		Ingulai	deposit on soil		1 hr 🔊	~Sh	🖉 6h	24 h
1	7	Ţ	100% 🖉 🔍 🕖	1	64.0	×12.5	68.4	77.1
2	22		100%	°%	y 93. J	x 77. 3	88.6	62.7
3	Ő,		10%	2	93.8 O	115.0	82.0	88.6
Mean		ŝ	×100%~ .~	Ŝ.	\$83.8	8 8.3	79.7	76.1
		~~ «			2. 2	S		

MI. Conclusion

The complete ecosystem especially the time of application, the target crop and the degree of soil coverage by plants should always be taken into consideration for an environmentally relevant assessment of the volatifization behaviour of plant protectants. The application in this trial was made onto an almost closed stand of winter wheat (flag teaf stage 37-39). Due to the high coverage of soil by plants only 6 to 17% of the total radioactivity applied reached the ground (soil and rim of vessels) immediately after spraying. The application of sproxamine EC 500 was performed under normal weather conditions and the volatilization rate of parent compound including possible volatile metabolites was determined to be 24%. Predominantly unchanged parent compound was becovered from the plant and soil extracts.

An assessment of the photochemical or idative degradability of spiroxamine in air was carried out. Based on calculations according to Atkinson the average chemical life was in the range of one to three hours.

Assessment and conclusion by applicant

Study meets the current gordance and the requirements in 283/2013.

The study provides supplementary information on the volatile behaviour of spiroxamine but is not based on a guideline compliant study design.



Data Point:	KCA 7.3.1/03
Report Author:	
Report Year:	1998 Volatilisation behaviour of KWG 4168 EC 500 in a field trial, treatment of byte
Report Title:	Volatilisation behaviour of KWG 4168 EC 500 in a field trial, treatment of pare
	soil
Report No:	MR-643/98
Document No:	<u>M-006028-01-1</u>
Guideline(s) followed in	BBA-Guidelines for the Testing of Plant Products in Registration Procedures,
study:	Part IV. 6-1 (July 1990)
Deviations from current	None V Q Q Q
test guideline:	
Previous evaluation:	yes, evaluated and accepted $\sqrt[n]{2}$
	RAR (2010), RAR (2017)
GLP/Officially recog-	Yes, conducted under GQP/Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	Yes O ^v O ^v A A A

Executive Summary

The volatilisation behaviour of the active ingredient spiroxamine formulated as EC500 was investigated in a registration study in accordance with the BBA Guideline IV 6-1. Field soil colleged from Lagenfield, Germany, was used to fill a number of plant containers consisting of 42 individual chambers for the conduct of the study. The experiment was carried out under field conditions with a target area of 1 m². Bare soil was treated.

Upon receipt of the 14C-spiroxamine, TLC analysis found that the test item was only 60% pure necessitating a preliminary clean-up step using TLC, giving a final radiochem parity of >99%. The spray application using [cyclohexyl-1]¹⁴C] formulated spiroxamine was made in June 6, 1998. The application equipment consisted of a mobile steel frame to which a vertically adjustable platform with the arrangement of spay nozzles was attached. The space between the plant container and nozzle platform could be sealed in order to avoid contamination of the environment during application. Practice-relevant application was simulated by spraying with a set of 3 individual nozzles at a distance of 50 cm each. The spray boom was driven by an electronically pulsed photor at a speed of 6 km/h over a distance of 100 cm (total container). During the entire test period of 24 hours, the local climatic conditions were recorded

The 12 vessels in the center were sampled Within 3 min after application of the test item, two of these vessels (A 3.1 and A 3.2) were taken for determination of the initial spray deposit. The sequence of removing vessels was:

- 0 h: vessels $A^{3.1}$ and $A^{3.1}$
- 1 havessels A 5.1 and AS.2
- Sh: vessels Ar.1 and A 1.2
- 6 h: vessels A 2.1 and A 2.2
- 24 h: vessels A 4.1; & 2.2; A 6.1 and A 6.2

The top 2-3 cm of the soil was scraped off with a spoon and extracted two times with acetonitrile (250 ml, 150 ml). Subsequently, the radioactivity and the content of active ingredient and metabolites were determined by two TLC methods. The quantification of a.i. and relevant metabolites was made by evaluation of the thin layer chromatograms developed with method I. Method II was used to confirm the qualitative exults obtained. The isomers A and B of spiroxamine were normally separated by TLC but calculated (quantified) together. The soil was extracted immediately after sampling. Extracts were analysed directly within 6 days (the detection limit for a single metabolite was $\geq 0.5\%$ of the applied radioactivity). The radioactivity in the extracted soil was determined by combustion. The measured radio-



active value immediately after application (mean value of vessels A 3.1 and A 3.2) was defined as applied radioactivity or applied amount of active ingredient for the further discussions.

The volatilisation of spiroxamine from bare soil was very low (2% of the applied compound after 24 hours). The analyses of the soil extracts indicated that the recovered radioactivity was predominantly unchanged parent compound after the period of 24 hours.

I. **Materials and Methods**

inthy international and intern A. Materials 1. Test Items [cyclohexyl-1-¹⁴C]-spiroxamine: notes positio Specific Activity: Radiochemical Purity: SU, CA Non radiolabelled spiroxamine Radiochemical Purity

¹⁴C-spiroxamine was dissolved in 2 meacetonitrile and analysed with TLC method I. Due to the radiochemical purity of only 60% of. (hypothesized to be caused by auto-radiolysis due to the high concentration of the test substance during storage the compound was purified with TLC method I prior to use of the material in the study. The purification was conducted by scraping the silica gel associated the radioactive zone corresponding to spiroxamine from the TEC plate and extracting the 14C-spiroxamine with 2 ml acetonitrile (stock colution). This purification led to a radiochemical purity of > 99% [with a ratio of the diastereomers \mathcal{A} : B = 3%: \mathcal{A}

For the treal, radioactivity labeled and non-tabelled spiroxamine were formulated as EC 500. 1.3 ml of the stock solution (10 mg 14C-spiroxamine equivalent to 7,057 kBq) and 297 mg of unlabelled spiroxamine were combined in acetonitrile (total volume 4.3 ml). The new specific radioactivity was 23.6 kBq/mg. After evaporating the solvent, spiror amine was thoroughly mixed with 298.9 mg blank formulation (formulation without a.). The formulation was then emulsified in 159.4 ml water with ultrasonication. Purity and content (radioactivary) of active ingredient was checked in the formulation before and after application. Please refer to Table CA 7.3.1-11:

	••••••••••••••••••••••••••••••••••••••	F		
Formulation without	14C-A.S.	12C-A.S.	Water	New specific ra- diochem
298.9 mg	1.9 mg; 7,057 kBq	297 mg	159.4 ml	23.6 kBq/ml

Table OA 7.3 2-11: Composition of spray application solution



2. Test Soil

Fresh soil was taken from a soil stack and used to fill a number of plant containers for the experiment. The soil characterisation details can be found in Table CA 7.3.1-12.

Table CA 7.3.1-12:	Physico-chemical properties of tes	st soil
--------------------	------------------------------------	---------

`			~~	
Parameter		1	Soil 🔊	S S
Geographic Location	<i>⊳</i> ∧			
City	S.	Langenfie	ld Rhinela	nd) 🖉
Country	Á,	Ó ^y Q	rmany	nd)
Textural Classification (USDA)	L Q	koa koa	my sand	ê û
Sand [50 - 2000 μm]			70° 6	
Silt [2 – 50 µm]	(%)	ja ja ja	€7.5 s	Ĵ,
Clay [< 2 μm]	$(%) \qquad (%) $		5.2	1 .
pH		Q	Ő "	
in CaCl ₂			5.9	S.S.
Organic Matter (%) *			2.41	Ő
Organic Carbon (%))
Cation Exchange Capacity (meq/10			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
Water Holding Capacity			×	
40% (g water/ 100 g dry weight soil)			10.8	
* Calculated by multiplying organic caro	n content by 1 🗹	29 ~ ~ ~ ~	Ŷ.	<u> </u>

B. Study Design

The objective of the present study was to determine the polatilization behaviour of the active ingredient in a practice-relevant trial vie. under field conditions in compliance with the valid guideline. The study was carried out in the experimental station and laboratories of Bayer AG. Monheim in accordance with GLP regulations.

The use of radioactive labelled a radiowed the quantitative determination of both nonvolatile degradation products as well as metabolites and parts of parent compound bound to soil matrices. These would not be detectable without the use of a tracer and hence would other wise be included in the overall balance as seemingly volationed and Since the use of radioactive isotopes in the free field is not permitted in Germany, for radiation protection and health reasons, the trial was carried out in a container under simulated field conditions in a controlled area. The bare soil was sprayed with the formulated a.i. in a manner reflecting common practice, i.e. using a set of nozzles. During the subsequent waiting period of up to 24 hours, the climatic conditions prevailing puring the test-period were recorded.

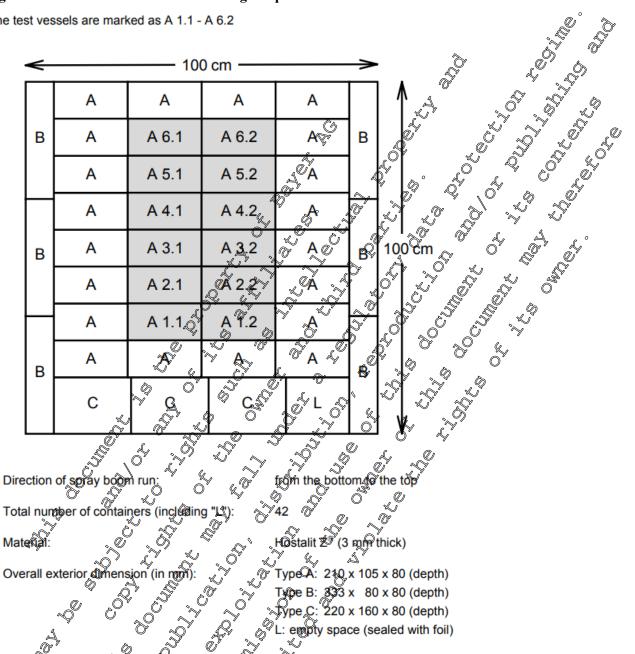
1. Experimental Conditions:

Fresh soil collected from the field was placed in containers for the purposes of the study conduct. Each PVC plant container of timensions 1 m x 1 m. The actual sampling space consists of 12 individual vessels with internal dimensions of 204 mm x 99 mm x 77 mm depth. These "sampling vessels" are surrounded by vessels simulating a field plot to minimise marginal effects. Please see Figure 7.3.1-2 for details.



Figure 7.3.1-2: Outline of trial design in pots

The test vessels are marked as A 1.1 - A 6.2



The appreation equipment consisted of a mobile seel frame to which a vertically adjustable platform with the arrangement of spay nozzles was attached. The space between the plant container and nozzle platform could be sealed in order to avoid contamination of the environment during application. The application (at agricultural relevant rates) was simulated by spraying with a set of 3 individual nozzles at a spacing of 30 cm each. The spray boom was driven by an electronically pulsed motor at a speed of 6 km/h over a distance of 100 cm (total container). Before and during application, the solution was kept in motion by mans of a magnetic stirrer in order to prevent inhomogeneity of spray solution in the supply vessel.

Re-calculations indicated, that about 30 ml spray solution was applied to the container. This spray solution was less than needed for the application of the total amount of spiroxamine. However, since spiroxamine the not sprayed directly onto bare soil, a reduced application rate for soil is appropriate (good agricultural practice). No additional pre-test was performed with the intended formulation to determine the exact amount of spray solution per m².



Application details are provided in Table CA 7.3.1-13:

Table CA 7.3.1-13:	Application details	
--------------------	---------------------	--

Number of sprays	Spray boom height	Number of nozzles	Distance be- tween noz- zles	Nozzle type	Préssure at Aozzle	Travel Aspeed
1	50 cm	3	50 cm	Lechler LU 120-04	3.5 bar 🖉	6 km/h
During the ent Co. weather sta	ire test period o ation:	of 24 hours the	following chim	atic data were	recorded using	a diambre cht
a) At the level	of the plant sta	nd:				
• -air te	mperature		u po		, ø ' ð' »	
• -humi	dity					.4
• -wind	velocity	×1		A.		
• -rainfa	all	Ű				
o) At 2 m abov	e ground:		y A D			
• -preva	velocity all ve ground: ailing wind dire velocity	ction				\sim
• -wind	velocity	Ţ, 'n	, '0' L		v v	
• -durat	ion of sunshine				inflational and a	
• -intens	sity of sunshine			A at any colored	, S	
The data for m	ind to Sugarative	o and Naumidate	. was Smarker	l at ana coord	informate and a	waragad awar

- -air temperature
- -humidity
- -wind velocity .
- -rainfall

- -prevailing wind direction
- -wind velocity
- -duration of sunshine

• -intensity of sunshine at one second intervals and averaged over C. C. C. ¢, periods of 10 min sich.

2. Sampling

 \bigcirc The 12 vessels in the center were used for sampling. Within 3 min after application of the test item, two Wweremaken for determination of the initial spray deposit. The sequence of these vessels (A 3.1 and A 3 of removing vessels was

- 0 h[.] vessels
- 1 h: vessels A
- Wessels & 1.1 and
- vessels A and
- h. vessel

3. Analytical Procedures

When sampling the soil in the container, the top 2-3 cm of the soil was scraped off with a spoon and extracted two times with accontrile (1 x 250 ml and 1 x 150 ml). Subsequently, the radioactivity and the content of active ingrodient and metabolites were determined by TLC using two methods:

> Method I: Silica F-254 Merck 60 gel plates. Solvent system of acetonitrile:water:ammonua (25%) 80:18:2 composition.

Method TI: Silica RP-18 F-254 S Merck plates. First solvent system of n-hexane: dichloromethane: 2-propyl alcohol: ammonia (25%) of 30:70:10:2 (v/v).

The quantification of a.i. and relevant metabolites was made by evaluation of the thin layer chromatograms developed with method I. Method II was used to confirm the qualitative results obtained. The



isomers A and B of spiroxamine were separated in the TLC system but calculated (quantified) together. The soil was extracted immediately after sampling. Extracts were analysed directly within 6 days (the detection limit for a single metabolite was $\geq 0.5\%$ of the applied radioactivity).

The radioactivity in the extracted soil was determined by combustion. The measured radioactive value immediately after application (mean value of vessels A 3.1 and A 3.2) was defined as applied radioactive ingredient for the further discussions.

The electro-spray ionisation mass spectra (ESI) via syringe were obtained with a TSQ 7000 instrument (Finnigan).

II. Results and Discussion

A. Data

The application was made on June 16, 1998 at 10.40 (a.m.) and the experiment lasted for 24 hours. The identity of the test substance 14C-spiroxamine was verified by TLC and MS. Normalising the radioactivity measured on the soil after application (θ h) to 100% allowed the calculation of losses due to yolatilisation from the soil surface during the course of the trial in percent of the initial deposit. After the maximum test duration of 24 hours the volatilisation rate was very low (2% See Table CA 7.3.1.4):

Table CA 7.3.1-14: Volatilisation of spiroxamine from plantsurfaces

Initial deposit on soil (0 hrs)	~~~ ?~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	ĝ.	0 1 hr 0	Secovery in %	و After: ک ولک	°۶۶ ۲۶۶ 24 h
100%	K,	.0	106,9	مچم <u>م</u> 96.8		98.2

Approximately 20% of the applied radioactivity was not extracted with acconitrile from the soil, proving the good binding of spiror amine to soil see Table C $\sqrt{7.3}$. (45). Re-calculations indicate that an amount, corresponding to 35% g at ha was sprayed onto bare soil. This represents about 50% of the maximum use rate (550 g 4 i./ha) Vinder the rules of good agricultural practice by far less than 50% of the application rate will reach the soil due to interception by the coop covering the soil. After 24 hours 68% of the applied radioactivity was found to be parent compound with all detected metabolites were each below 10% of the applied radioactivity (see Table CA 7.30-15).

a de la companya de l	<i>♥</i>	. U) ×				
Sampling Date	\sim	() (111)	Ů, Y, K ≪	, <u>Ś</u> ĥ	6 h	24 h
Extracted portion	Э× 4	× \$3.2 ~	″ ?® 7.0 O″	75.5	84.9	79.4
opnonamin	a J	Sn.d.	∾ n.d.	2 72.2	n.d.	68.1
M01 (spiroxanane sethyl)	U a	n.đ×	n ng.	1.1	n.d.	2.4
M02 (spiroxamine desprop	- (a)	Ön.d.	~~~ n.d. ~~	0.7	n.d.	1.8
M03(spiroxamine- ide)	N-0x-	nze.	nya.	1.6	n.d.	5.5
Unknown (≤1)	(⁽	Cn.d.	On.d.	n.d.	n.d.	1.6
Unextracted portio	n 🔬 💊	0n.d.	Q 19.9	21.3	18.2	18.8
TOTAL	Ž,	<u>5 106-0</u> , <u>5</u> ~	106.9	96.8	103.1	98.2
		* × 1	I. Conclu	usion		

Table CA 7.3.1-15: Composition of soil extracts by TSC

The spray application of spiroxamine EC 500 was performed under normal weather conditions onto bare soil. The volatilisation of parent compound including possible volatile metabolites from bare soil was very low (2% after 24 hours). Predominantly unchanged parent compound was recovered from the soil extracts.



Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study provides supplementary information on the volatile behaviour of spiroxamine buoss no based on a guideline compliant study design.

CA 7.3.2 Transport via air

Due to low volatility and degradation of spiroxamine residues in air by OH radicals, transport vicair is expected to be negligible.

CA 7.3.3 Local and global effects

Due to low volatility and degradation of spirosamine residues in arrow QB radicals; transport via air is expected to be negligible.

CA 7.4 Definition of the residue

CA 7.4.1 Definition of the residue for risk assessment

Based on the route of degradation studies presented under Point CA 7.9.1 (for soil) and Point CA 7.2 (for the aquatic environment) and the overview of metabolites observed in the various studies presented in Table CA 7.4.1-1, the following residue definitions for risk assessment are proposed for soil, ground-water, surface water, sediment and air

Soil: Spiroxamine and metabolites Mol (spiroxamine-desethyl), M02 (spiroxaminedepropy), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid)

Groundwater: Opiroxamine and metabolites M01 (spiroxamine-desethyl), M02 (spiroxaminedesptøpyl), M03 (spiroxamine-Noxide) and M46 (spiroxamine-acid)

Spiroxanine and metabolites M01 (spiroxanine-desethyl), M02 (spiroxamine-desptopyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid)

tite M06 (spiroxamine-acid)

Sediment:

Surface water:

Air:

Table CA 7.4.1-1: Overview of maximum levels of spiroxamine and metabolite observed in environmental fate studies [% AR]

Component			aximum level o	observed (% AI	R)			
Ó		Soil studies	•	A	Aquatic studies ^C			
		Anaerobic soil ^A	Soil photo- degrada- tion ^A	Photolysis ^B	W/S layers ^A	Whole sys- tem ^A		
Spiréxamine		-	-	-	- water 69.2 sed.	-		
MOD	12.0 [8.8]	7.6 [- ^E]	9.1 [9.1]	4.5 [4.5]	1.2 water [n.a.] 3.9 sed. [n.a.]	4.3 [<10 ^G]		



Component		Ν	aximum level (bserved (% Al	R)		
		Soil studies ^C		Aquatic studies ^C			
	Aerobic soil ^A	Anaerobic soil ^A	Soil photo- degrada- tion ^A	Photolysis ^B	W/S layers ^A	Whole Sys-	
M02	9.2 [9.2]	5.8 [- ^E]	6.1 [6.1]	4.5 [4.5]	1 water (n.a.] (n.a.] (n.a.]	3 A <10 S	
M03	7.9 [7.9]	3.3 [- ^E]	6.2 [6.2]	4.0 [4.0]	11.3 water [11.3] 1.5 sed [1.5]	15 Y [n.a. Of	
M06	5.3 ^D [3.5 ^F]	9.9 [- ^E]	not observed [2007 ob- served] °	not observed not ob- Served	28,7 water [25.6] 23.0 scol.	44.5 n.a. 1	

n.a. not available; sed. - sediment

- A Major metabolites are defined as >10% AR; 5% AR at consecutive timepoints; or >5% AR and increasing at end of study
- B Major metabolites are defined as >10% A
- C Proposed new LoEP for renewal [existing LoEP DAR 204]
- D Maximum level observed at last sampling integral in study
- E Existing LoEP (RAR 2017) does no proposed endpoints for degradation of spinoxamine under anaerobic conditions
- F Existing LoEP (RAR 2017) does not provide a max observed value of metabolite Mor and the default minimum (0.0001) is used for PECsw calculation. However, in the disting study KCP 7.1.1.1/01 (M406135-04-1) metabolite M06 is observed at a maximum of 3.5% AR
- M06 is observed at a maximum of 3 5% AR
 G Existing LoEP (RAR 2017) quotes V0% AR as maximum observed value for metabolites M02 and M02 and the default minimum (0.0001) is used for PECswoalculation. However, in the existing studies KCA 2.2.3/01 (M-006015-01-1) and KCA 7.2.2.3/04 (M-34) 324-01-1) the maximum observed ramount in the whole system of metabolites M01 and M02 is 1.9 and 13% AR as pectively
- and M02 is 1.9 and 1.9% AR respectively H Existing LoEP (RAP 2017) does not quote a Chole system maximum observed mount of metabolite M03. However, in the existing studies KCA 7.2.2.3(2) (M_DO015-01-1) and CA 7.2.2.3(04 (M-303324-01-1)) the maximum observed amount in the whole system of metabolite M03 is M.3% AP
- I Existing LoEP (RAR 2017) does not quote a whole system maximum observed amount of metabolite M06. However, in the existing studies KCA, Q.2.2.3/0 (M-006015-01-) and KCA 7.2.23/04 (M-303324-01-1) the maximum observed amount in the whole system of merabolite M03 is 31-3% AR

CA 7.4.2 Definition of the residue for monitoring

Based on the information considered for the definition of the residue for risk assessment and the persistence and relative toxicity of the components involved, the following residue definitions for monitoring purposes proposed for soil groundwater surface water sediment and air.

Soil:

Spiroxamine only

(metabolites M01 spirovamine-desethyl), M02 (spirovamine-despropyl), M03 (spirovamine-N-ocide) and M06 (spirovamine-acid) can be concluded as sufficiently less toxic than parent spirovamine in the terrestrial environment, see CP $\ge 10.4.1$

Groundwater.

Spinoxamine only

(metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) can be concluded as sufficiently less toxic than parent spiroxamine in the terrestrial environment, see CP 10.4.1., and the aquatic environment, see CP 10.2.

Surface water:

Spiroxamine only

(metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03



(spiroxamine-N-oxide) and M06 (spiroxamine-acid) can be concluded as sufficiently less toxic than parent spiroxamine in the aquatic environment, see CP 10.2.

Sediment: Spiroxamine only

(metabolite M06 (spiroxamine-acid) can be concluded as sufficiently test than parent spiroxamine in the aquatic opping to the second se than parent spiroxamine in the aquatic environment, see CP 10.2.

Air: Spiroxamine only

CA 7.5 **Monitoring data**

Monitoring data from databases in the EU

, soid r y No central EU databases are available for monitoring data in surface water, grandwater, soil and air for plant protection active substances. Therefore, on unsystematic database search was conducted by searching monitoring databases or monitoring reports available from e.g. Ovironmental agencies of several Member States to conclude on Wailable moniforing data.

	KCA 7.502
Data Point:	KCA 7.502
Report Author:	
Report Year:	
Report Title:	Spiroxantine and metabolites: Public environmental monitoring data (groundwa-
2	rer, surface water, drivering water, soil, air and sediment)
Report No:	EnSa-21-0063
Document No:	
Guideline(s) followed in	None of the transferred to the t
study:	None S S S S S S S S S S S S S S S S S S S
Deviations from current	None & A A A A A A A A A A A A A A A A A A
test guideline	
Previous evaluation: ¹⁰	No, not previously submitted a submitted
GLP/Officially recog-	No not conducted under 6 P/Officially @cognised testing facilities
nised testing facilities	
Acceptability/Reliability:	Yes in a of a
Executive Summary	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

Searches for public monitoring data were performed to provide an overview of residue concentrations of spiroxamine (SPX, parent) and its metabolites spiroxamine-desethyl (M01), spiroxamine-despropyl (M02), spiroxamine-N-9xide QM03) and spiroxamine-acid (M06) in the environmental compartments groundwater, surface water, drinking water, soil air and sediment in the frame of the EU approval renewal of spiroxamine according to 110702009 and 2020/1740. The search was predominantly based on internet sources identifying databases and reports which are publicly accessible e.g. from the Environmental Agencies of European countries. The parent SPX as well as its metabolites were the subject of this overview of monitoring results. Available monitoring data was analysed for exceedance of regulatory thresholds appropriate for the compartment and the results summarised. The search revealed that monitoring information is not generally publicly available in all European countries and not necessarily available at amational level, while in some cases being available at federal state/region/province level. In terms of concentration thresholds, this report facilitates analysis within the context of the Water Framework Directive (2000/60/EC) and the associated Groundwater Directive (2006/118/EC), the Drinking Water Directive (1998/83/EC) and the Plant Protection Products Directive (1107/2009/EC). Key Regulatory Acceptable Concentrations (RACs) for SPX are considered for surface water (0.188 μ g/L) and for sediment (712 μ g/kg). For groundwater, a value of 0.1 μ g/L applies for SPX. As part of



the EFSA conclusion (2010) for SPX, SPX-desethyl (M01), SPX-despropyl (M02) and SPXN-oxide (M03) are classified as a non-relevant metabolites. Metabolite SPX-acid (M06) is tentatively regarded as relevant for water unless the relevant algae study is submitted and demonstrates nonrelevance. This conclusion was derived by applying the guidance document for the assessment of the relevance of metabolites in groundwater within the EU (Sanco/221/2000 rev. 10 Feb 2003) as corrently valid guidance document. No monitoring data are reported for the metabolites SPX-desethy (M01), SPX-desproy/ (M02), SPX-N-oxide (M03) and SPX-acid (M06) in any database/report under consideration. Monitoring data for SPX was found in databases (and reports) of Austria, Denmark France, Germany, Italy, the Netherlands and Sweden, plus the Danube river database The groundwater monitoring data search resulted in a compliance rate of 99.99% with the threshold of 0.1 µg/L Q 9 analyses @ 130,633 analyses in total), with a maximum concentration of 20.76 µg/2. The surface water monitoring eata search re sulted in a compliance rate of 100% with the Tier ARACSW of @188 ug/L (Sanalyses of 1,004,326 analyses in total were reported above the RAC) with a maximum concentration 7.2 Jug/L For the air compartment, 792 analyses with SPX concentrations above the LOQ (0.000 -0.0, & ng/m, as stated in the databases) were found (14.0% of 5,677 analyses). The median value of the quantified analyses amounted to 0.36 ng/m3. The reported maximum psidue concertation amounted to 65.93 mg/m3. For the sediment compartment, the 435 analyses found reported SPX concentrations under LOQ (0.2 5.0 µg/kg d.w. as stated in the databases). Monitoring of SOX is not docomented for driving water and soil. It cannot be discounted that some of the detections identified in groundwater surface water, air and sediment are erroneous given they originate from non-GLP monitoring networks and programmes of unknown quality. Overall, it can be concluded from a sessment of readily available public monitoring datasets that spiroxamine (SPXF does not pose a concern for the investigated environmental compartments.

E Materials and Methods

A. Materials

1. Test Items

y g y g y g y This study reports the findings of a review of National member sate databases on residues of spiroxamine and metabolites in environmental compartments. All applications of spiroxamine related to environmental monitoring are resultant from applications of commercially available formulations in the field to good agricultural practice.

2. A. Study Design

In accordance with commission Regulation (FU) 2020/1740, Bayer AG, Crop Science Division will submit a dossier to support the renewal of the approval of the active substance spiroxamine (SPX, parent). At present, there is no guidance to indicate what adention should be paid to publicly available monitoring data, if any, and how the validity of this data should be assessed for such submissions. In order to ensure a complete data package is submitted and demonstrate the safety of this active substance, an overview of potential findings of parent SPX and its metabolites in databases reflecting 'public' monitoring programs is provided. This search included the following European countries with monitoring programs in place: Austria, Czech Republic Denmark, France, Germany, Greece, Ireland, Italy, the Netherlands, Portugal, Komania, Slovenia, Spain, Sweden, Switzerland, and United Kingdom. The search also ingluded (supra gational) i.e. R and river basin databases, for which Public Monitoring Programs anotheir data accessible via a bink on the internet. Evaluation of these data should be undertaken with caution as they are collected from monitoring points of unknown quality and to unknown quality standard@and experience from using these data suggests that they contain false positive findings. Monitoring data for SPX was found in databases (and reports) of Austria, Denmark, France, Germany, Italy, the Netherland's and Sweden, plus the Danube river database.

2. B. Data Collection

Public monitoring databases and associated monitoring reports were investigated for several countries covering groundwater and/or surface water and to a lesser extent drinking water, soil, sediment and air. The information in the databases and/or reports was collated and/or evaluated for the European country's



agency/organisation on the search list. An overview of the monitoring situation is compiled in Table 3.1. For the sake of completeness, countries with public monitoring program but where no relevant public monitoring data on SPX were available are also listed in Table 3.1, but not further mentioned in the results. For databases not reported in English language and/or some key words in drop down menus not translated, these terms were translated using 'Google' translate functions, De. for Denmark, Germany, Italy, the Netherlands, Czech Republic, Romania, Slovenia and Sweden, See Table CA 7.5-1

~	Č.	s and Outcome.
Country	Data Source/Organisation	Monitoring Data Available
Europe	NORMAN – EMPODA Database	No monitoring data reported
1	Danube River Basin Water Quality Database @	Aves &
	European Environment Agence – Status and quality of	Not considered due to rept-
	Europe's water database (Waterbase)	cation oondividual MS data
Austria	Austrian Federal Ministry for Sustainability and Four- ism – H2Q Water Database	No monitoring data reported
	Austrian Federal Environment Agency and Ministry for Sustainability and Fourism Several reports	Yes & Yes
zech Republic	IS Arrow – Assessment and Reference of water moni-	No monitoring data reported
Denmark	Geological Survey of Denmark and Greenland – Groundwater database (Supiter)	Yes Yes
	"Danish Pesticide/Leaching Assessment Programme"	No monitoring data reported
France	ADES National Groundwater Quality	Yes
	Porta Naïades – National Surface Water Quality Data	Yes
	ATMO SNational network of associations for the air	Yes
	CVEP - National presticide monitoring plan in air	Q Yes
Germany	Sachsen Environment Agency – Surface wall ter/Groundwater Quarty Portal (IDA) and report	Yes Yes
O ^r ,		Yes
	Rheinland Falz Environmental Agency Annuabre-	Yes
Ky .	Rheinland Pfalz Environmental Agency – Annual re- ports of stations for water investigation	Yes
	ment interactive data and map service (ODO)	No monitoring data reported
	German Federal agency for hydrology – Rhine river	No monitoring data reported
<i>A</i>	Elbe Biver Basin - Data information system	Yes
	AWA Working Group on water issues of the Fed- C Aeral States and the Federal Government	No monitoring data reported
y x	Baxarian Environmental Agency – Environment atlas	Yes
L.	Schleswig-Holstein – Agency for Agriculture, Envi-	Yes
Greece	Greek Ministry of Emergy and climate Change – Re- porton quatity of surface and groundwater of the coun- try	No monitoring data reported
Italy	A Irish Trivironmental Protection Agency – Annual re-	No monitoring data reported
Ital	Itakan National Institute for Environmental Protection	Yes



Country	Data Source/Organisation	Monitoring Data Available
		[yes/no]
Netherlands	Dutch Institute of Environmental Sciences - Atlas for	Yes
	pesticides in surface water	
	Water Quality Data portal of the Netherlands	res of a
	Ground Water Quality Reports	No ponitoring data reported
	"Research on exposure of residents to pesticides in the	No monitoring data reported
	Netherlands"	
	Groundwater Atlas for Pesticides – pesticide model	No monitoring data reported
Portugal	Portuguese Environment Agency – Report on state of	No monitoring data reported
	environment	
Romania	Romanian National Administration Apele Române" –	No monitoring data reported
	Several reports	
Slovenia	Slovenia Environment Agenco – Several reports and	No monitoring data reported
	raw@data @°	
Spain	"Ríos hormonados Amplin presencia de plaguicidas	No monitoring data reported
	distuptores endocranos en ags nos aspanotes	
	Spanish Water framewort Junta de Andalucía	No monitoring data reported
	Hydrographic confederation of Ekro	No monitoring data reported
	Hydrographi@confederation of Guadalquivit	No monitoring data reported
	Hydrographic confederation of Júcas	No monitoring data reported
	Hydrographic confederation of Segura	No monitoring data reported
	Basque Water agency	No monitoring data reported
Sweden	Swedish Oniversity of Agricultural Sciences - Posticide) d'és
	Database of the second	<u> </u>
	"Long-term Data from the Stredish National Environ-	No monitoring data reported
	mental Monitoring Program of Pesticides in Surface	
0 1 1	Waters Waters	
Switzerland	Swiss National Environment Seency Several report	No monitoring data reported
Ĵ.	Regional Environment Agency of Canton Solothurn -	No monitoring data reported
	Ševeral faw dáta S	
Inited Kingdom	England Environment Agency Wates quality archive	No monitoring data reported
le la	UK Water Quality Sampling Plarmonsed Monitoring	No monitoring data reported
N N	Drinking Water Inspectorate of England and Wales –	No monitoring data reported
je G ^u	Chief hypector Annual Reports and regional over-	
« ¥	Views Views	NT- manifesting 1 ()
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Pesticide Monitoring Bulletin	No monitoring data reported

## W Results and Discussion

Spiroxamine was barely quantified (car 99.99% of the analyses showed residue levels below LOQ) in groundwater and surface water analyses referenced from readily available public monitoring databases spanning 2005 - 2020 for seven European countries, namely Austria, Denmark, France, Germany, Italy, the Netherlands and Sweden, plus the Danube over database. In the cases where it was quantified with residue levels above the LOQ, there were only rarely findings above the applied thresholds.

#### Groundwater ~

For SPX, a total of 130.693 groundwater analyses were investigated, of which 119 analyses quantified SPX (with residue levels at or above LOQ). A compliance rate of 99.99% with the regulatory threshold was observed with 19 analyses exceeding the regulatory threshold of 0.1  $\mu$ g/L. These exceedances were only found in analyses from France where they represent 0.015% of all analyses. The maximum concentration was reported as 20.76  $\mu$ g/L (in France). See Table CA 7.5- 2.



Table CA 7.5- 2:	Summary of public monitoring results for spiroxamine (SPX) in groundwa-	
	• • •	

						_OČ 🎓	2
Country	Data source/	Monitor-	Anal-	Quantifica-	≥0.1	20.1	Ĵ
	Organisation	ing Period	yses	tions* ( $\geq$ LOQ)	μg/L	jong/L ℃	
						0 (%)	
Denmark	Groundwater database (Jupi-	2016	39	0 🔊	0	∘Q ^{©y}	
	ter)			1	S.		
France	ADES – National Groundwa-	2006 -	125,422	×113	:49	<b>0</b> .015 🖉	
	ter Quality Portal	2020	<u> </u>				Ø
	Sachsen Environment	2012-2020	1,885	Q 5			1
	Agency – Water Quality Por-	a start			, Q		
	tal (IDA)	A	L.		d.	Û, Û	
	Rheinland Pfalz – Geoportal	2000-	438	$\begin{bmatrix} & & & & & \\ & & & & & & \end{bmatrix}$	Ŏ ^Ÿ O Ø	004	
		2016		X & A		<i>A</i>	
	Rheinland Pfalz Environmen-	2011-2012	"120 ,		0%	, ~~ <u>0</u>	
	tal Agency – Annual reports				Å i		
	Bavarian Environmental	2013-2020~	©2,191		0 0		
	Agency – Environment atlas	$\sim$	́ "О"			. S	
Italy	Italian National Institute	2011-2016	12,8211	0 <u>9</u> 11 5	<u>, (e)</u>	00	
	Environmental Protection	2018	S O		Q' n		
	and Research (ISPRA)	r N			S v	/	
Sweden	Swedish University of Agto	2000-201	588		Ŭ Ŭ	0	
	cultural Sciences Pesticide	O' Å			×,		
	Database 🕺 🔌				0°		
* ~							

* Quantifications represent the number of analyses with residue levels  $\geq LOQ^{\vee}$ ¹In the reports from Italy, a total number of 16,420 analyses were investigated in 2011-2018. For the years 2011-2016 and 2018 (total analyses: 13,821), no analyses were shown to be ≥ 0.1 by L. For 2017 (2,599 analyses, 69 analyses above LOO) a maximum value of 0.4 bit discussed but discusses to a local discusses of 0.4 bit discusses and the discusses of 0.4 bit discusses above LOO). LOQ), a maximum value of 0 fug/L was indicated, but the could not be determined how many of the analyses were =  $0.1 \mu g/L$ . Therefore fue year 2017 has been excluded from the statistics.

is D D

#### Surface Water

Ş A total of 1,004326 analyses of surface water were investigated excluding Germany - Rheinland Pfalz reports and the Netherlands- Atlas for pesticides in surface water), of which 595 analyses quantified SPX (with residue levels at or above LOQ). & compliance rate of 100% with the Tier 1-RACSW of 0.188 µgd was observed, with analyses exceeding of the regulatory acceptable concentration (Tier 1-

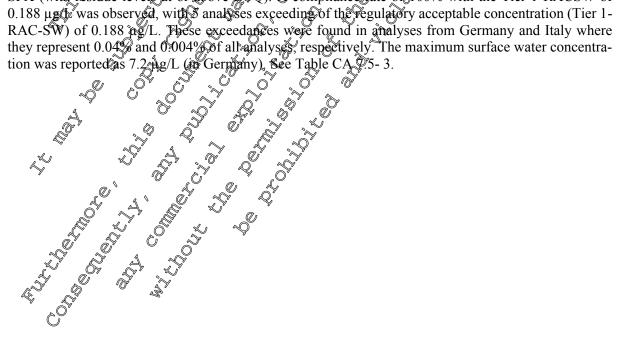




Table CA 7.5- 3: Summar	v of public monite	oring results for Sp	oiroxamine (SPX)	) in surface water
	J			, ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~

Country	Data source/	Monitor-	Analyses	Quantifica-	≥RAC	≥RAC	×
-	Organisation	ing Period	-	tions* (≥LOQ)		s. (🔊 🕯	Ő
EU	Danube River Basin Water	2013	211	0	0	6 ³ 0 0	ŕ
	Quality Database			, and the second	.0	Ø 5	
Austria	Austrian Federal Environ-	2013-2015	844,0861	0 💞	0	~Q\$~	
	ment Agency – reports			1			ゐ
France	Naïades – National Surface	2005-2019	121,638	×0 ³	$\sim 0$	2°0 ×	4
	Water Quality Data Portal		<u> </u>		N A		.C
Germany	Sachsen Environment	2012 -	[%] 10,028	Q 274	୰4ୖୢୣୣୣୖ	0:04	S
	Agency – Water Quality Por-	2020 🕺			Q,	Ô K	$\mathcal{O}$
	tal (IDA)	4	Ĺ		, v	<u>č</u>	
	Elbe River Basin - Data in-	2012 <b>-20</b> 19	294	10 Q .	0°0	0.0	
	formation system	~~	·	N N A		Ś	
	Rheinland Pfalz Environ-	2006-2010	526	Č Ž Š	-27	_~2	
	mental Agency – Annual re-				Ó L		
	ports				0	Î Î	
	Schleswig-Holstein –	2018-2020	,″2 <b>2</b> ∰	J, 10° ×		. <b>Q</b>	
	Agency for Agriculture, Ma-	in the				Ő	
	vironment and Rural Areas		Ž.		Q [°] A	-	
Italy	Italian National Institute for a	2005-2018	^{\$\$} 25,2 <b>4</b> 3	<u>مَ</u> 305	S 1 5	0.004	
	Environmental Protection		8				
	and Research @SPRA		Ŭ,		×,		
Netherlands	Dutch Institute of Environ-	2006-2019	¥,803,0	° © -3	©-3	-3	
	mental Sciences - Atlas for		di s		ð		
	pesticides in surface water	A DA			4		
	Water Quality Data portal of	3006-2008	£589 &	. <u>*</u> 2 8	0	0.0	
	the Netherlands						
Sweden	Swettish University of Agri	2010 2019 ~	1,168		0	0.0	
	cultural Serences Pesticide	~ ~	ġ,				
	Database (	N L					
· Ouantification	propresent the number of an luces an	The residua lave	> 100%	ither "zero" nor "".	OO'') The	value of	

* Quantifications represent the number of analyses with residue levels 2 LOQ meither "zero" nor ""<LOQ"). The value of the LOQ depends of the analytical method specified and is therefore variable (EOQ ranged from 0.002 to 0.15  $\mu$ g/L and in some databases LOQ value is not specified and is therefore variable (EOQ ranged from 0.002 to 0.15  $\mu$ g/L

** RAC value for SPX: 0.188 µg/L

¹ In the Darube river Datalase one malysis was done from the measuring site Oberloiben", a measuring point found also in the reports from the Austrian Federal Environment Agency. In order to avoid redundancy, this analysis was excluded

² In the annual reports of the German Rheinland Pfalz Kovironmental Acency, surface water data were only compared to 0.1 μg/L, therefore no statistics are possible (14 analyses ≥ 04 μg/L)
³ In the database from the Dutch Institute of Environmental Sciences - Atlas for pesticides in surface water, surface water data were only presented a "average" per year", all \$200 (\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$0.002 μg/L). No data about "maximum per vear" were available on the website

Drinking

Analyses of spiroxamine in water are not documented drinking

Ø

Soil

piroxamine in Soil are not documented Analyses of

Air

A total of 5,667 analyses of mr were investigated, of which 792 analyses quantified SPX (with residue levels at or above DOQ, with LOQ ranging from 0.0001 to 0.14 ng/m³ as stated in the databases). See Table CAS.5-4.



	<b>C P</b>			• • •	
Table CA 7.5- 4:	Summary of p	ublic monitoring	data for Sj	piroxamine ()	SPX) in air

Country	Data source/	Monitor-	Anal-	Quantifica-	Quantifica 🖉 📎
	Organisation	ing Period	yses	tions* ( $\geq$ LOQ)	tions* (%)
France	ATMO – National network of	2005-	4,2931	728	
	associations for the air quality	20171		, Or	<i>©</i> 6
	CNEP - National pesticide	2018-2019	1,348	54	4.0
	monitoring plan in air			1	
Sweden	Swedish University of Agri-	2017-2018	36	×10	27.8 4
	cultural Sciences - Pesticide		C)	Ű	
	Database		<b>∮</b> ″	Q. O	

* Quantifications represent the number of analyses with residue levels ≥ LOQ (neither "zero" nor " * LOQ") The value of the LOQ depends on the analytical method specified and is therefore variable (LOQ ranged from 0.0001 to 0 fr ng/m)

¹In the ATMO database, a total number of 6,714 analyses were investigated in 2005-2019. For the years 3018-2019, an over lap was observed with the analyses presented in the COCP database and therefore the analyses from ATMO database for these years are excluded from the statistics.

#### Sediment

A total of 435 analyses of sediments were investigated (see Table 4.13) of which no analyses quantified SPX (with residue levels at or above LOO, 0.3-5.0 µg/ag d w as stated in the databases) See Table CA 7.5-5.

Table CA 7.5- 5:	Summary of public monitoring data for s	nicoxamine (SPX) in sediment
	Summary of public monitoring during bi	

			v 0.		) <i>(</i> .	
Country	Data source/ 😽	Monitor-0	Anal-	Quantifica-	≥RA©**	≥RAC**
	Organisation 🔬	ang Period	vses 🗸	tions* (≥LOQ)		(%)
France	Naïades – National Strface	2015-2018	405		2 ⁹ 0	0.0
	Water Quatriy Data Portal				2	
Sweden	Swedisk University of Ag-	2003-2078	s,3€		0	0.0
	$\cdot 1 \otimes \alpha \cdot \beta $	o S	«"ľ			
	ricultural Sciences – Resti-		ð v			

* Quantifications represent the number of analyses with residue devels  $\geq 4$   $\mathcal{O}Q$  (norther "zero" nor ""<LOQ"). The value of the LOQ depends of the analytical method specified and is therefore variable (LOQ ranged from 0.0001 to 0.14 ng/m³) ** RAC value for SPX: 7.02  $\mu$ g/kg@.w.

#### Detailed results can be found in the original report?

III. Conclusion

The groundwater monitoring data search esulted in a compliance rate of 99.99% with the threshold of 0.1  $\mu$ g/L (19 analyses of 130,629 analyses in total), with a maximum concentration of 20.76  $\mu$ g/L. The surface water monitoring data search resulted in a compliance rate of 100% with the Tier 1-RAC_{SW} of 0.188  $\mu$ g/L (S analyses of 1004,326 analyses in total were reported above the RAC), with a maximum concentration 7.2  $\mu$ g/L. For the au compartment, 792 analyses with SPX concentrations above the LOQ (0.0001-00.14 ng/m³ as stated in the databases) were found (14.0% of 5,677 analyses). The median value of the quantified analyses amounted to 0.360 g/m³. The reported maximum residue concentration amounted to 65.93 ng/m³. For the sediment compartment, the 435 analyses found reported SPX concentrations under LOQ (0.3²⁰ 5.0  $\mu$ g/kg d.w. as stated in the databases). Monitoring of SPX is not documented for drinking water and soil, it cannot be discounted that some of the detections identified in groundwater. Surface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and soil, it cannot be discounted that some of the detections identified in groundwater ourface water and sediment are erroneous given they originate from non-GLP monitoring networks and programmes of unknown quality. Overall, it can be concluded from assessment of readily a tailable public monitoring datasets that spiroxamine (SPX) does not pose a concern for the investigated environmental compartments.



#### Assessment and conclusion by applicant:

Study meets the current guidance and the requirements in 283/2013.

The study addresses the requirement to review Member State data on spiroxamine monitoringin th environment. The study is considered valid.

Data Point:	KCA 7.5/01
Report Author:	
Report Year:	
Report Title:	Storage stability of KWG 4) 🚱 in water 🖉 🖉 🖉
Report No:	MR-690/96
Document No:	<u>M-006018-01-1</u>
Guideline(s) followed in study:	None quoted
Deviations from current test guideline:	None A A A A A A A
Previous evaluation:	
GLP/Officially recog-	Yes, conducted under GLP Officially recognised testing facilities
nised testing facilities:	
Acceptability/Reliability:	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
<b>Executive Summary</b>	

Ø The storage stability of spirøxamine in water was investigated in samples which were refrigerated (5°C) and frozen (<-18°C) for a maximum storage duration of 75 weeks. The purpose of the study was to determine the storage stability of spiroxamine from aquatio toxicity tests when stored under refrigerated and deep frozen conditions. Water used in the study was prepared by adding salt stock solutions to demineralised water (conductivity <0.24 mho/cm) with a pHof between 7.9-7.5.

The test was performed with at two concentration (J11.1 µg/L and 1.11 µg/L). For each test solution 21 bottles we prepared fren bottles were stored in a freezing changer (548°C) and ten bottles were stored in cold storage (5°C). One bottle of each test solution was used to determine the actual concentration of 6 T spiroxamone. S 0

Samples were taken from refrigerated and deep frozen conditions at study initiation, 1, 2, 4, 8, 21, 32, and 77 weeks after study initiation. Analysis of the samples was carried out in accordance to method 00252 M001. The method describes the determination of spiroxamine in water using gas chromatography and mass spectrometry (GC-MS) analysis

The method was validated by recoveries, which were performed with each set of samples. The recoveries were between 80 and 146%. The results are not conjected by the recoveries. For both concentrations no

were between 80 and 146%. The results are not corrected by the recoveries. For both concentrations no significant degradation of spiroxamine was observed during the storage by refrigeration or deep frozen.



#### I. **Materials and Methods**

#### A. Materials

1. Test Items

Spiroxamine

Batch

Purity:

#### 2. Test System

A Charter to a cha Water used in the study was prepared by adding salt stock solutions to demineralise water (conductivity  $<0.2 \ \mu$ mho/cm) with a pH of between 9.0-7.5? The prepared media was representative of that used in aquatic toxicity studies.

#### **B. Study Design**

#### 1. Experimental Conditions

The test was performed with at two concentration (111,  $\mu g/L$ ), and 1.  $\Omega \mu g/L$ ). The test solutions were prepared by adding defined volumes of the stock softition to the test water. For each test solution 21 bottles we prepared. Ten bottles were stored in a freezing chamber (<-18°C) and ten bottles were stored in cold storage (5°C). One bottle of each test solution was used to determine the actual concentration of spiroxamine

#### 2. Sampling

Samples were taken from refrigerated and deep frozen conditions at study initiation, 1, 2, 4, 8, 21, 32, and 77 weeks after study, initiation.

L

#### 3. Analytical Procedmes

Analysis of the samples was cartied out in accordance to method 00252 M001 (M-00849002-2). The method describes the determination of spiroxamine in water using gas chromatography and mass spectrometry GC-MS) analysis.

Prior to the analyses the samples were extracted by solid phase extraction. For this purpose C18 cartridges were conditioned with columns of 20 mil of methanol and 20 ml milli-Q-water. Then different volumes (100 mill respectively 10 mol depending on the nominal concentration) of the samples were sucked through the preconditioned eartridges. After drying for one hour the cartridges were eluted with a volume of 10 ml of methanol and ammonia solution (990:10). After evaporating to dryness the residue is dissolved in offerent volumes (depending on the nominal concentrations) of a mixture of 50% nbutyl-acetate, 49.5% methanol and 0.5% ammonia solution (25%).

The method was validated concurrently with the test solution analyses. The relative standard deviations were between 0.04 and 0.2 for the peak areas and between < 0.001 and 0.006 for the retention times of both isomers.



#### II. Results and Discussion

#### A. Data

Table CA 756.

Full details and acceptable validation data to support this method (Method 00252 M001 are presented) in Document M-CA 4, Section 4.1.2 (M-00849002-2). The method complies with the EU regulatory requirements outlined within SANCO/3029/99 rev. 4 and is suitable for the petermination of spice-amine and its metabolites in soil samples by HPLC/MS/MS.

The method was validated by recoveries, which were performed with each set of samples. The recoveries were between 80 and 116%. The results are not corrected by the recoveries.

Table CA 7.5-7 shows the stability of spiroxamine. The data show to significant decline in the concentration of KWG 4168 during the storage for 77 works when stored deep trozen ( $<-18^{\circ}$ ) or refrigerated (5°C).

Sample Time (week)	Nominal concentration (µg/L)	(Average %)
0	spiroxamine, results shown is a Nominal concentration (pg/L) V 1.11 V 1.11	<u> </u>
•	<u> </u>	
1		<u> </u>
2		
4	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
8 \$ \$ \$		83 108
	$\overline{\mathbb{V}}$	108
	₩ 1084	
$ \begin{array}{c} 4 \\ 8 \\ 21 \\ 32 \\ 77 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9 \\ 9$	0     0     111     0     1       0     111.4     0     4       0     124     0     4       0     124     0     4       0     124     0     4       0     1084     0     4       0     1084     0     4       0     0     993     0       0     993     0     0       0     993     0     0	108 91 97
32		Ø/ 84
	<u>1</u> 0.9999	<i>J</i> 94
	99, <u>8</u> 9 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	96



<b>Table CA 7.5-7:</b>	Results of spiroxamine storage stability conducted (results shown as ave	er-
	age, μg/L)	<i>°</i>

8,		1	&
Test system	Sample Time (week)	Average (µg/L) for	Average (μg/L) for 111.1 μg/b
-	1 ( )	1.11 µg/L	
*	0	0.921	91.8
	1	1.30 🖉	90.0 N
	2	1.19	<u> </u>
	4	0.989 🔊	<u>`~90.0</u>
Refrigerator	8	1.12	
	21	1.13	. 0 950 ~ 6
	32	0.978	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	77 4	1.98 °	δ <u>ξ</u> 86.2 <u></u>
	1 20		
	2 4		25.2 ×
	4 0 ^V 0 [°]	× 1.29 m	90.0 g
Deep Frozen	8	6936 0	
		N a 1.05 A a	106
	\$2 × 1	<u>1.06</u>	2108 2 ⁵
	<u> </u>	<u>× k04 × </u>	Ø \$91.2 O
Sample of 0 day, no storage		1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06 1.06	Š. Š. L
			Č ^v
	S MII. Conc	lusions and a	8 ×
		· . ·	$\lor$

The storage stability of spiroxamine in water was investigated in samples, which were stored in a refrigerated (5°C) and frozen ( $\ll$ 18°C) for a maximum storage duration of 77 weeks. For both concentrations no significant degradation of spiroxamine was observed during the storage by refrigeration or deep frozen. L,

Study meets the current grindance and the requirements in 283 2013 The study was not conducted to any study guidelines. The study is considered supportive information

the requirements in 2834 the requirements in 2834 the stability of spiroxanine inwatersample the construction of the stability of spiroxanine inwatersample the construction of the stability of spiroxanine inwaters and the spiroxanine inwaters a



#### Page 354 of 654 2021-03-31 Document MCA – Section 7: Fate and behaviour in the environment Spiroxamine

Appendix 1: Su	bstances and metabolites: structure, codes, synonyms the N3 document (Substances and metabolites: structure, codes, synonyms) is reproduced here Description IUPAC name: N-[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl)methyl]-NOP	e for information only is the faith
Code Number (Synonyms)	Description	Compound found in (level):
AE 1344273	ethylpropan-1-annue (TOPAC) 8-(1,1-dimethylethyl)-N-ethyl-N-propyl-1,4-diox- aspiro[4.5]decane-2-methanamine SMILES notation: CC(C)(C)C1CCC2(CC)OCC(CC)OCC InChiKe: 1S/C18H35NO2/c16-12-19( $V-2$ )13-16-D4-20- 18(21-16)10- $V-3$ 45(9-11-18)17(3,4) $O$ h15-164,6-14H2,4-	
M01 Spiroxamine-desethyl KWG 4168-desethyl FHW 0104H KWG 4557	5H3 IUPAC name: N-[(8-tert-butyl-1,4-dioxaspiro]4.5]dec-25VI) methylppro- pan-1-amine (HUPAC) SMILLS notation: CC(C)(C)C1CCC2(CC)OCC(CN(CC)O2; C,	Present in <i>in vitro</i> incubations with rat, dog and human hepato cytes Livestock Eggs hen (11.5% TRR) Muscle hen (9.3% TRR) Sub-cutaneous fat hen (8.4% TRR Liver hen (21.3% TRR) Plants Banana pulp (0.9% TRR) Banana pulp (1.1% TRR) Grapes (1.1% TRR) Grapes (2.1% TRR)



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Code Number	Description	Structural formula	Compound food in (leve):
(Synonyms)	Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Description Descr		
(« j « j» )		10 ² 00 ²	Spring where straws (2% TRR)
		Bar Lok	Spring wheat grain (0.5% TRR)
			Spring wheat forage (3.25.1% TR
			M01 not esolved from M05)
			Winterwheat strew (5.2% TRR-
	SOC SOC		Mol not resolved from M05)
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	E B A B AR	Winter wheat forage (4.8-7.1% The MOS)
			with work resolved from with 5)
		a 's with work of a off	
		and the the	Confined rotational crops
	E E CE	Silve aller - 9170 Were	Swiss chard leaves (11.6-12.1%
		et the to the	IRR- MUI not resolved from MU
	TUTUE Our H.S. SWI	e a ref fo and	Wheat straw (2.4-4.5% I KK- MU)
		20 ⁵ × 20 20	Turnin roots (3 7-4 4% TRR- M0
			not resolved from M05)
	AND F. A.		Turnip root (11.14.8% TRR- M01
			not resolved from M05)
			Swiss chard immature leaves (3.1-
			12.6% TRR)
		the why the	Swiss chard mature leaves (4.0-
	ve of ere or or		12.3% TRR)
	A CONAUTHORE THE		Wheat forage $(9.3-20.0\% \text{ TRR})$
77			Wheat may $(7.4-10.4\% \text{ TKR})$
A B			Wheat straw $(5.6-15.1\% \text{ TRR})$
P	With the second of the second		Turnip roots (1 5% TRR)
			Turnip tops (3.1-9.3% TRR)
	This and or rights on all of the copy the copy the copy the correct to the copy the copy of the copy o		Soul Coul
-702	" ALL ACT OCT SOF		Soil aerobic (12% AR)
ne ^r '	the mer ne E Mit		Soil anaerobic (7.6% AR)
at the all	SIT Ollon LIP. OL.		Soil, photo-degradation (9.1% AR
	This document is the proper and for tights such the subject of the own to the subject of the own to the subject of the own the subject of the own distr document on distr document on distr document on distr document on the option of this publication of this publication of this publication of the prohibited an any the permission an without be		
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Code Number	Description	Structural	Compound forbit in (level)
(Synonyms)	Description	15°	Compound found in (level):
		of Bayer propert	Water Of A.P.
		BOT	Photokysis water (4.5% AR)
			Water/sediment, aerobie (4.3% AR)
M02	IUPAC name: N-[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl) methyl]eth- anamine SMILES notation:		Present in vitre acubations with
Spiroxamine-despro-	N-[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl) methyl]eth-		rat dog and brunan hepatocytes
byl	anamine	E CONTRACTOR OF THE CONTRACTOR	Livesteck
KWG 4168-despropyl			Livestock Eggs hen (10 26 TRR)
KWG 4669 WAK 6174	SMILES notation: CC(C)(C)C1CCC2(CC1)OCC(CNCC)O2		Muscle hen (11.3% TRR)
Despropyl-KWG		ADOUDA A A A A A A A A A A A A A A A A A A	^O Sub culaneous fat hen (3.4% TRR)
o spiop y i k v o	InChiKe: 18/C15H29NO2/c1-5-16-1043-11-1045(18-		Liger hen (21.7% TRR)
	13)8-6-12(7-9-15)14(2,3)4/h12-4,3,16H,5-11H2,1-4H3	a a contraction a statille	en Plants Plat
	The other of the		Banana pulp (0.4% TRR)
	Chr. 102 WE OW		Banana pulp (0.4% TRR) Banana pulp (0.5% TRR)
		Jer Jel Maile a fr	^(*) Grapes (0.5% TRR)
	ante alle alle vi		Grapes (1.5% TRR)
	Cir. Cr Jr	NOUT OF E TH NES	Spring wheat forage (4.3-4.6% TRR Spring wheat straw (3.2% TRR)
		the of it	Spring wheat grain (3.0% TRR)
			Winter wheat forage (3.3-4.6 %
	gover give our	The way is the	TRR)
	no not en not an		Winter wheat straw (4.2% TRR)
		the adt	Rotational crops
	the solution the start s		Swiss chard leaves (7.5-14.2% TRR
Å			Wheat straw (2.9-3.5% TRR)
	White out the ison of		Turnip roots (2.6-3.3% TRR)
			Turnip tops (16.7-17.7% TRR)
	anamine SMILES notation: CC(C)(C)C1CCC2(CC1)OCC(CNCC)O2, $Dein ChiKe: 1S/C15H29NO2/c1-5-16-1013-11-10 F5(18-13)8-6-12(7-9-15)14(2,3)4/h12-03,16H,5-4(H2,1-4H3), ChThisdODeD$		Swiss chard immature leave (11.0-
	all act of a pr		50.0% TRR) Swiss chard mature leave (19.0-
*	et att aller we south		51.2% TRR)
an the	aler other the other		Wheat forage (23.4-46.6% TRR)
Filler	anamine SMILES notation: CC(C)(C)C1CCC2(CC1)OCC(CNCC)O2, De its InChike: 1S/C15H29NO2/c1-5-16-10+73-11-10+75(18- 13)8-6-12(7-9-15)14(2,3)4/h12+0516H,5-10H2,1-4H30, Ch and OC to the standard of the officer officer of the officer of the officer of the officer officer of the officer of		Wheat hay (15.2-30.9% TRR)
-704			• • • •



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Code Number	Description	Structural formula	Compound foond in (lever):
(Synonyms)	Description	Structuraportinuia	
M03 Spiroxamine-N-oxide XWG 4168-N-oxide WAK 6301 WAK 6301/1 XWG-N-oxide	Description IUPAC name: [(8-tert-butyl-1,4-dioxaspio][4.5]dec-2.9]) me [(8-tert-butyl-1,4-dioxaspio][4.5]dec-2.9]) me sMILES notation: CC(C)(C)CACCC2(CC1)OCC(C[N+]([0-DiCC)CCC)]2 InChiKe: 15/C18H35N(9/c1-6-122H9(20,7-2)]3-16-14H2/1- SHILES notation: CC(C)(C)CACCC2(CC1)OCC(C[N+]([0-DiCC)CCC)]2 InChiKe: 15/C18H35N(9/c1-6-122H9(20,7-2)]3-16-14H2/1- SH3 De COP UPAC name: InChiKe: 15/C18H35N(9/c1-6-122H9(20,7-2)]3-16-14H2/1- SH3 De COP UPAC name: InChiKe: 15/C18H35N(9/c1-6-122H9(20,7-2)]3-16-14H2/1- SH3 De COP UPAC name: Inchi De COP UPAC name: Inchi De COP UPAC Inchi De De UPAC UPAC Inchi Inchi <td< td=""><td>of Bayer property of the source of the sourc</td><td>Wheat grain (4.8% TKR) Wheat straw (14,347,4% TRR) Turnip roots (2.9% TRR) Turnip tob (14.5-24,1% TRR) Soil, aerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, photo-degradation (6.1% AR) Water Photolysis water (4.5% AR) Water Photolysis water (4.5% AR) Water/sectment, aerobic (3.2% AR) Rat Eiver (0.12 mg/kg) Livestock Not reported Plants Banana pulp (1.2% TRR) Banana pulp (0.8% TRR) Grapes (2.9% TRR) Grapes (4.7% TRR) Spring wheat forage (8.0-9.0% TRR) Spring wheat forage (8.0-9.0% TRR) Spring wheat straw (22.0% TRR) Spring wheat grain (17.8% TRR) Winter wheat straw (20.9% TRR) Winter wheat straw (20.9% TRR) Winter wheat grain (1.2% TRR)</td></td<>	of Bayer property of the source of the sourc	Wheat grain (4.8% TKR) Wheat straw (14,347,4% TRR) Turnip roots (2.9% TRR) Turnip tob (14.5-24,1% TRR) Soil, aerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, anaerobic (5.8% AR) Soil, photo-degradation (6.1% AR) Water Photolysis water (4.5% AR) Water Photolysis water (4.5% AR) Water/sectment, aerobic (3.2% AR) Rat Eiver (0.12 mg/kg) Livestock Not reported Plants Banana pulp (1.2% TRR) Banana pulp (0.8% TRR) Grapes (2.9% TRR) Grapes (4.7% TRR) Spring wheat forage (8.0-9.0% TRR) Spring wheat forage (8.0-9.0% TRR) Spring wheat straw (22.0% TRR) Spring wheat grain (17.8% TRR) Winter wheat straw (20.9% TRR) Winter wheat straw (20.9% TRR) Winter wheat grain (1.2% TRR)

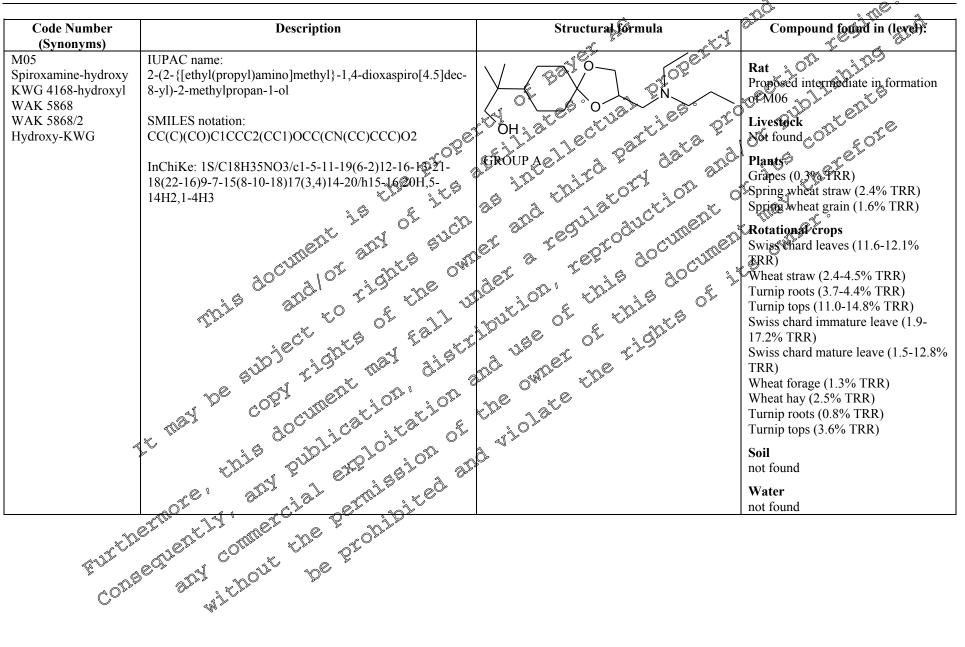


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Code Number (Synonyms)	Description	Structura	Compound for in (level):
		Structural formula	Turnip top(4.8-9.9% TRR) Wheat bay (1.7-20% TRR) Wheat grain (4.3% TRR) Wheat strow (1.4-50% TRR)
	The proper	ety of be provide and provide and and the provide and the provide and the provide and	Soil, aerobie (7.9% AR) Soil, anaerobie (8.9% AR) Soil, photo-degradation (6.2% AR)
	is to it	er and regulate duction	Water Photolysis water (4.0% AR) Water/sectment, aerobic (113% AR)
M04 Spiroxamine-N- formyl-desethyl	N-[(8-tert-butyl-1,4-dioxaspiro[4.9]dec-2-vi)methyl]-N-	A CONTRACTOR OF THE OF	Eivestock Not found
KWG 4168-N-formyl- desethyl WAK 6782 N-formyl-desethyl- KWG	IUPAC name: N-[(8-tert-butyl-1,4-dloxaspiro]4/S]dec-2-yd)methyll-N- propylformamide SMILES fileration: CC(C)(C)C1CCC2(CC1)OCC(CN(C=0)CCC)O2 allow InChiKe: 1S/C17H50NO3/cle5-10-18(13X9))11-1532-20- 17(21-15)8-6-14(7-9-17)b6(2,3)4/h18-45H,5-1242,1-4H3 COCCUME A CONTRACT OF A C	GROUPA the owner the the tights the owner the the	Plants Spring wheat forage (2.1-5.3% TRR) Spring wheat straw (7.5% TRR) Spring wheat grain (6.9% TRR) Winter wheat forage (4.6-5.8% TRR) Winter wheat straw (9.7% TRR)
	t may b correction to a the off	the late	Rotational crops Wheat straw (7.5-9.2% TRR) Wheat hay (1.5% TRR) Wheat grain (1.5% TRR) Wheat straw (2.8-6.4% TRR)
	more 1 and octal permit teo		Soil not found
A CONTRACTOR	ert the the the topologic		Water not found
E Use	Bear any thout be		



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Code Number (Synonyms) Description Structural formula Compound folded in (lgref) M06 [UPAC name: 2-(2-1[eth/[(popy])amino]methyl]-1.4-dioxaspiro[4.5]dec 8xi0-2-meth/propanoic acid Present informula Present informula WG 4168-acid WAK 5708/P ECW 80511 SMILES notation: 0=C(0)C(C)(C)(C)C1CCC2(CC1)OCC(CN(CC)CCC)O2 ECW 8046 ⁶ Present informula Rat of the state of the state of the state of the sta
M06 IUPAC name: Spiroxamine-acid KWG 4168-acid 2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec- KWG 4168-acid 8-yl)-2-methylpropanoic acid
WAR 5708 SMILES notation: OF OH, etc., or the state of the state o



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Description	Structural formula	Compound foond in (leve):
IUPAC name: 2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec- 8-yl)-3-hydroxy-2-methylpropanoic acid SMILES notation: O=C(O)C(C)(CO)C1CCC2(CC1)OCC(CN(CC)CCC)O2 InChiKe: 1S/C18H33NO5/c1-4-10-19(5-2)11-15-K023- 18(24-15)8-6-14(7-9-18)17(3,13-20)16(21)22/104- 15,20H,4-13H2,1-3H3,(H,21,22) InChiKe: 0 0 0 15,20H,4-13H2,1-3H3,(H,21,22) 15 0 0 15 0 0 0 0 15 0 15 0 15 0 15 0 0 0 15 0 15 16 17 18 19 19 10 10 10 10 10 10 10		Present in <i>pvitro</i> includions with mouse, rat, dog and human hepato- cetter Livestock Milk goat (10.9% TRR) Diver goat (1.7% TKR) Kidne goat (16.0% TRR) Muscle goat (10.3% TRR) Fat goat (9.7% TRR) Fat goat (9.7% TRR) Pkotts not found Soil Not found Water not found
2-(2-{[ethyl(propyl)amino] $(0, 0, 0, 1)$ }-8-hydroxy-1;4-diox- aspiro[4.5] dec-8-yl)-2-methylpropanoic acid SMILES notation: O=C(O)C(C)C1(O)CC2(CCC)OCC(CCC)CC)CCOO2		Rat Excreta (0.6-12.0% AD) Livestock Liver goat (1.2% TRR) Kidney goat (2.3% TRR) Plants not found Soil not found Water not found
	2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec- 8-yl)-3-hydroxy-2-methylpropanoic acid SMILES notation: O=C(O)C(C)(CO)C1CCC2(CC1)OCC(CN(CC)CCC)O2 InChiKe: 1S/C18H33NO5/c1-4-10-19(5-2)11-15-K23- 18(24-15)8-6-14(7-9-18)17(3,13-20)16(21)22/104- 15,20H,4-13H2,1-3H3,(H,21,22)	$\begin{array}{c} 2-(2-\{[ethyl(propyl)amino]methyl\}-1,4-dioxaspiro[4.5]dec-\\ 8-yl)-3-hydroxy-2-methylpropanoic acid \\ \\ SMILES notation: \\ O=C(O)C(C)(CO)C1CCC2(CC1)OCC(CN(CC)CCC)02 \\ \\ InChiKe: 1S/C18H33NO5/c1-4-10-19(5-2)11-15-H223-\\ 18(24-15)8-6-14(7-9-18)17(3,13-20)16(21)22/04-\\ 15,20H,4-13H2,1-3H3,(H,21,22) \\ \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $



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Code Number (Synonyms)	Description	Structural formula	Compound found in (level):
M09 Spiroxamine-hydroxy- despropyl KWG 4168-hydroxy- despropyl	IUPAC name: 2-{2-[(ethylamino)methyl]-1,4-dioxaspiro [4.5]dec-8-yl}-2- methylpropan-1-ol SMILES notation:	V C C C C C C C C C C C C C C C C C C C	Livestace not bund Plants D Spring wheat straw (0.3% TRR)
WAK 6079/1 WAK 6079-1 Hydroxy-despropyl KWG	CC(C)(CO)C1CCC2(CC1)OCC(CNCC)O2	GROUPA JECT Part. A FOR	Spring wheatOforage (15% TRR – M09 net resolved from unknown me- tabolite 9) Winter wheat forage (0.2-0.6% TRR-
	IUPAC name: 2-{2-{(ethylamino)methyl]-1,4-dioxaspiro [4.5]dec-8-yl}-2- methylpropan-1-ol SMILES notation: CC(C)(CO)C1CCC2(CC1)OCC(CNCC)O2 InChiKe: 1S/C15H29NO3/c1-4-16-9-13-10-18-15(DF13)7- 5-12(6-8-15)14(2,3)11-17/h12-13,16-17H,4+142,1-3H3 100 100 100 100 100 100 100 10	as and the guilator document	M09 not resolved from unknown me- tabolite 9) Winter wheat straw (0.4% TRR- M09 not resolved from unknown me- tabolite 9)
	This and or right or	der on trais door i	Rotational crops Free M09 not detected [M09 = aglycon of M39] Soil
	se supje right may dist	and when the riss	not found Water not found
M10 Spiroxamine-hydroxy- N-oxide	IUPAC name: 2-(2, dethyl(propyl)nitror, (methyl), 104-diox, aspiro[4.5]dec-8-yl)-2-methylpropan-1-ol		Livestock not found
KWG 4168-hydroxy- [《] N-oxide	SMILES notation: CC.CC(C)(CO)C1CCC2(CC1)OCC(C[N+1(f0- D)(CCCCC)02	ОН О О	Spring wheat- Free M10 not detected [M10 = aglycon of M20 and M21]
a th	2mChiKe 18/C18H3 404.C2H6/c1-5-11 (9(21,6-2)12-16- 13-22+8(23-16)9-7-15(8-10-18)17(3-4)14-20;1-2/h15-	GROUP A	Soil not found
Colle Enr	10,20H,5-J4H2,1-4H3,1-2H3 0,111 0,111 0,111 0 0 0 0 0 0 0 0 0 0 0 0 0		

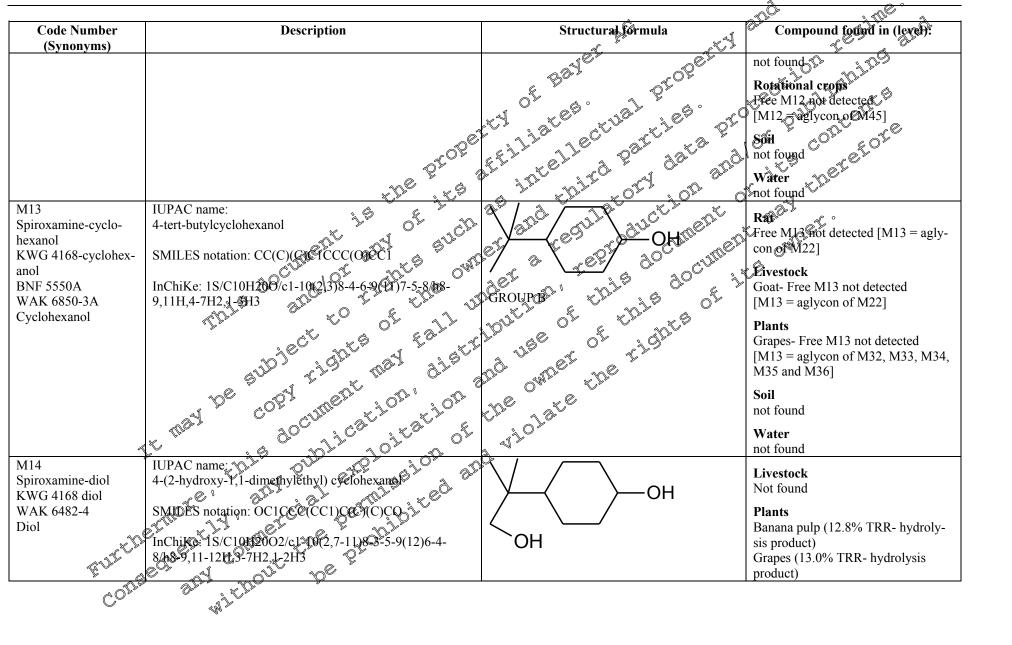


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Code Number (Synonyms)	Description	Structural	Compound found in (leve):
M11	IUPAC name:		Present in <i>Wvitro</i> incubations with
Spiroxamine-desethyl	$\begin{array}{c} 2\text{-methyl-2-} \{2-[(\text{propylamino})\text{methyl}]-1,4-\text{diox-aspiro}[4.5]\text{dec-8-yl}\}\text{propanoic acid} \\ \text{SMILES notation:} \\ O=C(O)C(C)(C)C1CCC2(CC1)OCC(CNCCC)O2 \\ InChiKe: 1S/C16H29NO4/c1-4-9-17-10-13-11-20-06(21-13)7-5-12(6-8-16)15(2,3)14(18)19/h12-13,17H4-11H2,15) \\ 3H3,(H,18,19) \\ & & & & & & & & & & & & & & & & & & $		Here and rat hereatory tes
acid	aspiro[4.5]dec-8-yl}propanoic acid		mouse and rat heratocytes Hart Excreta (8.4-13% &D) Givestock Milk geat (5.5% TRR) Liver for at (3.8% TRR)
KWG 4168-desethyl			Everete 13% R
acid	SMILES notation:		Exclements (5.4-13 (a teal)
ECW 8044	0=C(0)C(C)(C)C1CCC2(CC1)OCC(CNCCC)O2		5 Birestock COr 6 OF
ECW 8044A	10×	GROUP A S PO 200	Milk goat (5.5% TRR)
ECW 8045	InChiKe: 1S/C16H29NO4/c1-4-9-17-10-13-11-20-06(21-		Liver goat (3.85 TRR)
ECW 8045A	13)7-5-12(6-8-16)15(2,3)14(18)19/h12-13,17HG-11H2,	inter the second states and the second secon	Kidney goat (5.8% TRR)
KNO 2222	3H3,(H,18,19)		Muscle goat (6.4% TRR)
KNO 22243	i i i i i i i i i i i i i i i i i i i	ate and and	Fatgoat (4.3% TRR)
WAK 5756 WAK 5756B	at aver		7 Plants P
WAK 5756P	aller alter a		not Dund
WAK 5750F			N Detational arous
	20° 210° 29° 200	der al mit de	Free M11 not detected
	is all in the w		[M11 = aglycon of M43]
	The to take	ANT OF THE	
		y ac a sta	Soil
			not found
	and a for all the		Water
		the Own the	not found
M12	IUPAC name:		Present in <i>in vitro</i> incubations with
Spiroxamine-despro-	A COLONIN ET TI		mouse and rat hepatocytes
pyl acid	SMALES notation:		Bat
KWG 4168-despropyl «	() 0=C(0)C(C)(C)C16CC2(CCHOCC(CNCO))02		Kai Excreta $(2, 1, 13, 20/2)$
acid	Will olde AP at 0"		Excreta (2.1-15.270)
BNF 5534	InChiKe: 1S/C45H27NO4/c1-4-16@ 12-10-49 15(20-12) -	6 011	Livestock
BNF 5534A	5-11(6-8-15)14(2,3)13(17)18401-12,164(4-10H2,10)	GROUP A	Liver goat (3.5% TRR)
ECW 8042	3H30P7,17,18)		Kidney goat (9.0% TRR)
ECW 8042A	er the the		Muscle goat (6.8% TRR)
KNO 2218A	Call office tipe of Or		Fat goat (6.2% TRR)
KNO 2218B			Plants
<u> </u>	2-methyl-2-{2-[(propylamino)methyl]-1,4-diox- aspiro[4.5]dec-8-yl}propanoic acid SMILES notation: O=C(O)C(C)(C)C1CCC2(CC1)OCC(CNCCC)O2 InChiKe: 1S/C16H29NO4/c1-4-9-17-10-13-11-20-06(21- 13)7-5-12(6-8-16)15(2,3)14(18)19/h12-13,17H4-11H2,L 3H3,(H,18,19) is of and or right and		· · · ·
COJE.	"Or" and the		
V			



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Code Number	Description	Structural formula	Compound found in (level):
(Synonyms)	L L		Compound found in (level):
		GROUP B	Spring wheat straw (0,2% TRR- hy-
		BOR SOF	drolvsisproduct
			Spring wheat grain (2,6% TRR- hy-
			drolysis acouct)
			Rotational crops a C
			Rotational crops Swiss chard leaves (8,9-13.2% TRF
		RE PERA	hydrolysis produce
			Wheat straw (\$.5-4% TRR- hydroly
	Elle " Ca	6 the the top to the	Wheat straw 9.5-4% TRR- hydroly Sis producty
		at was at at	Turrep tops (4.4-13.0% TRR- hy-
		Site aller give aller	drolysis product)
	en an an	et te ato dur de	Soil Soil
	WILL'S A CHI SHE	a der go dun	pot found
		30 ² 30 ³ 30 ³ 30 ³	Water
	Description Description Description Description Description Description Description Description		not found
A15	IUPAC namenta to of the state o	Structural formula GROUP B OF Bay CT CT CT CT CT CT CT CT CT CT	D - 4
piroxamine-ketone	4-tert-butylcyclohexanone		Present as an artefact of sample wo
KWG 4168-ketone	AC MET AT AT		un in rat excreta
WAK 5428	SMILES notation: Q C PCCC(CC)(CO)		
Cyclohexanone		the Olyn. Chr.	Livestock
	InChike: 15(2)0H180(4-10(2,3)8-4-6-9(114)-5-8/n8H4-	GROUP B *	Not found
			Plants
			Grapes (1.3% TRR- hydrolysis pro
			uct)
	The start of the s		Spring wheat straw (5.5% TRR- hy
			drolysis product)
	a te during the tee		Spring wheat grain (4.6% TRR- hy
	atter at a to a		arorysis product)
~	per att and ne - oper		Soil
~~ ^K	The column the off		not found
E Vien	IUPAC name: document: any of and or any of the own 4-tert-butylcyclohexanone SMILES notation: Q PCCC(CO)C(C)(Q) InChiKe: LS/CI0H180/CI-10(2,3)84-6-9(11)75-8/h8H4-7 H2,1-3H3 CO-000000000000000000000000000000000000		Water
	2 The Flores		•



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		· · · · · · · · · · · · · · · · · · ·	pp ⁰
Code Number (Synonyms)	Description	Structural formula	Compound foond in (leve):
		JOF JOF	not found the state
M16 Spiroxamine-hydroxy- ketone	IUPAC name: 4-(2-hydroxy-1,1-dimethylethyl)cyclohexanone		Livestock Not found Plants Grapes (0.5% TRR-hydrolysis prod- uct)
KWG 4168-hydroxy- ketone	SMILES notation: OCC(C)(C)C1CCC(=O)CC1	the the true to be got	Plants
BNF 5569B BNF 5544B Hydroxyketone	IUPAC name: 4-(2-hydroxy-1,1-dimethylethyl)cyclohexanone SMILES notation: OCC(C)(C)C1CCC(=O)CC1 InChiKe: 1S/C10H1802/c1-10(2,7-11)8-3-5-9(12)6-4 O^{20} 8/h8,11H,3-7H2,1-2H3 C^{1} C	GRONDE WITTO OT BATCH	uct) Spring wheat graw (1.0% TRR- hy- drolysis product)
	i i o i v	as and wild auction	Spring wheat grain (7.6% TRR- hy- drovysis product)
	CUMPERT STRY SUC	er a reproviduren	Rotational crops Swiss chard leaves (15.6-29.3% FRR- hydrolysis product)
	This and to right the up	DUTION FULLS OF T	Wheat straw (8.9-11.6% TRR- hy- drolysis product) Turnip tops (11.7-37.3% TRR- hy-
	subject nav taletr	the use ot tight	Soil not found
	at the color annear to a ' to a		Water not found
M17 Spiroxamine-ketone acid	IUPA@ name: 2-methyl-2-(4-oxocyclonexyl)propanoic acid		Livestock Not found
KWG 4168-ketone acid	SMILES notation: O=C1CCC(CC1)C(C)(C)C(=0)O		Plants not found
WAK 6131-2-7	InChike: InChI=1\$7C10H1609/c1-10(2)9(12)13)75- 8(19)6-4-7/h7H3-6H2 1-2H3,(H,12,43)	GROUP B	Soil not found
EULTER	equent: contains the prob		Water not found
Colle	and the second		



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			and the state of t
Code Number (Synonyms)	Description	Structural formula	Compound found in (leve):
M19 Spiroxamine-acid glu- curonide	IUPAC name: 1-O-[2-(2-{[ethyl(propyl)amino]methyl}-1,4-diox- aspiro[4.5]dec-8-yl)-2-methylpropanoyl]hexopyranuronic		Rat O ^D Excrete (0.4-1, 79, AD) Eivestoel
WG 4168-acid glu- uronide	acid	201 200 ALDER OF DE CO	Liver goat (3.5% ÅRR)
ECW 80802 KNO 1634 KNO 1634/A	SMILES notation: O=C(0)C1OC(OC(=0)C(C)(C)C2CCC3(CC2)OCC(CO(C)) C)CCC)O3)C(0)C(0)C10		Khaney goat @.0% TBR Muscle goat (6.8% PRR) Fat goat (6.2% PRR)
	InChiKe: 1S/C24H41NO10/c1-5-11-25(6-242-15-13-32- 24(35-15)9-7-14(8-10-24)23(3,4)22(31)94-21- 19(29)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)94-21- 19(20)1(22(31)9-21- 19(20)1(22(31)9-21- 19(20)1(22(31)9-21- 19(20)1(22(31)9-21- 19(20)1(22(31)9-21- 19(20)1(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9-21- 19(20)1)(22(31)9)(22(31)9)(22(31)9)(22(31)9)(22(31)9)(22(31)9)(22(31)9)(22(31)9)(22(31)9)	SROUPA this at of a to the court	Plants not tound
	24(35-15)9-7-14(8-10-24)23(3,4)22(3,1)94-21- 18(28)16(26)17(27)19(33-21)20(29)30/h14-19,91,26- 28H,5-13H2,1-4H3,(H,29,30)		Noil not found Water not found
		der son rer do do do do	not found
A20 Spiroxamine-hydroxy-	IUPAC names & J 2-(2-{[ethyNoropy])nitroryI]methyP-1,4-diog-		Livestock Not found
N-oxide glucoside KWG 4168-hydroxy- N-oxide glucoside glucoside of hydroxy-	SMILES notation:	EROUP ALLE , DE	Plants Spring wheat forage (0.7% TRR) Spring wheat straw (2.0% TRR)
N-oxide	IUPAC name IUPAC name 2-(2-{[ethx10ropy1)nitrory1]methy1}-1,4-diox- aspiro[4.5]dec-8-y1)-2-methytoropy1 hexopyranoside SMILES notation: OC1C(O)C(O)C(CO)OC1OCC(C)(C)C1CCC2(CCP)OCC(C[N+]([O-])(CC)CCC)O2 InCh(Ref. 1S/C24H45NO9(4)-5-11-23(0),6-2)12(17-14-32- 24(34-17)9-7-16(8-10-24)23(3,4)15-31-22- 21(29)20(28)19(27)78(13-26)32-22/h16-32,26-29H5	CROUP, ATLET, the Till of the	Rotational crops Swiss chard leaves (2.5% TRR) Wheat straw (2.1-2.6% TRR) Turnip tops (8.4-10.4% TRR)
	21(29)20(28)19(27)48(13-26)33-22/h16-92,26-29165 15H2,1-4H3 * 1 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 - 2 -		Soil not found
	MOTE! all's cial permit bites		Water not found
EUITTI	In Chike: $1S/C24H45NO9(0-5-11-2500,6-2)12217-14-32-24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-7-16(8-10-24)23(3,4)15-31-22-300-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24)24(34-17)9-22(24-17)9-22(24)24(34-17)9-22(24-1$		

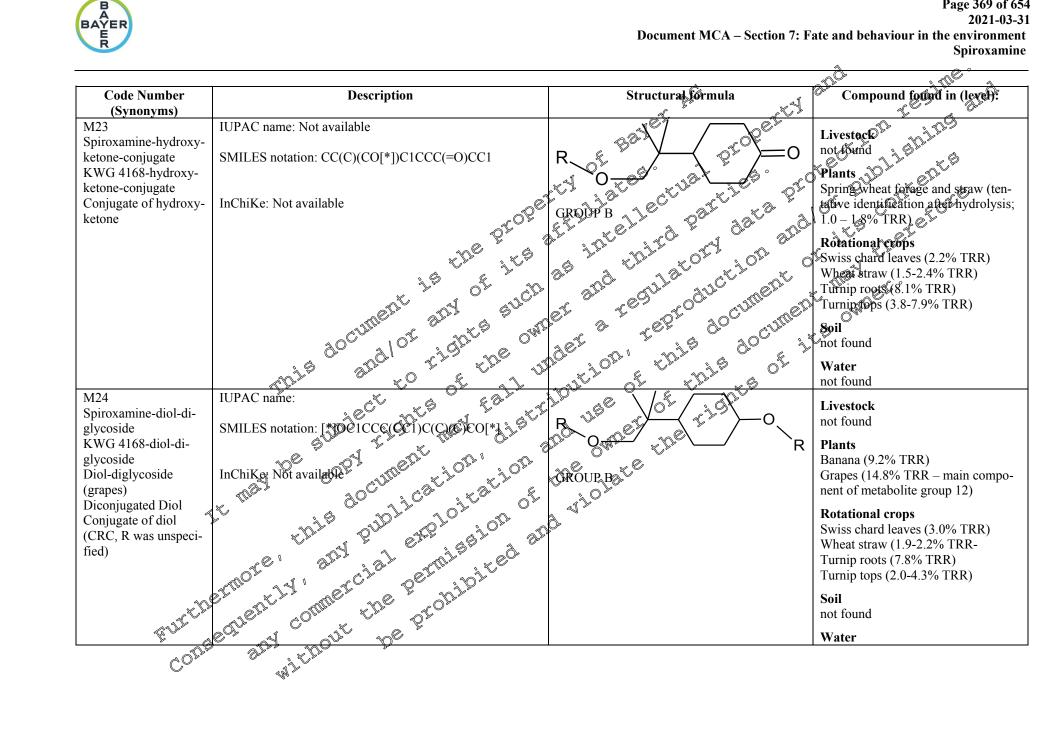


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		8	
Code Number (Synonyms)	Description	Structural formula	Compound found in (level):
M21 Spiroxamine-hydroxy- N-oxide malonyl glu- coside KWG 4168-hydroxy- N-oxide malonyl glu- coside	Description IUPAC name: 2-(2-{[ethyl(propyl)nitroryl]methyl}-1,4-diox-aspiro[4.5]dec-8-yl)-2-methylpropyl 6-O-(carboxyace-tyl)hexopyranoside SMILES notation: O=C(O)CC(=O)OCC1OC(OCC(C)(C)C2CCC3(CC2)/00C (C[N+]]([O-])(CC)CCC)O3)C(O)C(O)C10 InChiKe: 1S/C27H47NO12/c1-5-11-28(35) 20(29)30/h17-19,22-25,32-34L(S-16H2,4)H3,(H,2930) IUPAC name: 4-tert-butylcyclohexyl hexopyranosiduronic acid SMILES notation: CC(C)(C)C1/CC(CC1)OC1OC(CO)C(O)C40)C(=0)Q IUPAC name: 4-tert-butylcyclohexyl hexopyranosiduronic acid SMILES notation: CC(C)(C)C1/CCC1/OC1OC(CO)C(0)C40)C(=0)Q InChiKe: 1S/C16H2807/e1Ci6(2,3)8,46-9(7-5-9)2-15- 12(19)10(17)11(18)13(2-15)14(21)21/h8-13,15,17-19104- 7H2,1-3H3,(H,20,21)	HOLO CONTROLOGIAL CLATTER	Livestack not found Plants Spring wheat forage (0.2-2.0% TRR) Spring wheat forage (0.2-0.9% TRR) Winter wheat forage (0.2-2.0% TRR) Winter wheat forage (0.2-0.9% TRR)
M22 Spiroxamine-cyclo-	IUPAC name: 4-tert-butylcyclohexyl hereopyranesidefonic acid ²		Soil not found Water not found Rat Excreta (0.6-1.7% AD)
hexanol-glucuronide KWG 4168-cyclohex- anol-glucuronide ECW 8081	SMILES notation CC(C)(C)C1CC(CC1)OC1OC(CO)C(O)C(O)C(=O)O InChite: 1S/C16H2807/OC6(2,3)8	GROUP B	Livestock Kidney goat (0.4% TRR) Plants not found
**************************************	12(19)10(17)11(18)13(23-15)14(20)21/h8-13,15,17-19HQ4-7H2,1-3H3,(H,20,24) P10	ð.	Soil not found Water not found
E JIC LIL	SMILES notations 1^{10} $1^$		



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Code Number	Description	Structural formula	Compound for in (lever):
(Synonyms)			Compound found in (lever):
(~)) ~)		al ^{OF} OF	not found to a the
M25	IUPAC name:		Present in vitra proubations with
Spiroxamine-sulfate	2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec-	pt y pt i	
KWG 4168-sulfate	8-yl)-2-methylpropyl hydrogen sulfate		Rat
ECW 8076			Everate (1.0.205% AD)
ECW 80772	SMILES notation: O=S(=O)(O)OCC(C)(C)C1CCC2(CC1)OCC(CN(CC)CCC))O2		Rat Che
KNO 22302	0=S(=0)(0)OCC(C)(C)C1CCC2(CC1)OCC(CN(CC)CCC	STROLIP A C A C AC	Livestock
)O2	Moor and a gar	Milk goat (8 1% TRR)
	InChiKe1S/C18H35NO6S/c1-5-11-19(6-2)12-16-13-23-	2 2 x Will work i Or	Mill goat (8 1% TRR) Liver goat 2.2% TRR) Kidney goat (1.6% TRR)
	1100000000000000000000000000000000000	at the states	Kidney goat (1.6% TRR)
	18(25-16)9-7-15(8-10-18)17(3,4)14-24 26(20,2) 22/h15- 16H,5-14H2,1-4H3,(H,20,21,22)	Sign and Sign Weight	Plants not four a
		at the don duit all	not found
	The dub the solution	HOLS-O-CO HOLS-O-CO CROUPACILLECTION CROUPACI	Soil
	ao ^{Co} lo ^T d ^D O ^V		not found
			Wator
	$\frac{16(25,14H2,1-4H3,(H,20,21,22))}{16H,5-14H2,1-4H3,(H,20,21,22))} = \frac{10(25,14H2,1-4H3,(H,20,21,22))}{10(25,14H2,1-4H3,(H,20,21,22))} = \frac{10(25,14H2,1-4H3,(H,20,21,22))}{10(25,14H2,1-4H2,1-4H3,(H,20,21,22))} = \frac{10(25,14H2,1-4H3,(H,20,21,22))}{10(25,14H2,1-4H2,1-4H3,(H,20,22))} = \frac{10(25,14H2,1-4H3,(H,20,22))}{10(25,14H2,1-4H2,1-4H3,(H,20,22))} = \frac{10(25,14H2,1-4H2,1-4H2,1-4H3,(H,20,22))}{10(25,14H2,1-4H2$		not found
М26	InChiKe1S/C18H35NO6S/c1-5-11-19(6-2)12-16-13222 18(25-16)9-7-15(8-10-18)17(3,4)14-2426(20,2)122/h15- 16H,5-14H2,1-4H3,(H,20,21,22) 10H,5-14H2,1-4H3,(H,2		Rat
Spiroxamine-desethyl-	IUPAC name: 2-methyl-2-{2-[(propylareino)methyl)+1,4-diox- aspiro[4.5]dec-8-yl}hopyl hydrogen sulface SMILES notation: O=S(=O)(O)OCC(C)CCCCCCCC2		Excreta (0.7-14.6% AD)
sulfate	aspiro[4.5]dec-8-y] popyl hydrogen sulface		
KWG 4168-desethyl-		The Contra the	Livestock Liver goat (1.9% TRR)
sulfate	SMILES notation: O=S(=Q)(O)OCC(C)CC(C)CC(C)CC(C)CC(C)CC(C)C)	HO-S-O-CT COROUPACT	Kidney goat (3.2% TRR)
	O=S(=Q)(O)OCC(C)(C)(C)C1CCC(C)OCC(C)CCC(O)O2	CROUP AS	Fat goat (3.5% TRR)
ECW 80822	InchiKe: 1S/C16H31N06S/c1-4-9-17-10-14-11-21-16(23-	10×	e (
KNO 2226 🦿	*mCniKe: 15/C16H31N@65/c1-4-9/1/-10-149/1-21-16(23-		Plants not found
•	14)/-3-13(0-0-10)(0-0(2,3))12-32-24(10,59)20/1113-74(11,4- 12H2 1-3H3 (4) 78 19 20)		
			Soil
	all other all all all all all all all all all al		not found
			Water
	2 ¹ of the me to pit		not found
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	aler column the off		
F Vett	$\frac{4}{14}$		
	athe tho y		
C ^O [*]			



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		<u>^</u>	
Code Number	Description	Structural formula	Compound foond in (level):
(Synonyms) M27 Spiroxamine-despro- pyl-sulfate KWG 4168-despro- pyl-sulfate ECW 80862 ECW 80873 KNO 2233B	IUPAC name:         2-{2-[(ethylamino)methyl]-1,4-dioxaspiro[4.5]dec-8-yl}-2-methylpropyl hydrogen sulfate         SMILES notation:         O=S(=O)(O)OCC(C)(C)C1CCC2(CC1)OCC(CNCC)O2         InChiKe: 1S/C15H29NO6S/c1-4-16-9-13-10-20-15022-13)7-5-12(6-8-15)14(2,3)11-21-23(17,18)19(h)2-13,16H4-11H2,1-3H3,(H,17,18,19)         1H2,1-3H3,(H,17,18,19)	HO S O S O TOPEN NH HO S O TOPEN N	Rat Excreta (0.3-11.3% AD) Uwestock Liver goat (4.7% TRR) Kidney goat (5.8% TRR) Pat goat (3.5% TRR) Plants Plants
KML 2202 Aminodiol	HUDAC nome: CUITIE OF GILLS ON	the det the this do the the	Rat         Excreta (2.2-5.6% AD)         Livestock         not found         Plants         Banana pulp (31.2% TRR)         Grapes (37.5% TRR)         Rotational crops         Swiss chard immature leave (1.8-
	ermore, this publication and and explored and and explored and and explored and and and explored and and and and and and and and and an		2.4% TRR) Swiss chard mature leave (3.9% TRR) Wheat hay (0.3-0.6% TRR) Wheat straw (0.2% TRR) Turnip roots (4.9% TRR) Turnip tops (0.9-3.3% TRR) Soil



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Code Number (Synonyms)	Description	Structural formula	Compound foond in (leve):
		C BONET OF OF	not found
		Å.	not found to the found of the f
29	IUPAC name:	the set of the set	Livesback
piroxamine-amino- ol-N-oxide	IUPAC name: N-ethyl-2,3-dihydroxy-N-propylpropan-1-amine N-oxide SMILES notation: CCC[N+]([O-])(CC(O)CO)CC_OCO InChiKe: 1S/C8H19NO3/c1-3-5-9(12,4-2)6-8(41)7 10/h8,10-11H,3-7H2,1-2H3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		Livestock of found Contract of Plants
WG 4168-amino-	SMILES notation: CCC[N+]([O-])(CC(O)CO)CC	N PO ADO	Plants (0 100 (0 100 )
ol-N-oxide /AK 6885	InChiKe: 15/C8H19NO3/c1_3_5_9(12.4_2)6*09117-		Grapes (0, 1% TRR)
minodiol-N-oxide	10/h8,10-11H,3-7H2,1-2H3	of a trating	<b>Rotational crops</b> Swass chard, immature leave (1.0-
	K Dr O'D	GROLEC OUL OUL TREIL	5.2% TRUE
	lein and sy	er re- or content	Swigs thard mature leave (0.8%
	CULL OF THE OWN	a ger a cor	ÆRR) Turnip roots (4.7-4.8% TRR)
	do del cior the	Der of the thirt of the	
	Mailes ar to the 1	GROUPE EVICO TO	not found
		i de of othic	Water
		A WE AF AF	not found
30 piroxamine-desethyl-	IUPAC name:	140 MD LD	Livestock
ninodiol		NE LE NH	not found
WG 4168-desethyl-	SMILES notation: CCCCCCOO)CO		Plants
ninodiol /AK 6894 -	MChiKe: InChI=15466H15NQ221-2-3-7-@6(9)5-84a6-	C POUD C	Banana pulp (0.6% TRR) Grapes (1.1% TRR)
esethyl-aminodiol	9H,2-5H2,1H3		Soil
			not found
	of the citar of the mitte		Water
	er zyz er z zyż		not found
~~ [~] ~ [~] [~]	The could be the prov		
EV.	IUPAC name: 3-(propylamipo)propane, 2-diol SMILES notation: CCCNCC(0)CO MChike: InChI=15/C6H15NO2c1-2-3-7-06(9)5-8/h6- 9H,2-5H2,1H3 2100 CCL CCL CCL CCL CCL CCL CCL C		
A OIL'	Orper , they a		



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Code Number (Synonyms)	Description	Structural formula	Compound found in (level):
M31 Spiroxamine-despro-	IUPAC name: 3-(ethylamino)propane-1,2-diol	HO pater (property	Livestach The share of the shar
yl-aminodiol			not tound
WG 4168-despro- yl-aminodiol	SMILES notation: CCNCC(O)CO	NH 200 ANH 200 AV	Plants D Banafig pulp (0,6% TRR)
AK 6893	InChiKe: 1S/C5H13NO2/c1-2-6-3-5(8)4-7/h5-8H,2-	HOTO	Grapes (1.20 TRR)
espropyl-aminodiol	4H2,1H3	HO to third part data and and third part to the to	<b>Rotational crops</b> Wheat forage (1.6% TRR) Wheat hay (1.4-1.7% TRR)
	IUPAC name:	HO HO CLUNH 105 OF GROUPSCE LINC PART OF GROUPSCE LINC PART OF CHO TO THE CONTRACT OF CONTRACT OF THE	Wheat straw (1.4-1.8% TRR) Turnip roots (6.1% TRR)
	CUIRED'S ADY BU	er a reproductiner	Turniprops (0.4% TRR) Soil Not found
	IUPAC name: 4-tert-butylcyclohexyl besopyranoside	Pet and regulate duc annener ader a reproduce document ader of this document hyper of this of the hyper of th	Not found Water
32	IUPAC name:		not found
piroxamine-cyclo- exanol glucoside	IUPAC name: 4-tert-butylcyclohexyl hexopyranoside SMILES notation	OH OH	Livestock not found
WG 4168-cyclohex-	SMILES notation		Plants
nol glucoside yclohexanol Gluco-		OH OH	not found [transient]
de	InChilde: 1S/C16H30O6/e106(2,3)9-@6-10(7-59)21-15- 44(20)13(19)12(18)11(@17)22-4.5/99-15.12-20H.4-8H20-	HO OH HO OH HO OH HO OH OH OH GROUP B	Soil not found
	CC(C)(C)CLCCC(CC1)OC1OC(CO)C(O)C(O)C1O InCh(&e: 1S/C16H30O6/e)O16(2,3)9-6-10(7-5-9)21-15- 14(20)13(19)12(18)11(&17)22-15/19-15,17-20H,4-8H2Q- 3H3		Water not found
133 piroxamine-cyclo- exanol-glucopyra-	HIDAC normal Mat area labla	НО ОН ОН	Livestock not found
piroxamine-cyclo- exanol-glucopyra- osyl-pentose	InCharles Not againable	O-Pentose	Plants Grapes (19.1% TRR)
EVer	InCharte: Not agailable the pro-		Soil



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Code Number (Synonyms)	Description	Structural formula	Compound for din (level):
WG 4168-cyclohex- nol-glucopyranosyl- entose Cyclohexanol-gluco- yranosyl-pentose Conjugate of cyclo- exanol 434 piroxamine-cyclo- exanol-glucopyra- osyl- lucopyranosyl-pen- ose CWG 4168-cyclohex- nol-glucopyranosyl- lucopyranosyl-pen- ose Cyclohexanol-gluco- yranosyl-glucopyra- osyl-pentose	IUPAC name: Not available SMILES notation: Not available InChiKe: No	PROUP B (position of glucopy ranosyl-pentose not speci- fied)	not found The state of the stat
Conjugate of cyclo- exanol 435 piroxamine-docosa- oic acid ester CWG 4168-docosa- oic acid ester A1345 Docosanoic acid ester	IUPAC name. 4-tert-putylcyclohexyl docosanoate SMILES notation: Not available in often in the	GROUP B	Livestock not found Plants Grapes (13.0% TRR) Soil not found Water



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Code Number (Synonyms)	Description	Structural formula	Compound found in (leve):
M36 Spiroxamine-tetraco- sanoic acid ester KWG 4168-tetracosa- noic acid ester PA1344 Tetracosanoic acid es-	IUPAC name: 4-tert-butylcyclohexyl tetracosanoate SMILES notation: Not available InChiKe: Not available	$\begin{array}{c} & & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & & \\ & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ &$	Livestect
M37 Spiroxamine-cyclo- hexenol KWG 4168-cyclohex- enol	IUPAC name:         4-tert-butylcyclohexen-1-ol         SMILES notation: CC(C)(C)C1C=CC(O)CC1         InChiKe: 1S/C10H18O/c1-10(2,3)8-4-6-9(11)7-53844,6,8-9,11H,5,7H2         9,11H,5,7H2         YH3	GROUP B OF THIS 5	Water not found Livestock not found Plants Grapes (3.2% TRR- hydrolysis prod- uct) Soil not found
M38 Spiroxamine-N- formyl-despropyl KWG 4168-N-formyl- despropyl	IUPAC name: N-[(8-tert-buryl-1,4-divxaspiro[4,5]dec-2 x0methyl]-NO Th ethylfotnamide SMILES notation: CC(C)(C)C1CQC2(CC1)QCC(CN(C+Q)CC)O2 InChik@15/C16H29NO3/c15517(12-18)P0-14-1129- 16(20-14)8-6-13(7-9-16)15(2,3)4/h12 14H,5-11P12,1-4H3 N ¹ +t Th O Th D ¹ +t Th O Th D ² +t Th O Th		Water         not found         Livestock         not found         Plants         not found
	InChik @15/C16H29NO3/c15217(12-16)40-14-1169- 16(20-14)8-6-13(7-9-16)45(2,3)4/h12-14H,5-14H2,1-4H3	GROUP A	Rotational crops Wheat hay (4.8-6.8% TRR) Wheat grain (2.7% TRR) Wheat straw (3.4-7.6% TRR) Soil not found



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Code Number	Description	Structural formula	Compound formed in (large)
(Synonyms)	Description	e tr	Compound foond in (leve):
		e Bayer or Oper	Water, OIL Julian
M39 Spiroxamine-hydroxy- despropyl glycoside KWG 4168-hydroxy- despropyl glycoside	IUPAC name:         glycoside of 2- {2-[(ethylamino)methyl]-1,4-diox-aspiro[4.5]dec-8-yl}-2-methyl         propan-1-ol         SMILES notation:         OC1C(O)C(O)C(CO)OC1OCC(C)(C)C1CCC2(CC1)OCC(         CNCC)O2         InChiKe: 1S/C21H39NO8/c1-4-22-9-14-14128-21(30-04)7-         5-13(6-8-21)20(2,3)12-27-10-18(26)17625)16(24)15(10-         23)29-19/h13-19,22-26(14-12H2)-3H3         IUPAC name:         glycoside of 2-(2-{fethyl(propyl) aminofmethyl}-K4-diox-aspiro[4.5]dec-8-yl)-2-methylpropart1-ol         SMILES notation:         OC1C(O)C(O)C(CO)OC1OCC(C)(C)C1CCC2(CC1)OCC(         CNCCOCO2         IUPAC name:         glycoside of 2-(2-{fethyl(propyl) aminofmethyl}-K4-diox-aspiro[4.5]dec-8-yl)-2-methylpropart1-ol         SMILES notation:         OC1C(O)C(O)C(CO)OC1OCC(C)(C)C1CCC2(CC1)OCC(         CN(CC)CCC)O2         Inchike: 15/C24H455/08/c1-5-11-25(6-2)(12-17-14-31-24(33-t7)9-7-16(45H0-24)(23(3-4))15-30-22-21(29)(20(28)(9(27))18(13-26)32-227016-22,26-29H,5-31-22,26-29H,5-31-22,14-13	HOLO A CONTRACTORY AND	<b>Livestock</b> not found <b>Plants</b> not found <b>Rotational crops</b> Swiss chard immature leave (2.0% TRN) Swiss chard mature leave (2.8% TRN) Wheat forage (1.6-2.1% TRR) Wheat forage (1.6-2.1% TRR) Wheat straw (0.5-1.6% TRR) Turnip tops (3.1-21.3% TRR)
M40 Spiroxamine-hydroxy	IUPAC name: glycoside of 2-(2-{[ethyl(probyl) aminofunethyl]=K4 diox-	HOHO ON DET THE THE NH	not found Water not found Livestock not found
glycoside KWG 4168-hydroxy « glycoside	$\begin{array}{c} \text{aspred}_{\text{respect}} \\ \text{SMILES notation}^{\text{aspred}_{\text{respect}}} \\ \text{SMILES notation}^{\text{aspred}_{\text{respect}}} \\ OC1C(O)C(O)C(CO)OC1OCC(C)(e)C1CCe2(CC1)OCC(e)C1CCe2(CC1)OCC(e)C1)OCC(e)C1CCe2(CC1)OCC(e)C1)OCC(e)C1CCe2(CC1)OCC(e)C1)OCC(e)C1)OCC(e)C1CCe2(CC1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC(e)C1)OCC($	GROUP A	Plants not found Rotational crops Swiss chard immature leave (0.8-
EULTU	162hiKe: 157c24H455008/c1-5-11225(6-2)12-17-14-31- 24(33-17)9-7-16(8-10-24)23(3,4)15-30-22- 21(29)20(28)19(27)18(13-26)32-221016-22,26-29H,5- 25H2,1-4H3		4.7% TRR) Swiss chard mature leave (0.8-3.8% TRR) Wheat forage (1.3-1.5% TRR)



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Code Number (Synonyms)	Description	Structural formula	Compound foond in (level):
		ety of Bayer reproperty	Wheat hay \$1.0-2.9% (FRR) Wheat straw (0.902.6% TRR) Turnip tops (10-7.6% TBR)
	PTOPE	EFiliates. productions pro	
	Q [¥]	EEIL BLEILE BOUNDARD	not found
M41 Spiroxamine-hydroxy- lesethyl	2-methyl-2-{2-[(propylamino)methyl]-1,4-diox-		Livestock de not found
KWG 4168-hydroxy- lesethyl WAK 6084/1	SMILES notation:	CROUPATEDICOUNTER	Plants
			<b>Rotational crops</b> No free M41 detected [aglycon of M42]
	3H3 THE CIT OF THE CALL	ADUTION THE THE THE OF	Soil not found
	gup jece the max distr	nd whet the t	Water not found
M42 Spiroxamine-hydroxy- lesethyl glycoside	IIIPAC name		Livestock not found
KWG 4168-hydroxy- lesethyl glycoside	SMILES notation	GROUP A	<b>Plants</b> not found
	O(1)O(1)O(1)O(1)O(1)O(1)O(1)O(1)O(1)O(1)		<b>Rotational crops</b> Swiss chard mature leave (0.4-1.6% TRR)
. Th	Inchike: 15/C22H41N08/c1-4-9-25-10-15-12/29-22(31- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(26)17(25)16(11-24)30-20/b14-20,23-27H,4- 19(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18(20)18		Wheat forage (1.6-3.4% TRR) Wheat hay (2.7-6.5% TRR) Wheat straw (0.8-4.7% TRR)
E Vet	19(20)18(26)1 (025)16(11-24)30-20(404-20,23-27)H,4- 09H2,1-3H3		Turnip roots (2.8% TRR)



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~			ALCON AND AND AND AND AND AND AND AND AND AN
Code Number (Synonyms)	Description	Structural formula	Compound foond in (level:
		of Bayer proper	Turnip top (3.2-14.6% PRR) Soil Cond Not found Water Bolt found Livestock
	l l	ty liates. that ies. pr	Water
M43 Spiroxamine-desethyl acid glycoside	IUPAC name: glycoside of 2-methyl-2-{2-[(propylamino)-methylPl,4-di- oxaspiro[4.5]dec-8-yl}propanoic acid		
KWG 4168-desethyl acid glycoside	SMILES notation: OC1C(O)C(O)C(CO)OC1OC(=Q)C(Č)(C)C1CCC2(CCQ)	GROUPA gulato duction	Plants netsfound Rotational crops
	OCC(CNCCC)O2 InChiKe: 1S/C22H398699/c1-4+9923-10-1462-29-22(32-4- 14)7-5-13(6-8-22)2H(2,3)29(28)31-19-C		Swiss chard immature leave (1.8% CPRR) Swiss chard mature leave (0.6%
	giycoside of 2-inethyl-2-{2-{(piopylainino)-inethylye1,4-di- oxaspiro[4.5]dec-8-yl}propanoic acid SMILES notation: OC1C(O)C(O)C(CO)OC1OC(=O)C(C)(C)C1CCC2(CC0) OCC(CNCCC)O2 InChiKe: 1S/C22H30\09/c1-4+923-10-14(12-29-22(32)) 14)7-5-13(6-8-22)2f(2,3)20(28)31-19- 18(27)17(26)16(25)15(11224)30-19/h13-19,23-27/H,4- 12H2,1-3f(3) UPAC name glycoside of 2-(2-{[ethyl(propyl)amino]methyl]-1,4-diax- aspiro[4.5]dec-8-yf)-2-methylpropanoic acid SMILES notation: OC1(CO)C(O)(CO)OC1OC(=O)C(C)(C)C1CCC2(CC1) OC1(CO)C(O)(C)C1OC(=O)C(C)(C)C1CCC2(CC1) OC1(CO)C(O)(C)(C)C1CCC2(CC1)		TRR)         Wheat forage (0.6-2.6% TRR)         Wheat hay (1.3-3.3% TRR)         Wheat straw (0.5-3.4% TRR)         Turnip roots (2.6% TRR)         Turnip tops (5.7% TRR)
	at be coet at 1000 at 1000	the late	Soil not found
~		8	Water not found
M44 Spiroxamine-acid gly- coside	IUPAC name glycoside of 2-(2-{[etbyl(propyl)amino]methyl}-1,4-dby- aspirol 3]dec-8-yl-2-methylpropanoic acid		Livestock not found
KWG 4168-acid gly- coside	SMILES notation; Mercine Der Oliver		Plants not found
ANK CH	0C1@(0)C(0)@(0)0C10@(=0)C(G)(C)C1CCC2(CC1) 		Rotational crops
Cont	and the post of th		



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Code Number	Description	Structural formula	Compound forfind in (lorge
(Synonyms)	Description	Structur apper muta	Compound foord in (lever):
M45 Spiroxamine-despro-	Description           InChiKe: 1S/C24H43NO9/c1-5-11-25(6-2)12-16-14-31-24(34-16)9-7-15(8-10-24)23(3,4)22(30)33-21-20(29)19(28)18(27)17(13-26)32-21/h15-21,26-29H,5-14H2,1-4H3           14H2,1-4H3           IUPAC name:           glycoside of 2-{2-[(cthylamit0)methyl]e 1,4-diox           glycoside of 2-{2-[(cthylamit0)methyl]e 1,4-diox           SMILES notation:           OC1C(O)C(O)C(CO)OC FOC(=OCCC)(C)C1CCC2(CCT)           InChiKe: hOff1=1S/C2PH37NQ921-4-22-9515-11-280	er and reproduction and reproduction and reproduction of the sector of t	Swiss chard immature leave (2.2- 4.6% TDR) Swiss chard mature leave (2.4-3.1% TRR) Wheat for age (0.9-2.3% TRR) Wheat straw (1.0-10.5% TRR) Turnip roots (1.9% TRR) Turnip tops (6.0-11.6% TRR) Soil Not found Livestock not found
yl acid glycoside KWG 4168-despropyl acid glycoside	IUPAC name:       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0 <td< td=""><td>HOHORA CE THOMAN THE THE THE THE THE THE THE THE THE THE</td><td>not found <b>Plants</b> not found <b>Rotational crops</b> Swiss chard immature leaves (2.6- 6.0% TRR) Swiss chard mature leave (1.8-5.5% TRR) Wheat forage (1.3-2.5% TRR) Wheat forage (1.3-2.5% TRR) Wheat straw (0.6-2.8% TRR)</td></td<>	HOHORA CE THOMAN THE	not found <b>Plants</b> not found <b>Rotational crops</b> Swiss chard immature leaves (2.6- 6.0% TRR) Swiss chard mature leave (1.8-5.5% TRR) Wheat forage (1.3-2.5% TRR) Wheat forage (1.3-2.5% TRR) Wheat straw (0.6-2.8% TRR)
EUICED	ermore, any e ermissized or ermore, any connercial permissized or equently, commercial permissized or		Wheat straw (0.0-2.3 % TRR)         Turnip roots (3.7-9.1% TRR)         Turnip tops (1.7-3.6% TRR)         Soil         not found         Water



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			Compound forther in (level):
Code Number	Description	Structural formula	Compound forged in (level):
(Synonyms)		×	Compound to the in (levely:
			not found the state of the second sec
* no need to include all metabolites for	bund in rat in case not found in the other matrices.	hua (TDR) for an gran montal comportments	ant/mimal maide and antista
** levels should be expressed as % of	applied radioactivity (AK) or total radioactive resid	iue (TKK) for environmental compartments and pi	ant/animal residues, respectively
		*1 × 0°	
			Profession
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th se ^{cr} a	pund in rat in case not found in the other matrices. Fapplied radioactivity (AR) or total radioactive residents applied radioactive (AR) or total radioactive (AR) or total radioactiv		
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\checkmark	AN THE REAL PROPERTY OF THE PR		



Appendix 2: Estimation of soil sorption Koc value based on Log Pow

The soil sorption Koc values of the separate A and B isomers was estimated from the corresponding C Log Pow values using KocWin, v2.00 (part of EPI suite).

2.9' i) Estimation if Koc for A isomer based on Log Pow value of 2.79 (pH 7 SMILES : C1CC(C(C)(C)C)CCC12(OCC(CN(CC)CCC)O2) CHEM : KWG 4168 MOL FOR: C18 H35 N1 O2 MOL WT : 297.49 ----- KOCWIN v2.00 Results -Koc Estimate from MCI: -----First Order Molecular Connectivity Index Non-Corrected Log Koc (0.5213 MCI #9.60) Fragment Correction(s): 3 Nitrogen to Carbon (aliphate) (-N-9)... **0:6**38 2 Ether, aliphatic (-C-O-Cc) Corrected Log Koc Estimated Koc: Koc Estimate from Log Kovô Log Kow (User entered) Non-Corrected Log Koc (0.55312, log Kogy + 0.9251 Fragment Correction(s) Ö) : -0:9654 3 Nitrogen to Carbon (aliphatic) (-N-CA. 2 Ether, aliphatic (-C-O-C Corrected Dog Koe ... Estimated K Estimation If Koc for Bosomer Dased on Log Pow value of 2.98 (pH 7) ii) SMILES : C1CC(C)(O)CHEM : KW& 4168 MOL FOR 2 18 H35 N1 (MOL WT 297.49 Koc Estimate from MCI: 9.883 First Order Molecular Connectivity Index Non-Corrected Log Kos (0.5213 MCI 0.60) : 5.7519 Fragment Correction(s): 3 Nitrogen to Carboy (aliphatic) (-N-C).. : -0.6382 Ether, atphatic (-C-O-C-) : -1.7432 2 Estimated Koc: 2347 L/kg <== Koc Estimate from Log Kow:



Sumi	Log Kow (User of Non-Corrected L Fragment Correct 3 Nitroger 2 Ether, al Corrected Log Ko Estimat	entered) 2.98 og Koc (0.55313 logKow + 0.9251) 2.5734 tion(s): n to Carbon (aliphatic) (-N-C) : -0.0654 iphatic (-C-O-C-) : 2.3269 ted Koc: 212.3 L/kg $<$
id.	CAS no.	SMILES code
A B	- 118134-30-8	$C1CC(C(C)(C)C)CCC12(\bigcirc CC(C)C)CCC)C(C)C(C)C)C(C)C(C)C)CCC12(\bigcirc CC(C)C)CCC)CCCC)CCCCCCCCCCCCCCCCCCCCC$
		entered)

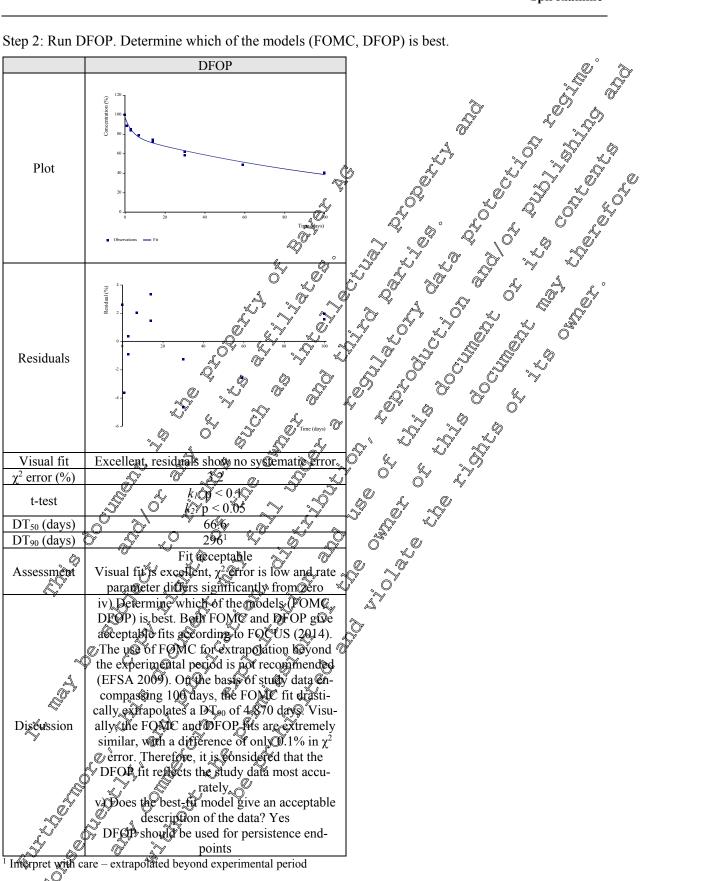


Appendix 3: Kinetic evaluation of laboratory soil studies **Appendix 3.1:** Kinetic evaluation for persistence/trigger endpoints Appendix 3.1.1. Degradation of 14C-cyclohexyl- labelled spiroxamine, M01, M02 and M03 in BE 2.2/Speyer 2.2 soil (KCA 7.1.1.1/01 (M-006135-01-1)) Appendix 3.1.1.1. Spiroxamine kinetics Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit? SFO FON Plot Residuals Time (days) Intermediate, residuals show systematic error Visual fit Excellent, residuals show no systematic error and final data point is underestimated ©ð.4 χ^2 error (%) 3.1 NA t-test < 0.05DT₅₀ (days) 65.8 DT₉₀ (days)≽ 4870^{1} Fit not acceptable \heartsuit Fit not acceptable \checkmark \checkmark χ^2 error is low and rate parameter differsig-Fit potentially acceptable Ò Visual fit is excellent and χ^2 error is low. Sig-Assessment nificantly from zero, however, visual fit is innificant extrapolation from study period to termediate (residuals show stematic error ~ DT90². and final data point is underest mated) B/SFO more appropriate than EOMC and gives acceptable fit? SFO is not considered acceptable. ii) Run morified fitting. Sto more appropriate than FOMC & fit acceptable (modified fit-Discussion ting)? Modified fitting not needed

iii) Deviation from SFO due to experimental artefact/decline in microbial activity? No Go to step 2 below

extrapolated beyond experimental period ¹ Interpret with@are – ² EESA (2009)



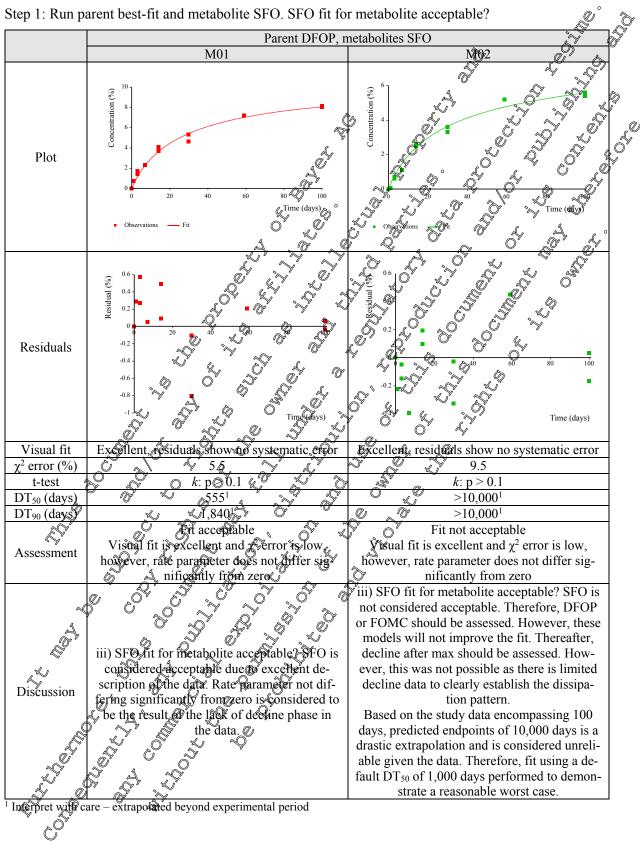


Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.

Summary:

For parent spiroxamine use DFOP. $DT_{50} = 66.6$ days, $DT_{90} = 296$ days.

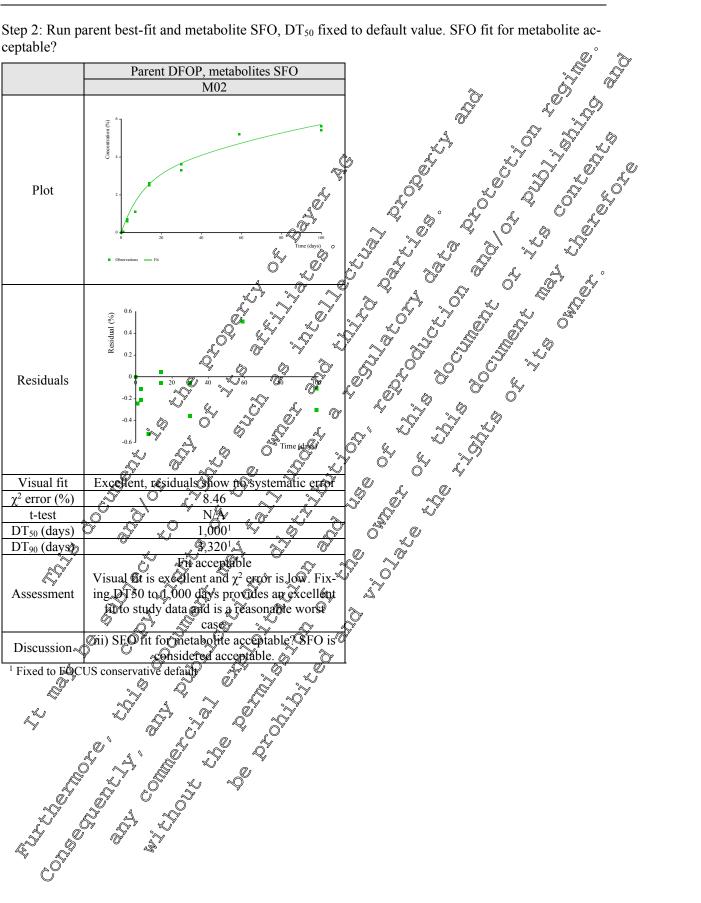




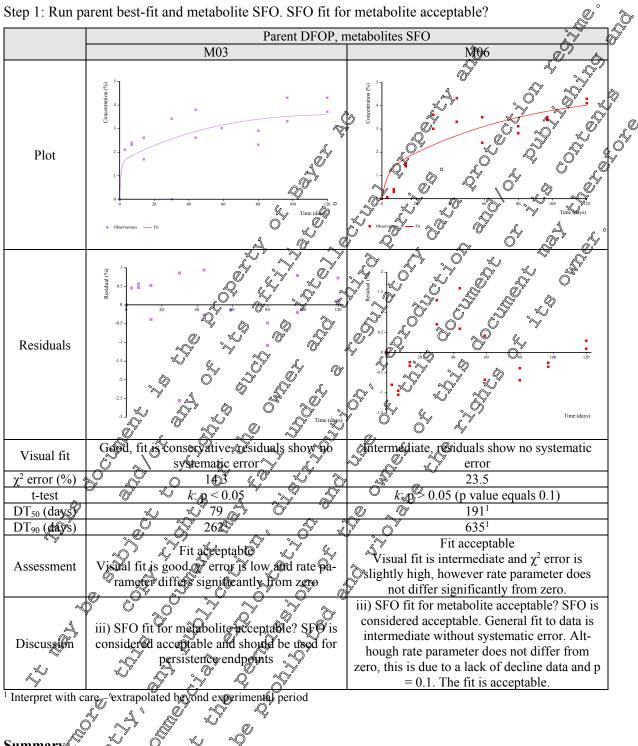
Appendix 3.1.1.2. Metabolite kinetics (M01 and M02)



Step 2: Run parent best-fit and metabolite SFO, DT₅₀ fixed to default value. SFO fit for metabolite acceptable?







Appendix 3.1.1.3. Metabolite kinetics (M03 and M06)

Summary

For MO Suse DOP/SFO. $DT_{50} = 70.7$ days, $DT_{90} = 235$ days. For M92 use $DFOP(SFO_{50} = 65.2 \text{ days}DT_{90} = 217 \text{ days}.$ For M03 use DFOP/SFO $DT_{50} = 79$ days, $DT_{90} = 262$ days.

For M@6 use DFOP/SFO $DT_{50} = 191$ days, DT90 = 635 days

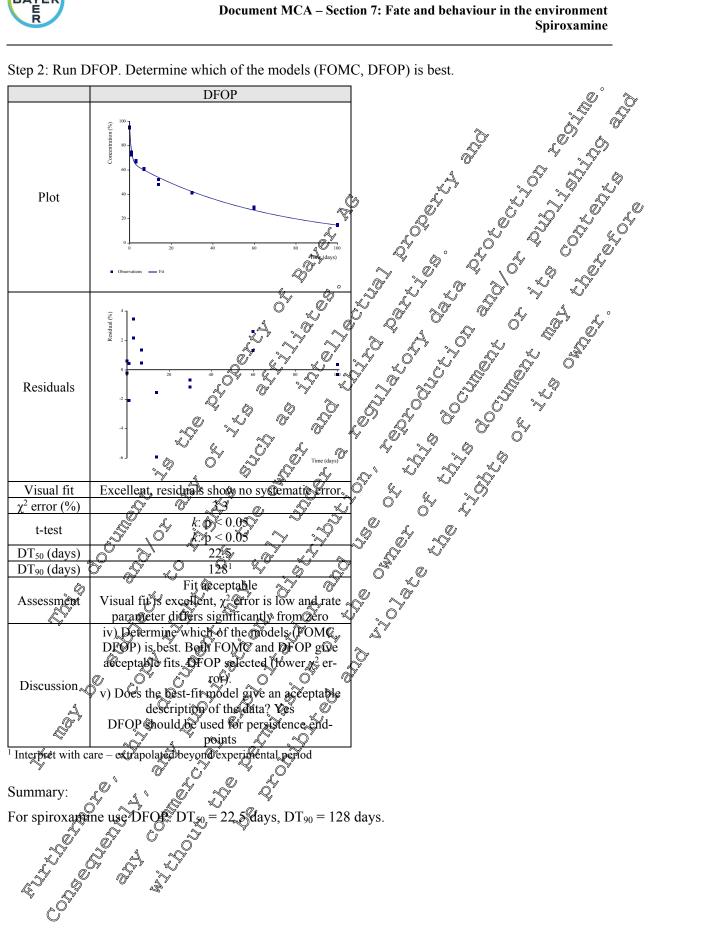


Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M02 in Appendix 3.1.2. Laacherhof soil (KCA 7.1.1.1/02 (M-006141-01-1)) Appendix 3.1.2.1. Spiroxamine kinetics Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit? SFO FOM oncentration (% Plot tesidual (%) Residuals 2 Intermediate, residuals show systematic error Good, residuals show no systematic error and Visual fit Ø Ø1 and fit not conservative fit is conservative $\chi^2 \operatorname{errop}(\%)$ 11.9 8.6 t-test *k*: pk\$ 0.05 NA DT₅₀ (days) 34 8 17.2 m 908¹ DT₉₀ (days) Ô 116 Fit not acceptable Fit acceptable χ^2 erfor is acceptable and rate parameter dif-Visual fit is good and χ^2 error is low. Signifi-Assessment fers significantly from zero, however, visual cant extrapolation from study period to fit is intermediate (residuals show systematic DT90². error and fit not conservative Ż i) SFO more appropriate than FOAC and gives acceptable fit? SFO is not more appropriate than FOMC. (i) Run modified fitting. SFO more appropriate than FOMC & fit acceptable (modified fit-Discussion ting." Deviation from SFO is not due to outliers or experimental artefacts (ii) Devotion from SFC due to experimental artefact/decline in microbial activity? No Go to step 2 below

¹ Interprets with cate – extrapolated beyond experimental period

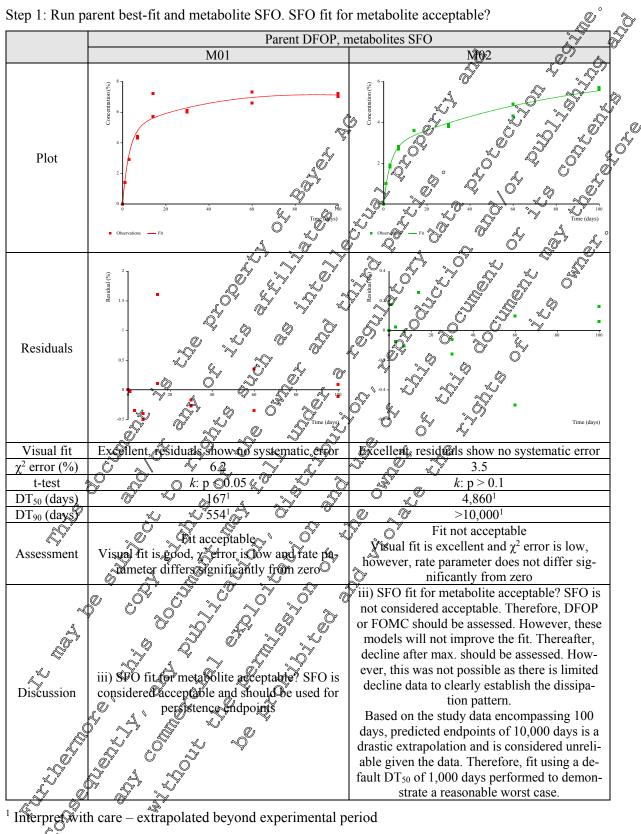
² EFSA((2009))





Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.

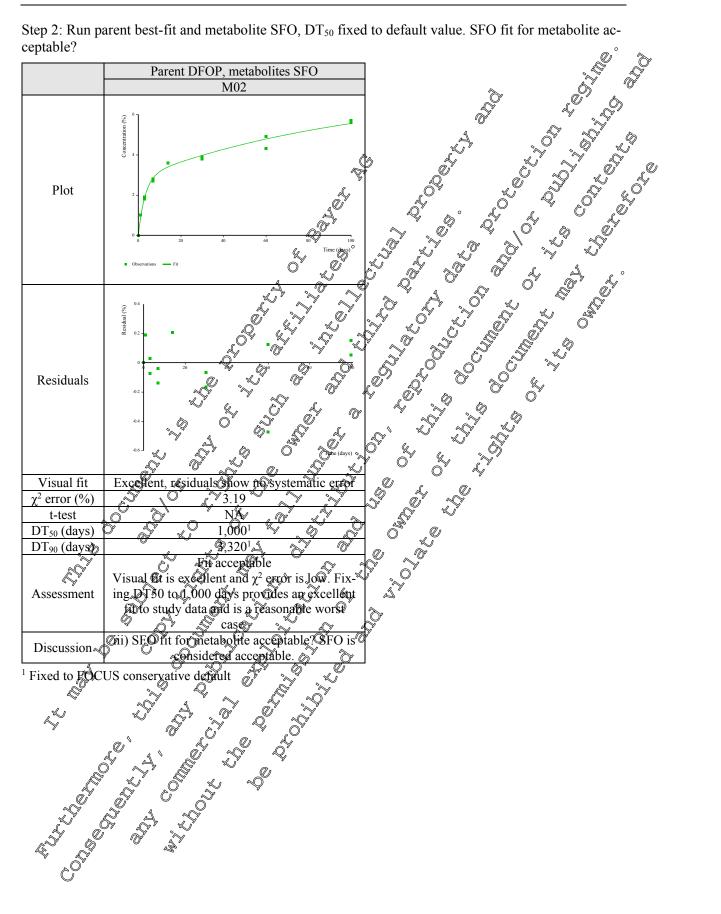




Appendix 3.1.2.2. Metabolite kinetics (M01 and M02)

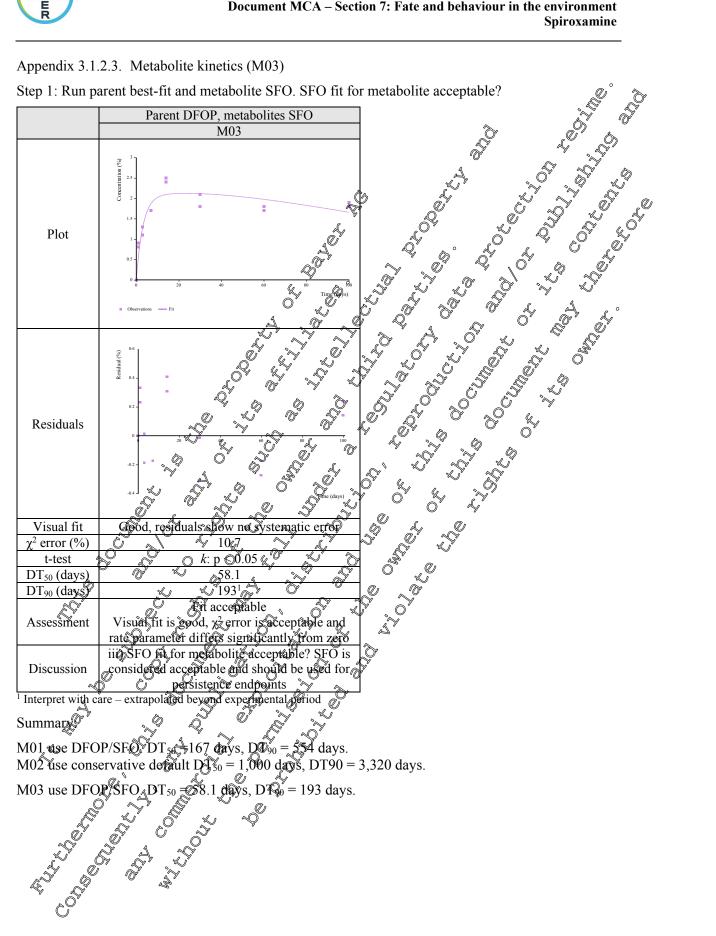


Step 2: Run parent best-fit and metabolite SFO, DT₅₀ fixed to default value. SFO fit for metabolite acceptable?







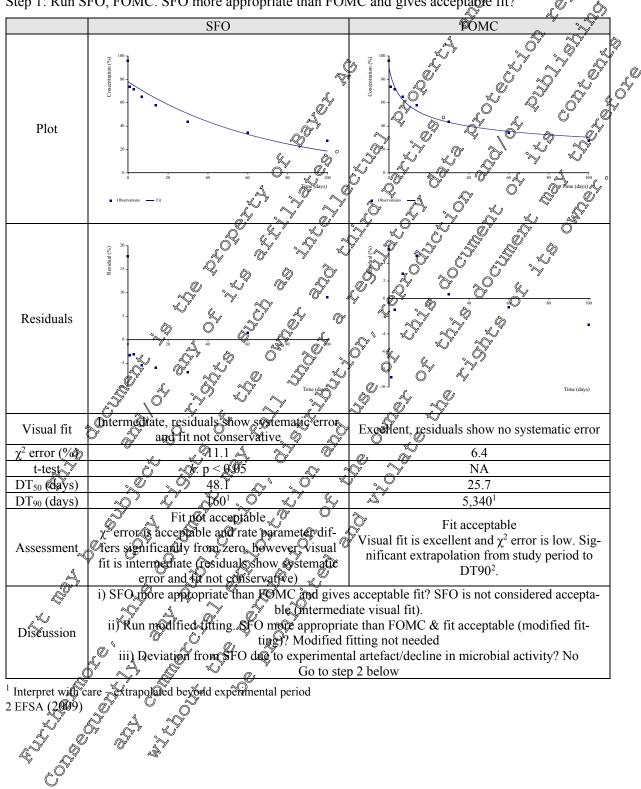




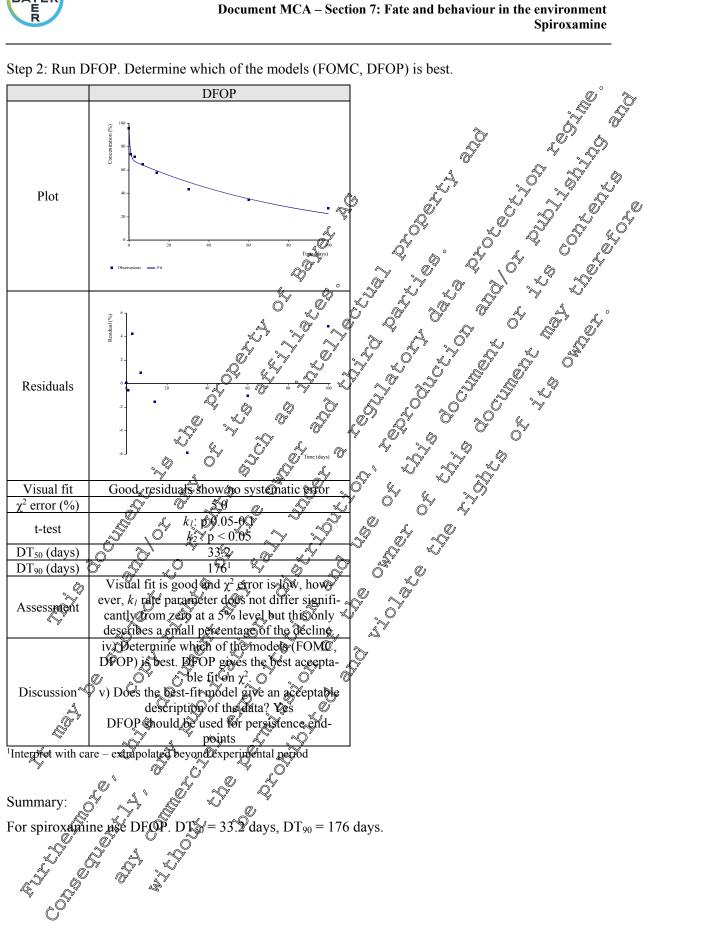
Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Mon-Appendix 3.1.3. heim 3 soil (KCA 7.1.1.1/02 (M-006141-01-1))

Appendix 3.1.3.1. Spiroxamine kinetics

Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit?







Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.



Step 1: Run parent best-fit and metabolite SFO. SFO fit for metabolite acceptable?			
	Parent DFOP, metabolites SFO		
	M01 N02		
Plot	Parent DFOP, metabolites SFO M01 M01 M01 M01 M01 M01 M02 M01 M04 M04 M04 M04 M04 M04 M04 M04		
Residuals	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$		
Visual fit	Intermediate, fit slightly under estimates the		
χ^2 error (%)	$\frac{6}{6} \frac{6}{2} \frac{1}{2} \frac{1}$		
t-test			
DT ₅₀ (days)			
DT ₉₀ (chay's)	<i>C S</i> 1,220 <i>S S S S S S S S S S</i>		
• • Assessment	Visual fit is intermediate with a high γ value. Rate parameter is not statistically different to zero. However, this is considered to be driven by the tack of adecline phase as opposed to data quality.		
Discussion	iii) SFO fit for metabolife acceptable? SFO is considered acceptable. In order to scaluate potential application of the OCUS default, a fit with M01 DC50 set to 1,000 days per- formed.		
Interpret with ca	Traplaced beyond experimental period		

Appendix 3.1.3.2. Metabolite kinetics (M01 and M02)



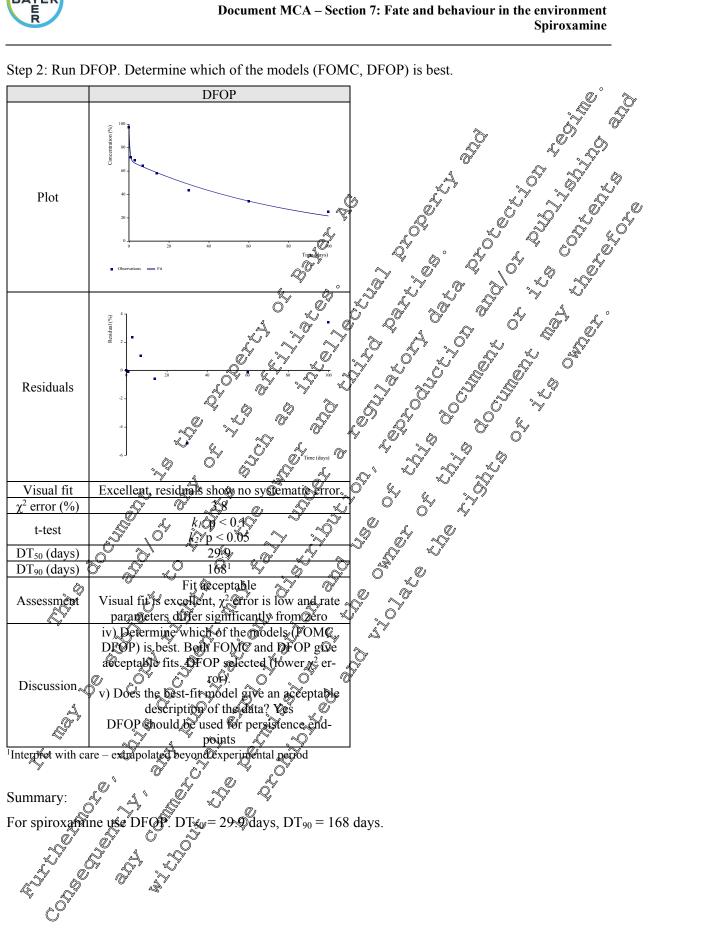
Step 2: Run parent best-fit and metabolite SFO, DT_{50} M02 fixed to default value. SFO fit for metabolite acceptable?

	Parent DFOP, metabolites SFO	Parent DFOP, metabolites SFO
	M01	M02
Plot	(c) 10 8 6 4 2 0 2 0 20 40 60 80 100 100 100 100 100 100 100	Parent DFOP, metabolites SFO M02 M02 M02 M04 M04 M04 M04 M04 M04 M04 M04
Residuals		A A A A A A A A A A A A A A A A A A A
Visual fit	Exceptent, residuaisconow no systematic error	
$\chi^2 \operatorname{error}(\%)$	N^{2} N^{2} N^{2} N^{2}	Solution Systematic error
t-test DT ₅₀ (days)		$\bigcirc \qquad \mathbb{Q} \qquad 1,000^1$
DT_{90} (days)		3,3201
Assessment	Fit mot acceptable. Use Whe J 000 days results in increased Chi ² versus previous Bodelling.	Fit acceptable χ^2 by χ^2
Discussion	with default DTS9 is nonconsidered accepta- Colle as increases Chi Versu Orevious esti-	(Aii) SFO fit for metabolite acceptable? SFO is considered acceptable.
Fixed to FQCU	Concomunitive defaulter des ()	·J
Append 3.1	.3.3. Metabolite kinetics (M05)	
Metabolite M	03 was not observed in this soil.	
For M01 use	\widetilde{DFOP} \widetilde{SFO} $\widetilde{DF}_{50} = 3$ days, $\widetilde{DT}_{90} = 1,220$ d conservative defaute $DT_{50} = 1,000$ days.	lays.
M03 Not obse	conservative default $DT_{50} = 1,000$ days.	
÷		



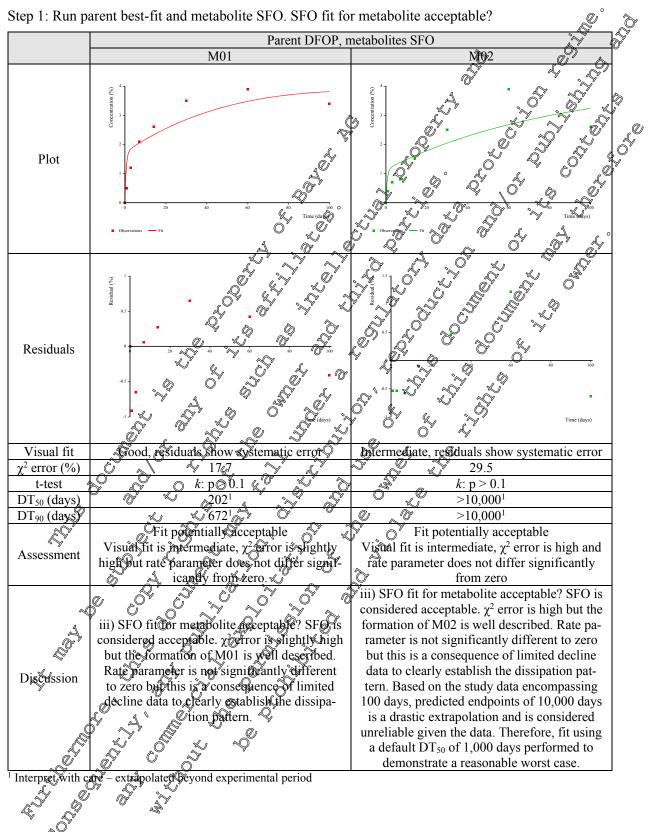
Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Howe Appendix 3.1.4. soil (KCA 7.1.1.1/02 (<u>M-006141-01-1</u>)) Appendix 3.1.4.1. Spiroxamine kinetics Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit? SFO FOMC Plot tesidual (%) Residuals Time (days) Good, residuals show no systematic error and Intermediate, residuals show systematic error Visual fit and fit not conservative fit is conservative $\chi^2 \operatorname{error}(\%)$ 119 8.0 L t-test pK\$ 0.05€ NA *k*: Q DT₅₀ (days) 21.2 46.5 \bigcirc DT₉₀ (days) 9,110¹ 155 Fit not acceptable Fit potentially acceptable χ^2 error is a coeptable and rate parameter diff. Visual fit is good and χ^2 error is low. Signififers significantly from zero, however, visual Assessment \$ 000 cant extrapolation from study period to fit is intermediate (residuals show systematic DT90². Firror and fit not conservative? Ż i) SFO more appropriate than FQAC and gives acceptable fit? SFO is not more appropriate than FOMC. © i) Run modified fitting. SFQ more appropriate than FOMC & fit acceptable (modified fit-Discussion ting? Deviation from SFO is not due to outliers or experimental artefacts (i) Devation from SEC due to experimental artefact/decline in microbial activity? No ¹ Interpret with care extrapolated beyond experimental period ² EFSA⁴(2009) Go to step 2 below





Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.





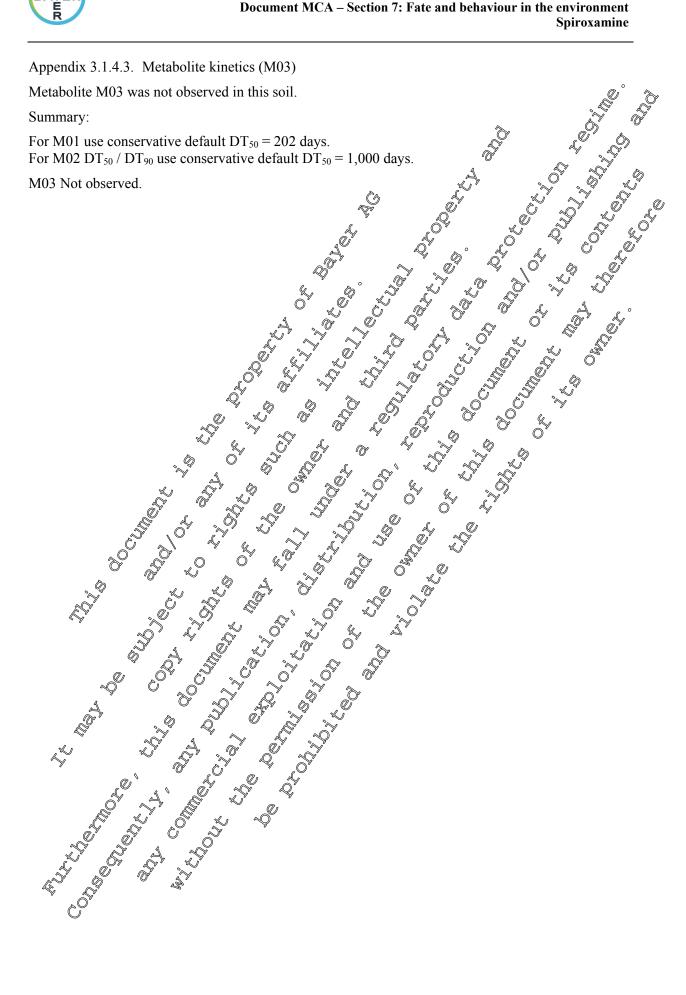
Appendix 3.1.4.2. Metabolite kinetics (M01 and M02)



Step 2: Run parent best-fit and metabolite SFO, DT_{50} fixed to default value. SFO fit for metabolite acceptable?

ceptable?		
	Parent DFOP, metabolite SFO	
	M02	
Plot	Concentrations — Fit	
Residuals		
Visual fit	Intermediate, residents show systematic erfor	
χ^2 error (%)	27.8° Y 27.8° Y 27.8°	
t-test	O O' ' NMA O' L'Y A	
DT_{50} (days)		
DT ₉₀ (days)	5,320 0 0 0	
	Visual tit is informediate and a error low	
Assessment	Use 1 000 day default provides a good fe-	5 Martin Contraction of the Cont
11550555110110	Use 1,000 day default provides a good de- scription of the story data and is oreasonable	~~
	Worst Pase. 2 A	
	Wii) SEO fit formetabolite acceptable? SFO us	
Discussion	ing default OT ₅₀ is considered acceptable de-	
	siduals are mall, 9	
· Fixed to FOCU	S conservative default	
st Sy −		
	Use of 1,000 day default provides a good de- scription of the starty data and is creasonable worst case. (7ii) SEO fit formetabolite acceptable SFO us ing default DT ₅₀ is considered acceptable de- sictuals are small.	



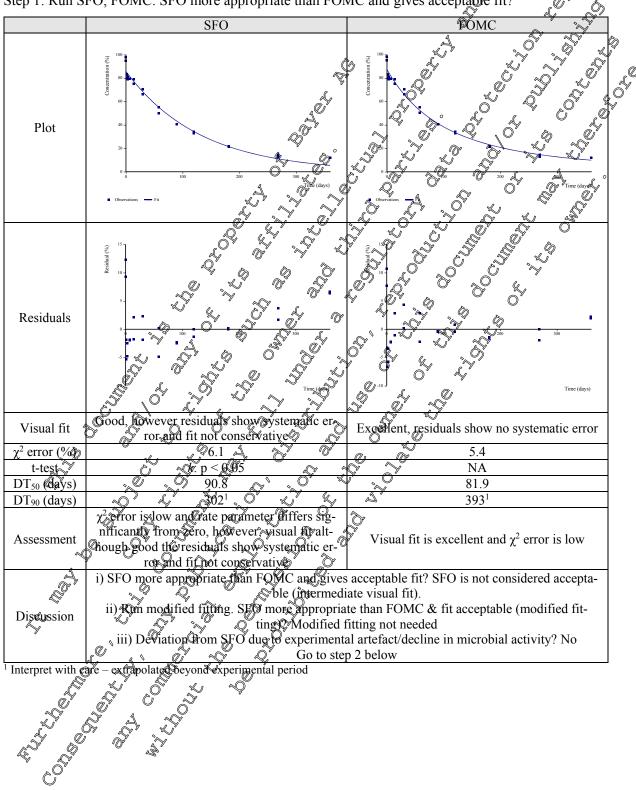




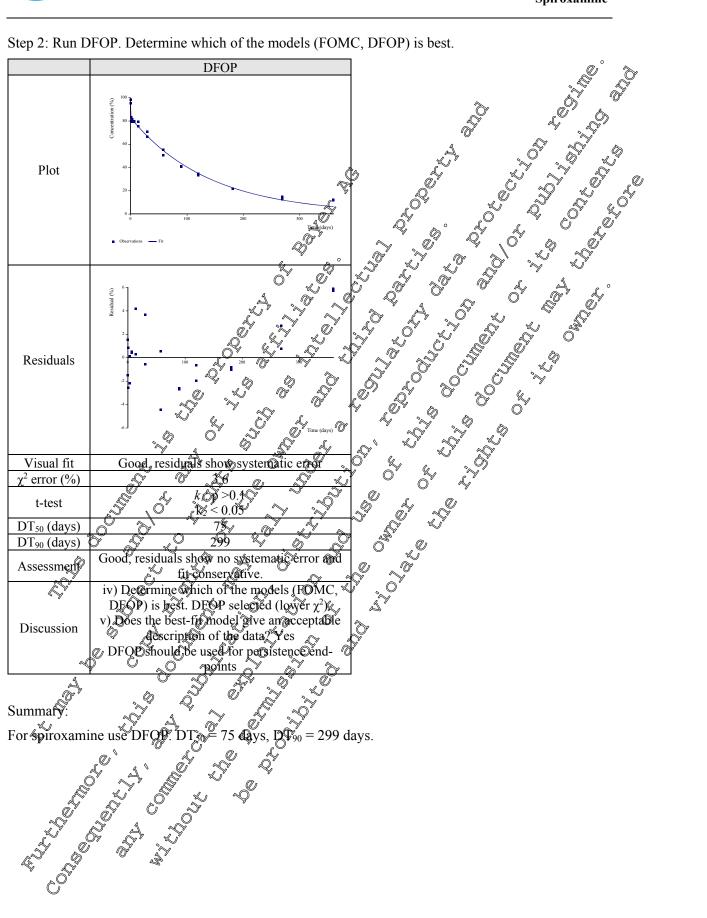
Appendix 3.1.5. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Wolf Ranch soil (KCA 7.1.1.1/04 (<u>M-006148-01-1</u>))



Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit?

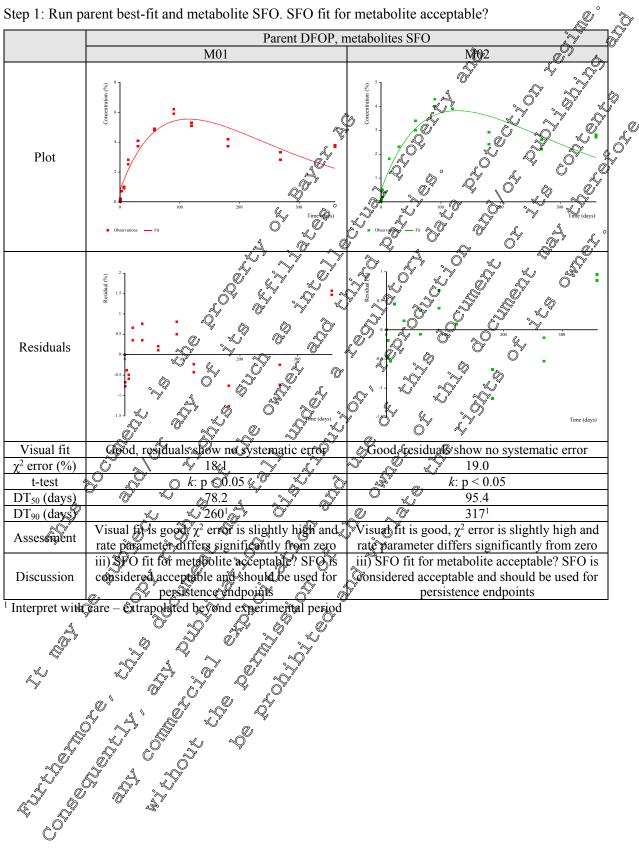






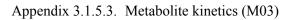
Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.

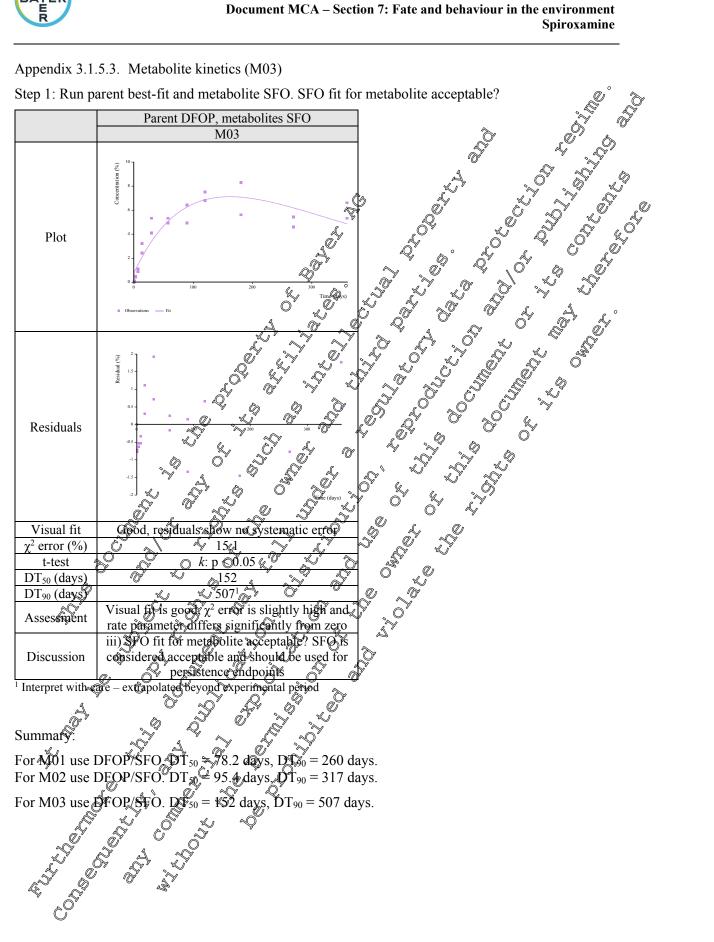




Appendix 3.1.5.2. Metabolite kinetics (M01 and M02)





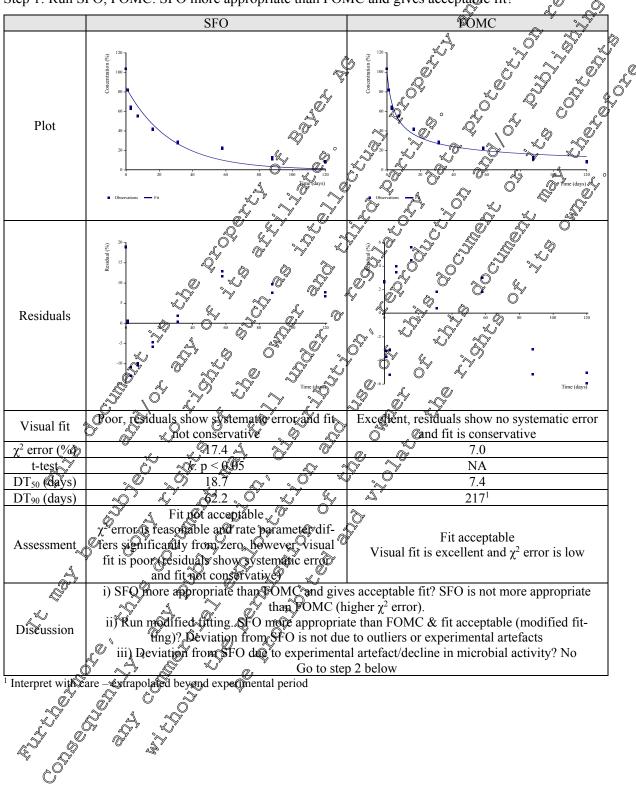




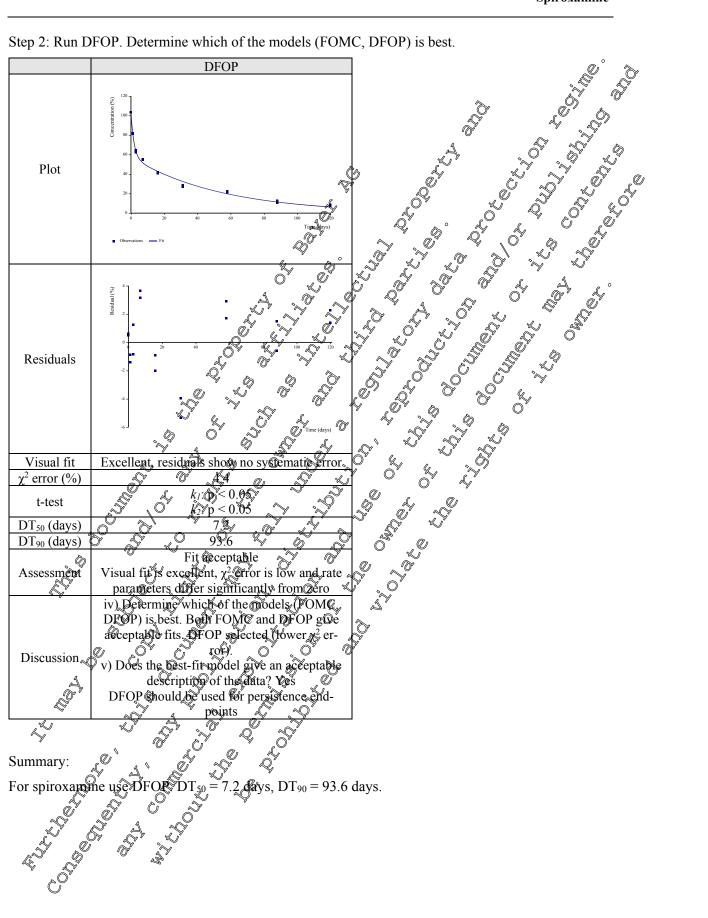
Appendix 3.1.6. Degradation of ¹⁴C-dioxolane labelled spiroxamine, M01, M02 and M03 in Hoefchen am Hohenseh soil (KCA 7.1.1.1/05 (<u>M-303803-01-1</u>))

Appendix 3.1.6.1. Spiroxamine kinetics

Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit?







Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.



Plot Plot		arent best-fit and metabolite SFO. SFO fit for metabolite acceptable?
Residuals Residuals Visual fit Good, residuals abov no systematic error Z'error (%) Ltest DT ₅₀ (days) DT ₅₀ (days) Considered acceptable and rate parameter differs significantly from zero iii)SFO Fit for metabolite deceptable? SFO is considered acceptable and should be used for persistence endpoints Interpret with care – extrapolated beyond experimental defined state of the provide acceptable and should be used for persistence endpoints Interpret with care – extrapolated beyond experimental defined or MOL use DEOP/SFO. DEP = 78.7 days, DT ₅₀ = 261 days. or MOL use DEOP/SFO. DEP = 78.7 days, DT ₅₀ = 261 days. or MOL use DEOP/SFO. DEP = 78.7 days, DT ₅₀ = 261 days. or MOL use DEOP/SFO. DEP = 78.7 days, DT ₅₀ = 261 days. or MOL use DEOP/SFO. DEP = 78.7 days, DT ₅₀ = 261 days.		Parent DFOP, metabolites SFO
ResidualsImage: construct of the second	Plot	$\left(\begin{array}{c} \mathbf{W} \mathbf{U} 1 \\ \mathbf{W} \mathbf{U} 1 \\ \mathbf{U} \mathbf{U} 1 \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \\ \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U} \mathbf{U}$
Visual fitGood, residuals abow no systematic errorGood desiduals show no systematic error χ^2 error (%)10.914.8t-testk: p < 0.05	Residuals	05 0 0 0 0 0 0 10 0 0 0 0 0 0 0 10 0 0 0 0 0 0 10 10 0 0 0 0 0 0 10 10 1 0 0 0 0 0 10 10 1 0 0 0 0 0 10 10 1 0 0 0 0 0 0 10 1 0 0 0 0 0 0 10 1 0 0 0 0 0 0 10 1 0 0 0 0 0 0 10
t-testk: p ≤ 0.05 DT_{50} (days)78.7 DT_{90} (days)78.7 DT_{90} (days)2611AssessmentVisual fit is good, χ^2 error is acceptableVisual fit is good, χ^2 error is acceptableVisual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zeroDiscussionii0 SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpointsDiscussionconsidered acceptable and should be used for persistence endpointsInterpret with care – extrapolated beyond experimental or iod M as not observed in this softummary: M as not observed in this softummary: M and M as not observed in this soft M as not observed in this soft M as not observed in this soft M as M and M as M and M as M and M		Good, residuals show no systematic error Good tesiduals show no systematic error
DT_{50} (days)78.778.8 DT_{90} (days)261'262'AssessmentVisual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zeroFit acceptableAssessmentVisual fit is good, χ^2 error is acceptable? sonsidered acceptable and should be used for persistence endpointsSFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpointsDiscussioniii) SFO fit for metabolite acceptable? persistence endpointsSFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpointsInterpret with care – extrapolated beyond experimental official ummary: or M01 use DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. DT $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.		
D1 ₉₀ (days) 261 262 ¹ Assessment Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero Fit acceptable Assessment Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero Discussion iiii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpoints nterpret with care – extrapolated beyond experimental period persistence endpoints persistence endpoints 103 was not observed in this soft 0 0 0 0 003 was not observed in this soft 0 0 0 0 0 003 was not observed in this soft 0 0 0 0 0 0 003 was not observed in this soft 0 0 0 0 0 0 0 003 was not observed in this soft 0		$\sum_{k=1}^{\infty} \underbrace{(k:p \otimes 0.05)}_{70.7} \underbrace{(k:p \otimes 0.05)}_{70.7} \underbrace{(k:p \otimes 0.05)}_{70.7} \underbrace{(k:p \otimes 0.05)}_{70.0} (k:p \otimes$
Assessment Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero ii Ω SFO fit for metabolite acceptable and should be used for persistence endpoints of persistence endpoints of the second experimental period Λ^2 error is acceptable and should be used for persistence endpoints of the second experimental period Λ^2 error is acceptable and should be used for persistence endpoints of the second experimental period Λ^2 error is acceptable and should be used for persistence endpoints of the second experimental period Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints of Λ^2 error is acceptable and should be used for persistence endpoints		
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Discussion considered acceptable and should be used for persistence endpoints Interpret with care – extrapolated beyond experimental period appendix 3.1.6.3. Metabothe kinetics (N003) 103 was not observed in this soft ummary: or M01 use DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. DT $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.		rate parameter differs significantly from zero rate parameter differs significantly from zero
ummary: or M0Cuse DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. DT $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.		considered acceptable and should be used for providered acceptable and should be used for
ummary: or M0Cuse DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. DT $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.	Interpret with ca	are – extrapolated beyond experimental period
ummary: or M0Cuse DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. DT $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.		
ummary: or M0Cuse DFOP/SFO. DT $_{50}$ = 78.7 days, DT $_{90}$ = 261 days. or M02 use DFOP/SFO. D4 $_{50}$ = 78.8 days, DT $_{90}$ = 262 days.	ppendix 3.1.	6.3. Détabolite kinerics (NO3)
or M02 use $PFOP(SFO, DT_{50} = 78.7 \text{ days}, DT_{90} = 261 \text{ days}.$	103 was not c	bbserved in this soft
103 was not observed in this soil.	or Mussuse I	$DOP/StO. DAPS_0 = 78.7 \text{ days, } D1_{90} = 261 \text{ days.}$
	103 was not a	be of $3 + 0$, $3 + 50 = 78.8$ days, $D + 90 = 262$ days.

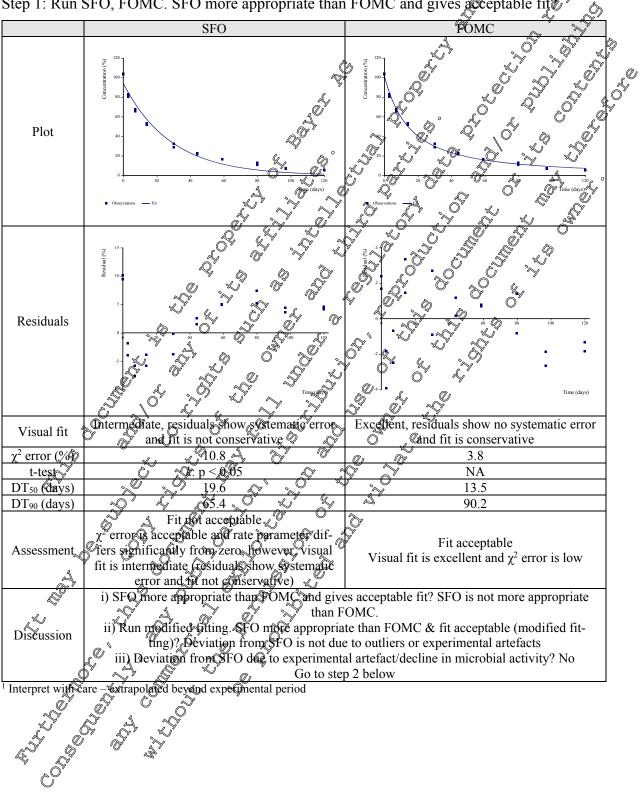
Appendix 3.1.6.2. Metabolite kinetics (M01 and M02)



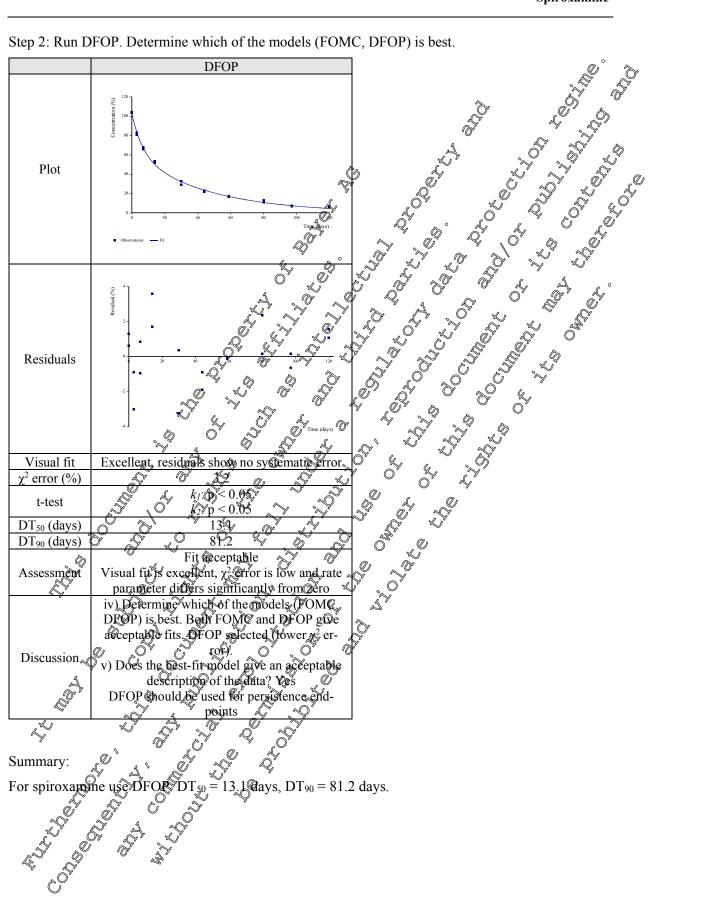
Appendix 3.1.7. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Longwoods soil (KCA 7.1.1.1/06 (M-762349-01-1))

Appendix 3.1.7.1. Spiroxamine kinetics

Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit

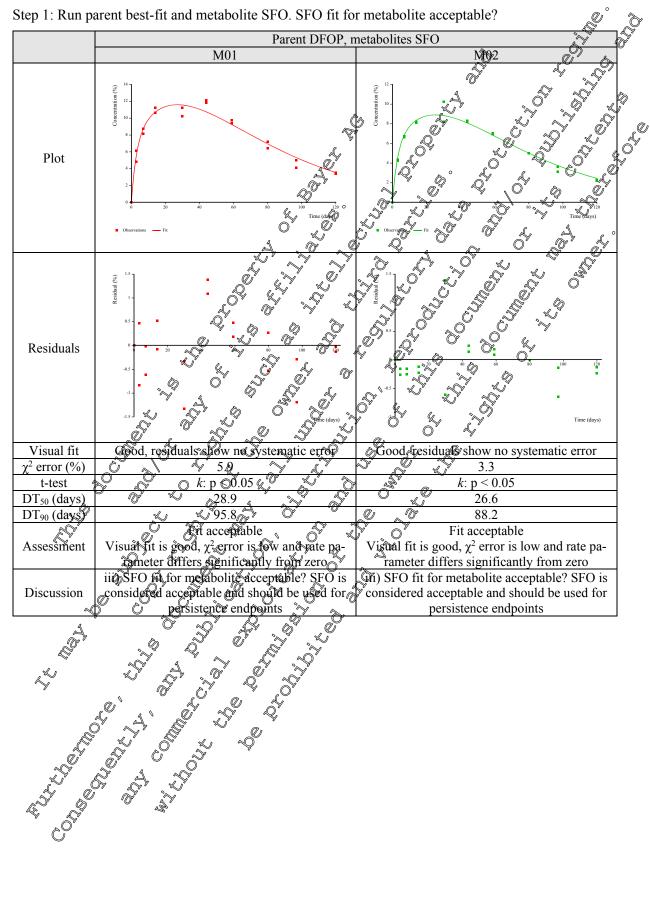






Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.





Appendix 3.1.7.2. Metabolite kinetics (M01 and M02)



Step 1: Run parent best-fit and metabolite SFO. SFO fit for metabolite acceptable?		
	Parent DFOP, n	netabolites SFO
	M03	M06
Plot	Concernations — Fit	netabolites SFO
Residuals		C C C C C C C C C C C C C C C C C C C
Visual fit	Sood, residuals show no systematic error	k intermediate, residuals show no systematic k is $p < 0.05$
$\chi^2 \text{ error (\%)}$		18.5
t-test	$\sum_{k:p} < 0.05$	
DT ₅₀ (days)	L L 16.7 D O	<u>Ø</u> <u>0</u> 49.6
DT90 (ctays)		165
Assessment	Visital fit is good, gerror is low and rate pa-	Fit acceptable Visual fit is good, χ^2 error is slightly high and Gate parameter differs significantly from zero
Diamaian	11) SFG tot for apetabolite acceptable? St O is	7 111) SFO fit for metabolite acceptable? SFO is
Discussion	p considered acceptable and should be used for	considered acceptable and should be used for persistence endpoints
		persistence enupoints
	DEOP/SFO. DT $_{50}$ = 28.9 days. DT $_{90}$ = 95.8 d	
Summary:		
For M01 use I	$DFOP/SFO^{D}T_{a} \stackrel{\sim}{=} 28 \ P days DT_{a} = 95 \ 8 \ d$	avs
For M02 use I	$DPOP/SFO.$ $DT_{20} = 26.6$ days, $DT_{90} = 88.2$ d	avs
For M03 use	$\text{Prop}(51, 27, 50) = 16.7 \text{ days, } \text{DT}_{90} = 55.4 \text{ d}$	avs.
For M06 use I	$DFOP/SFQOT_{50} = 49.6 \text{ davs. } DT_{90} = 165 \text{ davs.}$	IVS.
	$DFOP SFO. DT_{50} = 16.7 days, DT_{90} = 55.4 dDFOP/SFODT_{50} = 49.6 days, DT_{90} = 165 da$	

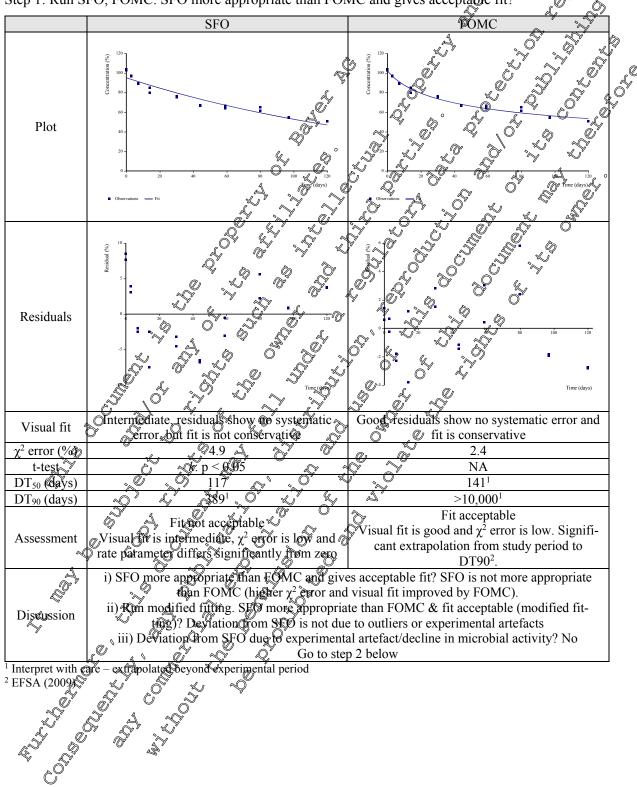
Appendix 3.1.7.3. Metabolite kinetics (M03 and M06)



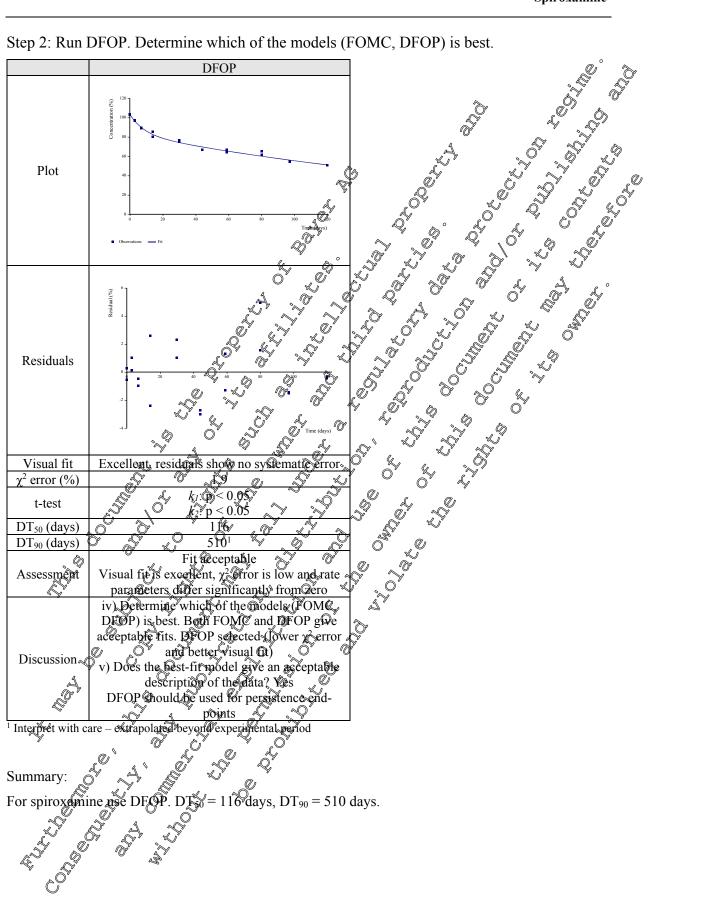
Appendix 3.1.8. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Refesol 02-A soil (KCA 7.1.1.1/06 (<u>M-762349-01-1</u>))



Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit?

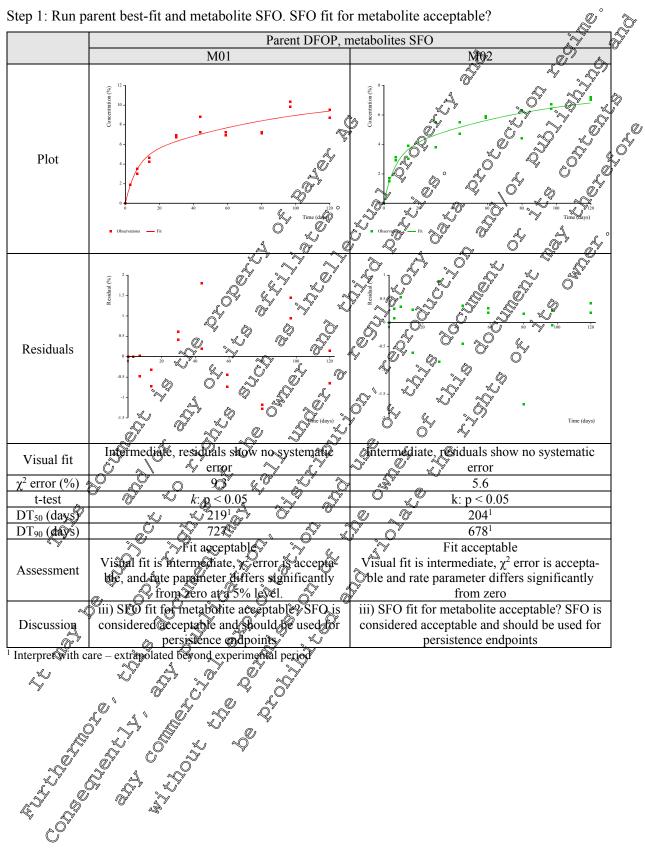






Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.





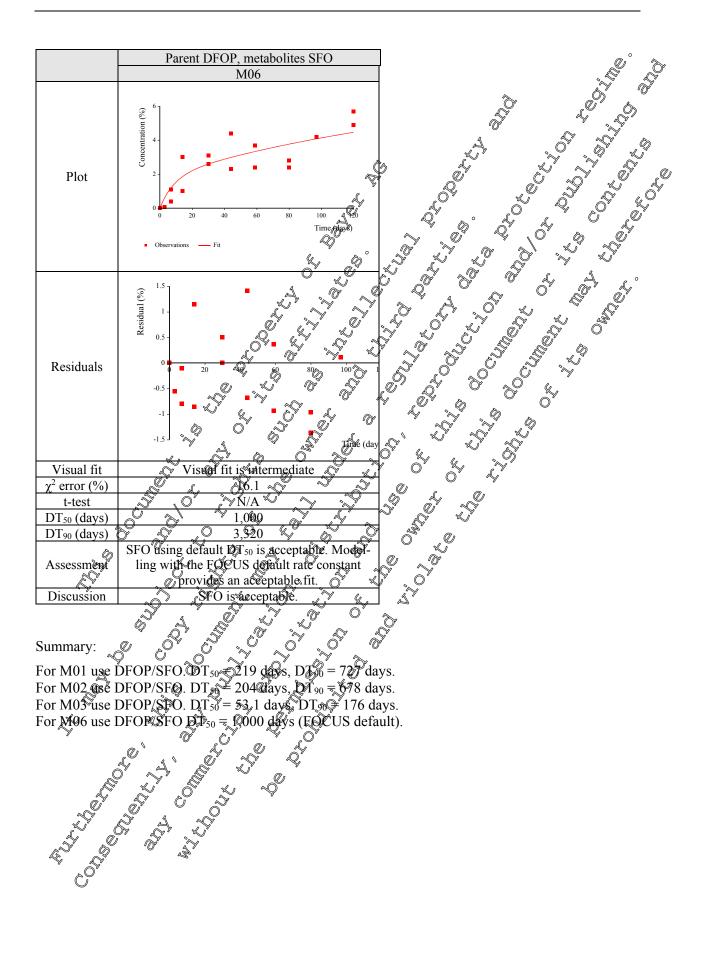
Appendix 3.1.8.2. Metabolite kinetics (M01 and M02)



Plot Plot	tep 1. Kull p	1: Run parent best-fit and metabolite SFO. SFO fit for metabolite acceptable?		
Plot Informediale, residuals show no systematic residuals Informediale, residuals show no systematic Visual fit Informediale, residuals show no systematic reference Informediale, residuals show no systematic <th></th> <th></th> <th></th> <th></th>				
ResidualsImage: state of the st	Plot	Concentration (%)		
Visual fitIntermediate, residuals show no systematic errorAssessmentIntermediate, residuals show no systematic error χ^2 error (%)10216.6t-test $k_{20} < 0.05$ $k_{20} > 0.1$ DT ₅₀ (days) 53.1 20000 DT ₉₀ (days) 176 $210,000$ DT ₉₀ (days) 76 76 AssessmentVisual fit is acceptable, χ^2 error is acceptable and rate parameter differ significantly from zeroFit potentially acceptable Visual fit is intermediate and χ^2 error is only slightly high, however rate parameter does not differ significantly from zero.iii) SFO fit for metabolite acceptable acceptable acceptable acceptable acceptable acceptable? SFO is considered acceptable and should be used for persistence endpoint.Discussion 600 M_{10} 1000 M_{10} 1000 M_{10} 10000 M_{10} 10000 M_{10} 10000 M_{10} 10000 M_{10} 10000 M_{10} 10000 M_{10} 100000 M_{10} 100000 M_{10} 10000000 M_{10} 10000000000 M_{10} $1000000000000000000000000000000000000$	Residuals		C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1 C 1	8
t-test $k.p < 0.05$ $k.p > 0.1$ DT_{50} (days) 53.1 $>10,000$ DT_{90} (days) 176 $>10,000$ Assessment Fit acceptable, γ^2 error is acceptable and rate parameter differs significantly from zero. Fit potentially acceptable Visual fit is intermediate and χ^2 error is only slightly high, however rate parameter does not differ significantly from zero. $iii)$ SF0 fit for metabolite acceptable? Fit potentially acceptable. Based on the study data encompassing 120 days, predicted endpoints of 10,000 days is a drastic extrapolation and is considered unreliablegiven the data. Therefore, fit using a default DT_{50} of 1,000 days performed to demonstrate a good	Visual fit	Intermediate, residuals show no systematic	Antermediate, residuals show no systematic	
D150 (dass) 35.1 10,000 DT90 (dass) 176 >10,000 Assessment Visual fit is acceptable, χ^2 error is acceptable and rate parameter differs significantly from zero. Fit potentially acceptable Visual fit is acceptable, χ^2 error is acceptable and rate parameter differs significantly from zero. Nisual fit is intermediate and χ^2 error is only slightly high, however rate parameter does not differ significantly from zero. iii) SFO fit for metabolite acceptable? iii) SFO fit for metabolite acceptable? iii) SFO fit for metabolite acceptable? Discussion considered acceptable and should be used for persistence endpoints iii) a considered acceptable and should be used for persistence endpoints 10,000 days is a drastic extrapolation and is considered unreliablegiven the data. Therefore, fit using a default DT ₅₀ of 1,000 days performed to demonstrate a good	$\chi^2 \operatorname{error}(\%)$		16.6	
DT ₅₀ (days) 35.1 >10,000 DT ₉₀ (days) 176 >10,000 Assessment Fit acceptable Fit potentially acceptable Visual fit is acceptable, χ^* error is acceptable Visual fit is intermediate and χ^2 error is only Sessment 200 Second fill Visual fit is acceptable, χ^* error is acceptable Visual fit is intermediate and χ^2 error is only Sessment 200 Second fill Visual fit is acceptable, χ^* error is acceptable Not differ significantly from zero. iii) SFO fit for metabolite acceptable SFO is considered acceptable and stould be used for persistence endpoints Second field SFO is considered acceptable and stould be used for persistence endpoints Second field SFO is considered acceptable and stould be used for persistence endpoints Second field SFO is considered acceptable and stould be used for persistence endpoints Second field SFO is considered acceptable and stould be used for persistence endpoints Second field Second field Second field		$\frac{1}{2} \frac{1}{2} \frac{1}$		
Assessment Visual fit is acceptable, χ ² error is acceptable, and rate parameter differs significantly from zero. Fit potentially acceptable Visual fit is acceptable, χ ² error is acceptable and rate parameter differs significantly from zero. Visual fit is intermediate and χ ² error is only slightly high, however rate parameter does not differ significantly from zero. iii) SFO fit for metabolite acceptable? iii) SFO fit for metabolite acceptable? iii) SFO fit for metabolite acceptable? Discussion considered acceptable and stould be used for persistence endpoints points of 10,000 days is a drastic extrapolation and is considered unreliablegiven the data. Therefore, fit using a default DT ₅₀ of 1,000 days performed to demonstrate a good	DT ₅₀ (days)			
Assessment Assessment Assessment Nisual fit is acceptable, χ^2 error is acceptable and rate parameter differs significantly from zero iii) SFO fit for metabolite acceptable of the study iii) SFO fit for metabolite acceptable of the study considered acceptable and should be used for persistence endpoints of 10,000 days is a drastic extrapola- tion and is considered unreliablegiven the data. Therefore, fit using a default DT ₅₀ of 1,000 days performed to demonstrate a good	DT90 (ctays)	<u> </u>		
biscussion biscus	44	Vistal fit is acceptable, χ^2 error is acceptable and rate parameter differs significantly from	Oslightly high, however rate parameter does not differ significantly from zero.	
Interpret with care - Strapolated beyond experimental period	Ş	considered aeceptable and should be used for	potentially acceptable. Based on the study data encompassing 120 days, predicted end- points of 10,000 days is a drastic extrapola- tion and is considered unreliablegiven the data. Therefore, fit using a default DT ₅₀ of 1,000 days performed to demonstrate a good fit to study data and establish a reasonable	

Appendix 3.1.8.3. Metabolite kinetics (M03 and M06)



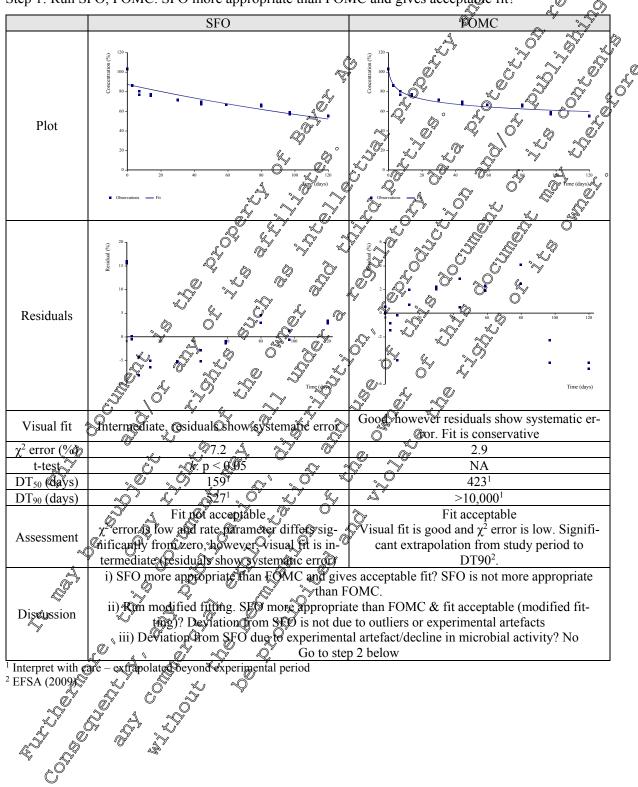




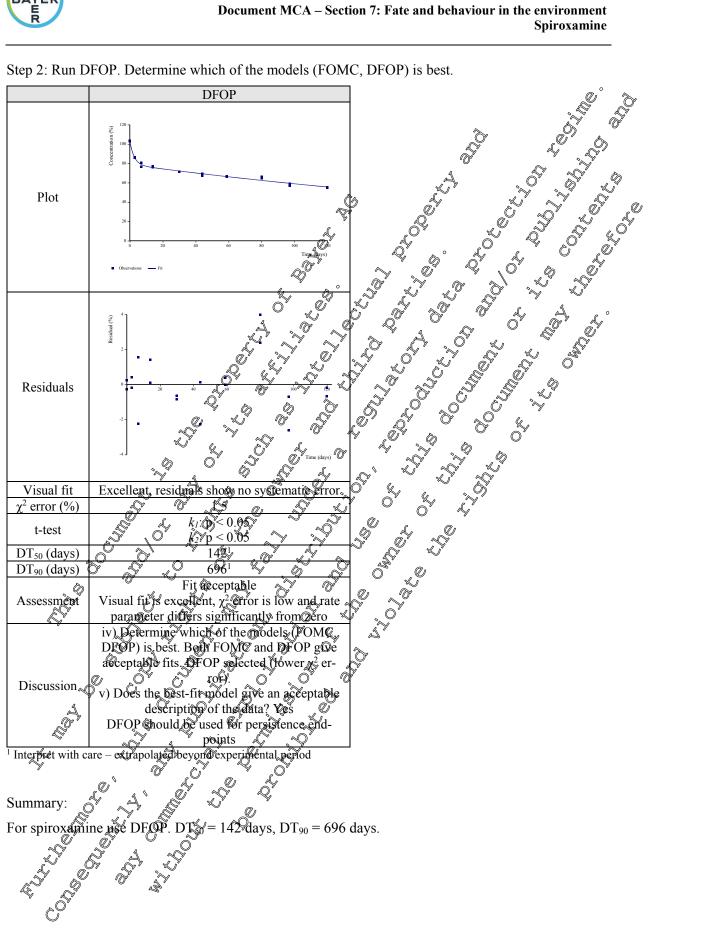
Appendix 3.1.9. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Refesol 03-G soil (KCA 7.1.1.1/06 (<u>M-762349-01-1</u>))



Step 1: Run SFO, FOMC. SFO more appropriate than FOMC and gives acceptable fit?

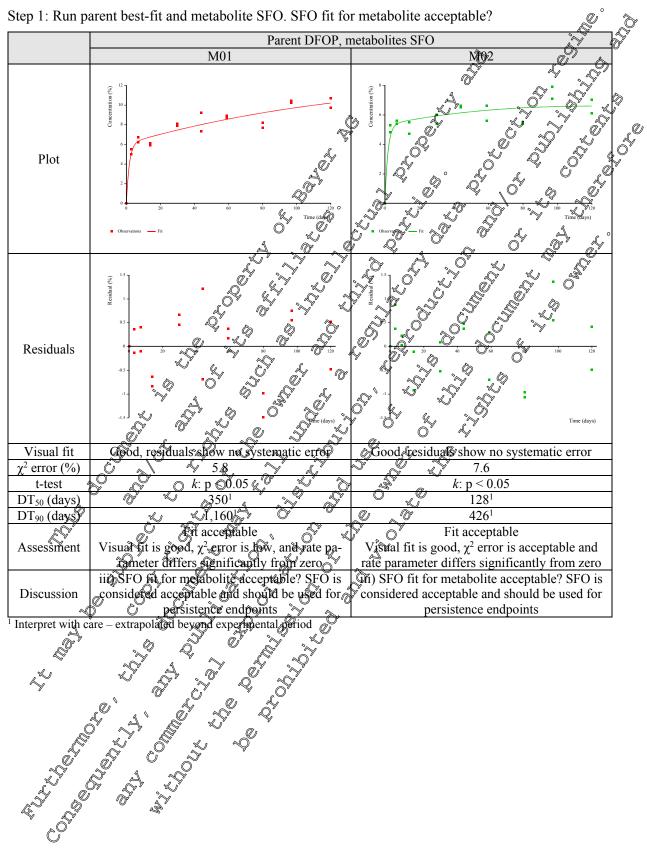






Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.





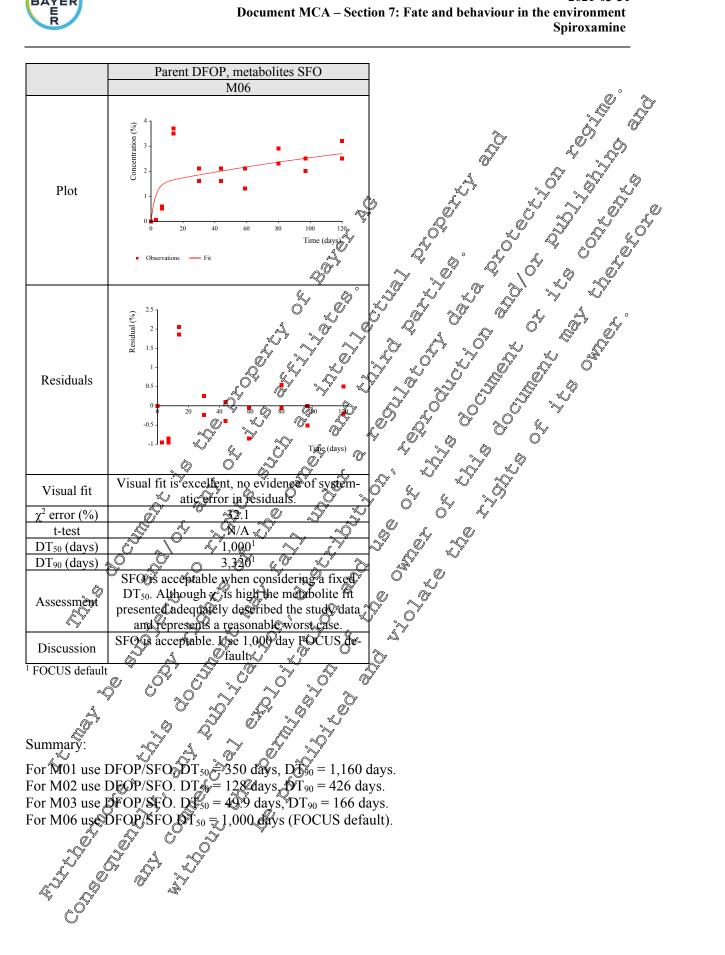
Appendix 3.1.9.2. Metabolite kinetics (M01 and M02)



Step 1: Run p	arent best-fit and metabolite SFO. SFO fit for metabolite acceptable?
	Parent DFOP, metabolites SFO
Plot	$\left(\begin{array}{c} 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ $
Residuals	Observations — Fit
Visual fit	Good, residuals show no systematic error
$\chi^2 \operatorname{error}(\%)$	
t-test	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
DT ₅₀ (days)	
DT ₉₀ (tays) Assessment	Fit acceptable Visual fit is good χ^2 error is high and rate parameter defines significantly from zero Fit not acceptable Visual fit is intermediate, χ^2 error is high and trate parameter defines significantly from zero from zero
Discussion	 iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpoints iii) SFO fit for metabolite acceptable? SFO is not considered acceptable. Use of DFOP and FOMC do not improve the fit and not possible to fit to decline phase. Therefore, fit using a default DT₅₀ of 1,000 days performed to demonstrate a reasonable worst case
	are extrapolated by ond experimental period

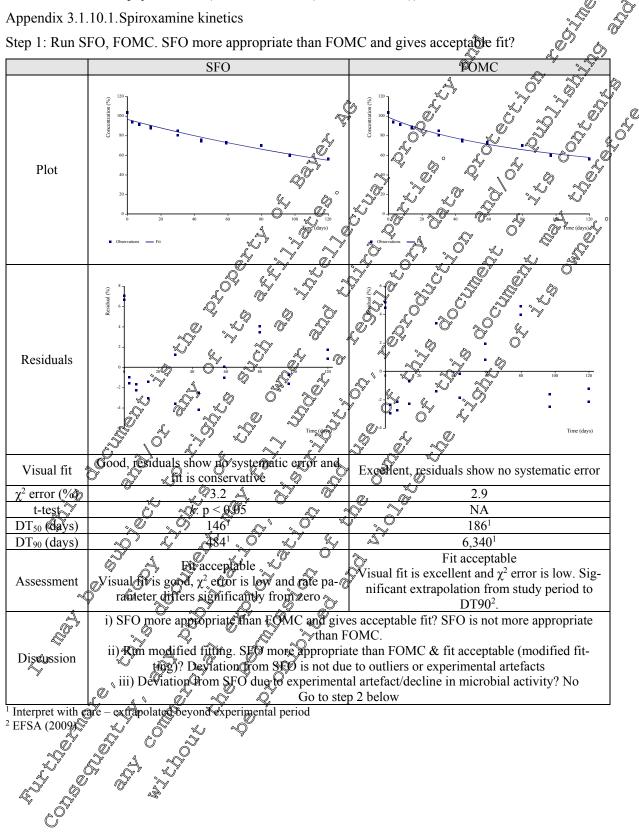
Appendix 3.1.9.3. Metabolite kinetics (M03 and M06)



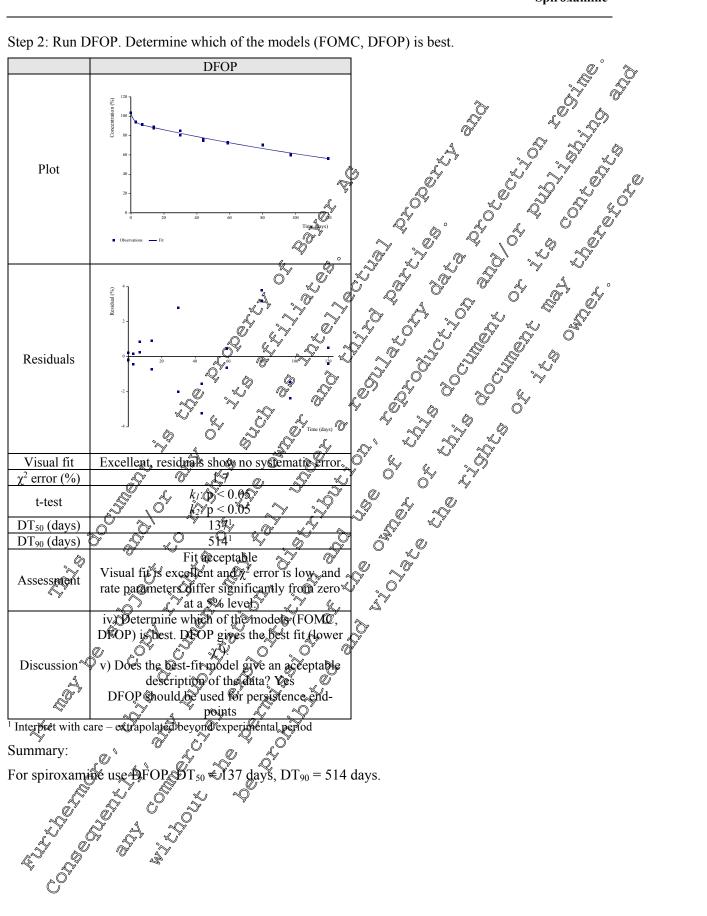




Appendix 3.1.10. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Speyer 6S soil (KCA 7.1.1.1/06 (<u>M-762349-01-1</u>))

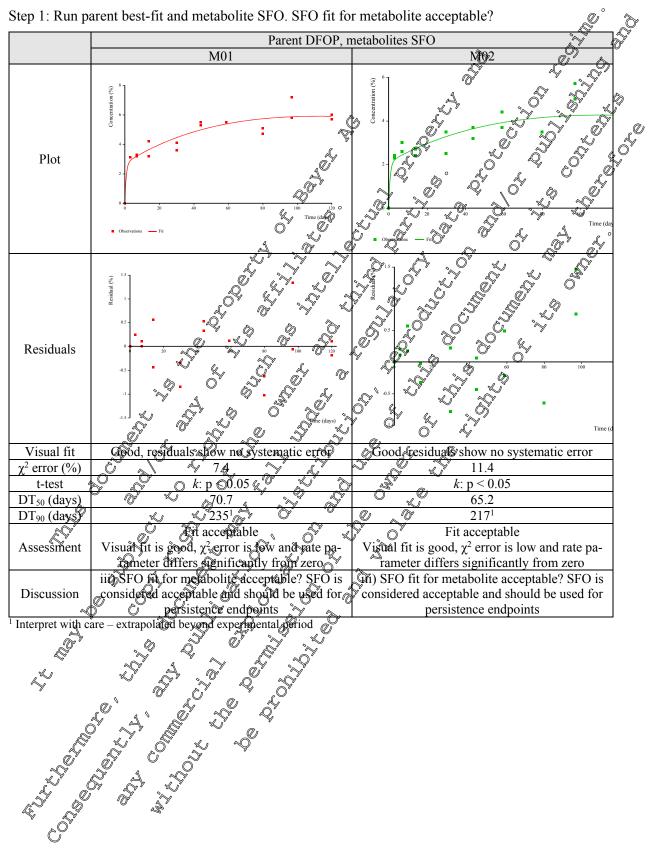






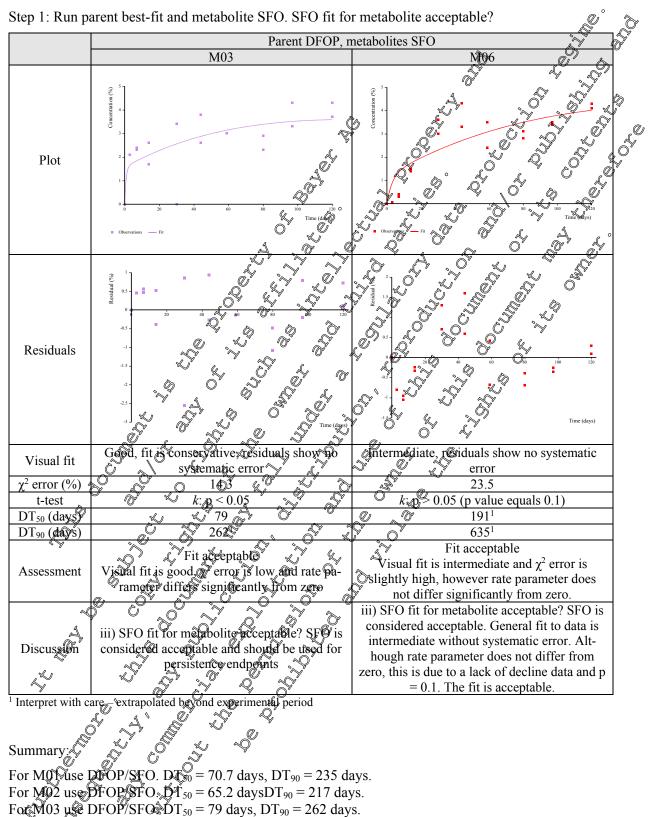
Step 2: Run DFOP. Determine which of the models (FOMC, DFOP) is best.





Appendix 3.1.10.2. Metabolite kinetics (M01 and M02)





Appendix 3.1.10.3. Metabolite kinetics (M03 and M06)

For M060 se DFOP/SFO $DT_{50} = 191$ days, DT90 = 635 days

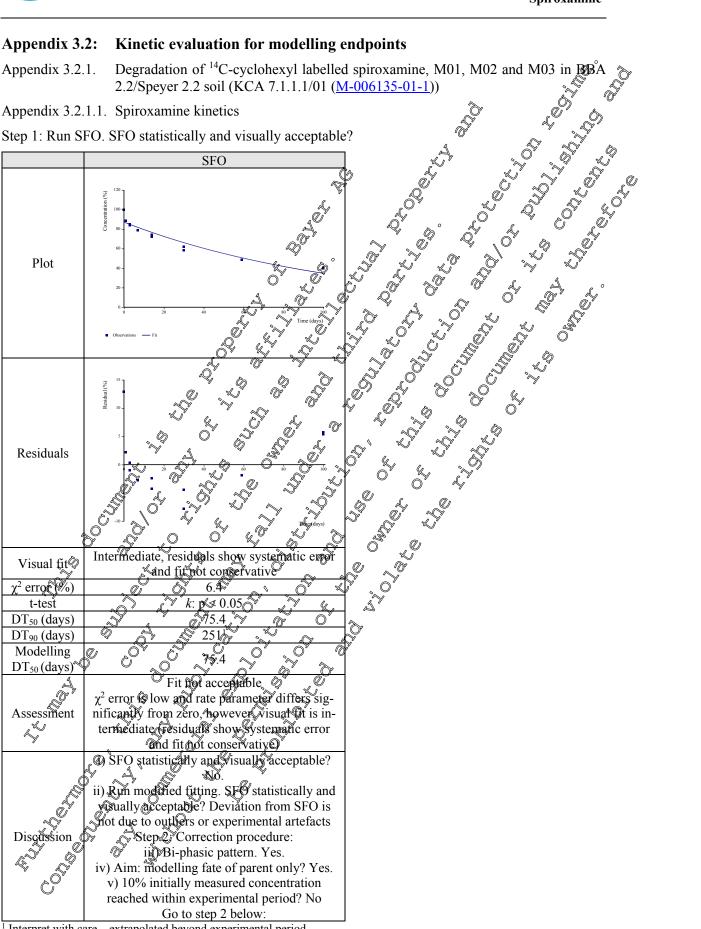


Appendix 3.2: Kinetic evaluation for modelling endpoints

Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in RBÅ Appendix 3.2.1. 2.2/Speyer 2.2 soil (KCA 7.1.1.1/01 (M-006135-01-1))

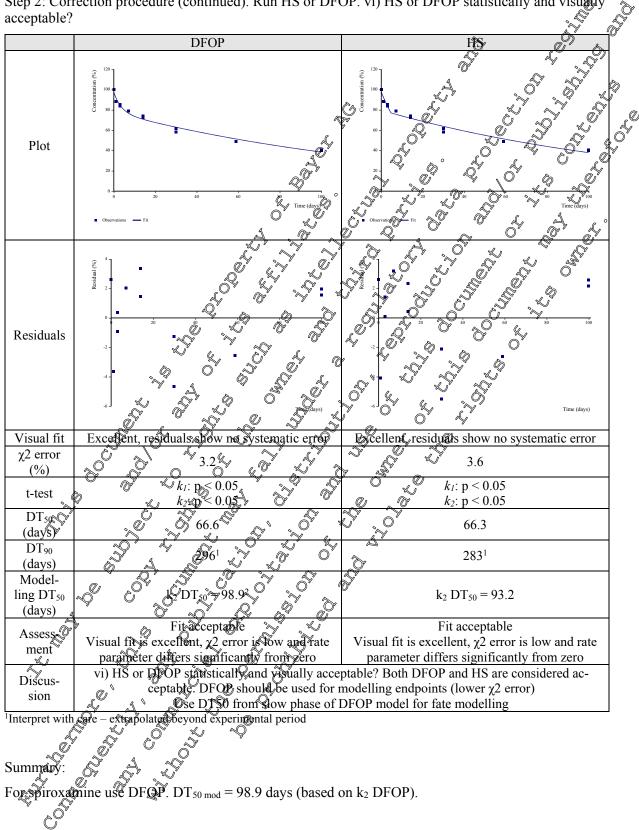
Appendix 3.2.1.1. Spiroxamine kinetics

Step 1: Run SFO. SFO statistically and visually acceptable?



¹ Interpret with care – extrapolated beyond experimental period





Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually

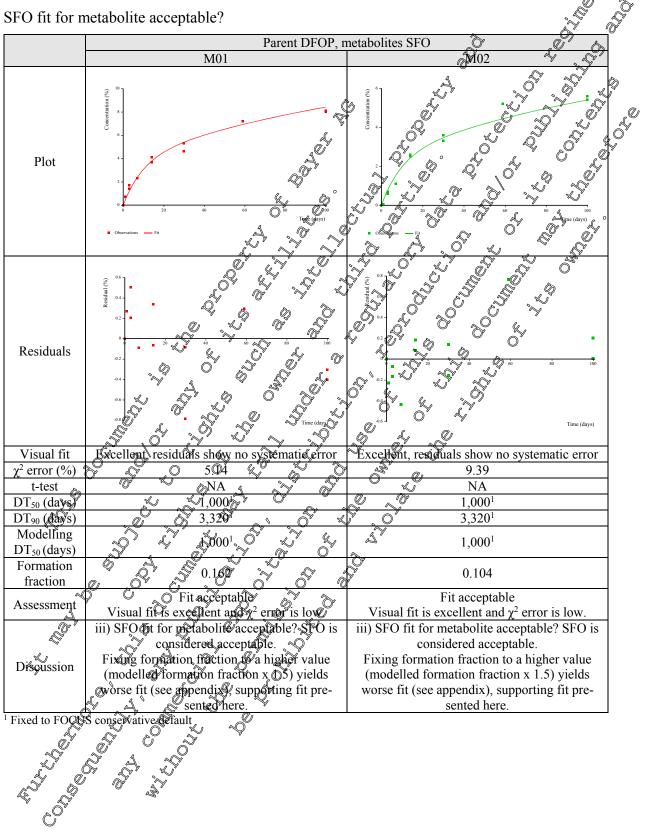


• •	Step 1: Run parent and metabolites all SFO. SFO fit for metabolite acceptable?	
	Parent DFOP, n	netabolites SFO
	M01	<u></u>
Plot	Constraints - Fit	etabolite acceptable?
Residuals	Conversions Fit	Time (days)
Visual fit	Excellent, residuals show to systematic, effor	Evallant racidials show no systematic arror
χ^2 error (%)	() × 56 × 1	$\frac{6}{2}$ 9.5 $\frac{k: p > 0.1}{2}$ >10,000 ¹
t-test	$ \begin{array}{c} $	<i>k</i> : p > 0.1
DT ₅₀ (days)	555 ¹ × × 555 ¹ × × × × ×	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$
DT ₉₀ (days)	<u> </u>	<i>©</i> ≥10,000 ¹
Modelturg DT ₅₀ (days)	, , , , , , , , , , , , , , , , , , ,	$ \begin{array}{c c} & > 10,000 \\ \hline & & > 10,000^1 \\ \hline & & > 10,000^1 \\ \hline & & > 10,000^1 \\ \hline & & \\ \end{array} $
Formation fraction		⊘ 0.104
Inaction	$\frac{2^{3}}{\sqrt{2}} \xrightarrow{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt{2} \sqrt$	0.104 Fit not acceptable
~		Visual fit is excellent and χ^2 error is low,
Assessment	however, rate parameter does not differ sig-	however, rate parameter does not differ sig-
	nificantly from zero	nificantly from zero
Ű,	iii) SFO/iit for metabolite acceptable? SFO is	iii) SFO fit for metabolite acceptable? SFO is
, K	not considered acceptable. Dierefore, DFOP	not considered acceptable. Therefore, DFOP
\sim	or FOMC abould be assessed. However, these	or FOMC should be assessed. However, these
	models are not approprate for metabolites	models are not appropriate for metabolites
	which are formed gradually. Thereafter, de-	which are formed gradually. Thereafter, de-
Discussion	cline after now should be a sessed. However,	cline after max should be assessed. However,
S.	this was not possible as there is limited de-	this was not possible as there is limited de-
	Wine data to clorily establish the dissipation	cline data to clearly establish the dissipation
	$\sum_{n=1}^{\infty}$ pattern. Therefore, use of default DT ₅₀ and	pattern. Therefore, use of default DT_{50} and
	modeled formation fraction of 0.162 investi-	modelled formation fraction of 0.104 investi- gated.
		ogied

Appendix 3.2.1.2. Metabolite kinetics (M01 and M02)



Step 2: Run parent DFOP and metabolite SFO with DT_{50} of 1,000 days and modelled formation fractions (conservative estimate).





Appendix 3.2.1.3. Metabolite kinetics (M03) Step 1: Run parent and metabolites all SFO. SFO fit for metabolite acceptable? Parent DFOP, metabolites SFO M03 Concentration Plot Residual (%) Residuals Office and the second s Good, residuals show no systematic error Visual fit χ^2 error (%) 18 <u>k: p</u>©ð.05 t-test DT₅₀ (days) 29.8 DT₉₀ (days) 98.8 Model 29 8 DT50 (days) Formation Visual fis good, χ^2 error is slightly high and χ^2 rate parameter differs significantly to the state of 0.125/ fraction Assessment iii) SFO fittor metabolite asceptable? SFO is Discussion considered acceptable and should be used for modelling endpoints Summary:

Summary: For M01 use BFOP/SFO (using conservative parameters). $DT_{50 \text{ mod}} = 1,000$ (conservative default), f.f. from parent $\neq 0.162$ For M02 use DFOP/SFO (using conservative parameters). $DT_{50 \text{ mod}} = 1,000$ (conservative default), f.f. from parent = 0.162For M03 use DFOP/SFO, $BT_{50 \text{ mod}} = 29.8$ days, f.f. from parent = 0.125.

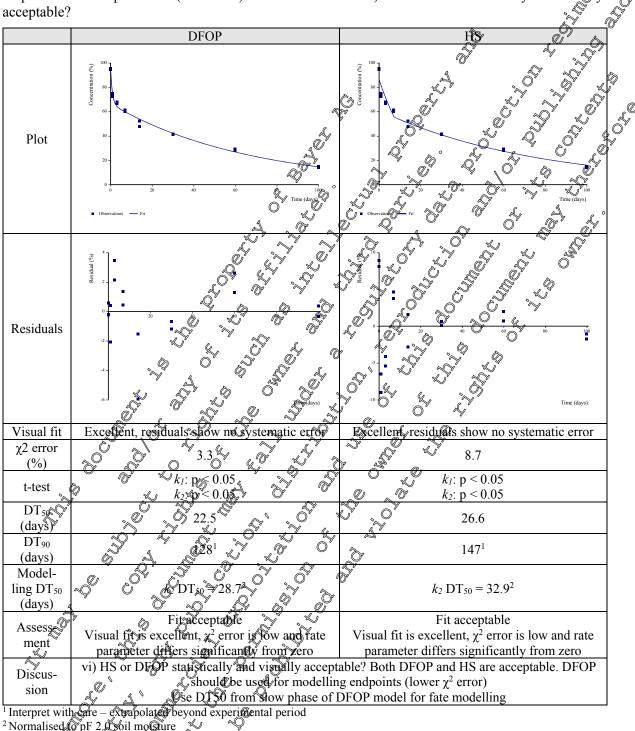


in A contraction of the traction of the tract Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Appendix 3.2.2. Laacherhof soil (KCA 7.1.1.1/02 (M-006141-01-1)) Appendix 3.2.2.1. Spiroxamine kinetics Step 1: Run SFO. SFO statistically and visually acceptable? SFO Plot tesidual (%) Residuals Ś Ontermediate, residuals show sortematic error Visual fit and fit not conservative χ^2 error (%) 🕅 1.9 🗳 t-test DT₅₀ (days) DT₉₀ (days) Modelling 21 DT₅₀ (days) Êit not acceptable χ^2 error is acceptable and rate parameter diff fers significantly from zero, however, visual Assessment fit is intermediate (residuals show systematic ė Serror and fit not conservative) i) SFO statistically and visually acceptable? Ň Run modified fitting SFO solistically and visually acceptable? Deviation from SFO is not due to Sutliers or experimental artefacts Step 2: Correction procedure: Discussion iii) Riphasic pattern. Yes. Aim: modelling fate of parent only? Yes. $\sqrt{910\%}$ initially measured concentration reached within experimental period? No Go to step 2 below:

¹Interpret with care – extrapolated beyond experimental period

² Normalised to pF 2.0 soil moisture





Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually

Ô

Summary:

For spirovamine use DFOP. $DT_{50 \text{ mod}} = 28.7$ days (based on k_2 DFOP of 45.4 normalised to pF 2.0).

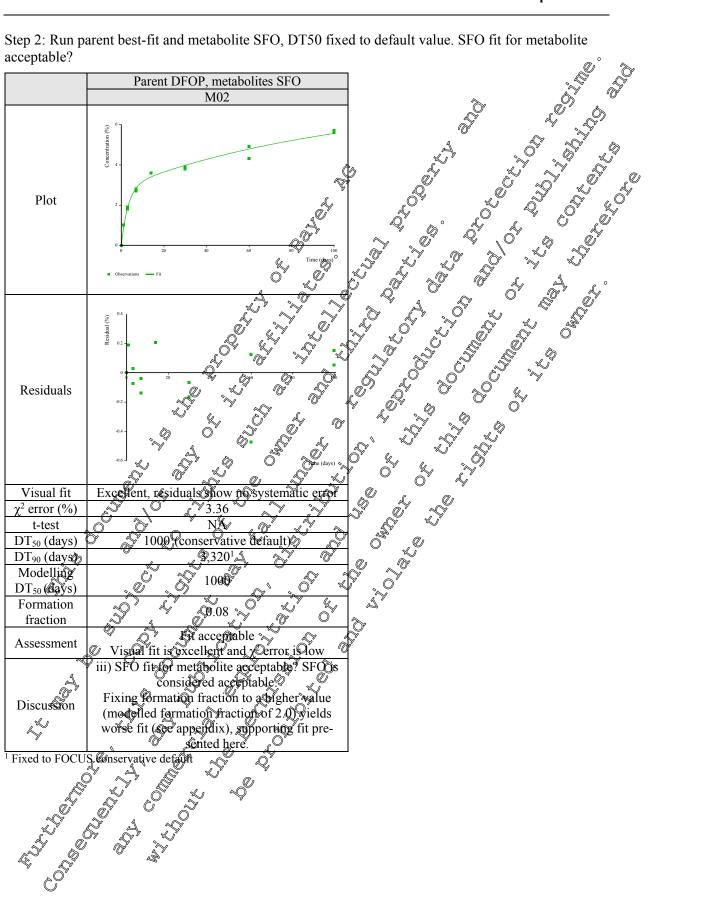


Plot Plot		Doront DEOD	netabolites SEO
Visual fit Excellent, residuals show no systematic error 2 error (%) 62 1-test 8. p 0.05 (model) DT ₅₀ (days) 167 0 (days) 167 0 (days) 105.5 ² 0 (days) 105.5 ² 0 (fays) 0.137 0 (fays) 0.137 0 (fays) 0.137 0 (fit is excellent and χ^2 error is low, however, rate parameter does not differ significantly, from zero 0 (fit or metabolite acceptable) Visual fit is pool, fit for pretabolite acceptable? SFO is not considered acceptable? SFO is nodel ling endpoints 0 (fit or metabolite acceptable? SFO is nodel ling endpoints in model led formation fraction of 0.08 as a realistic worst case investigated.		M01	Mineration Mineration Contraction of the second sec
Visual fit Excellent, residuals show no systematic error 2 error (%) 62 1-test 8. p 0.05 (model) DT ₅₀ (days) 167 0 (days) 167 0 (days) 105.5 ² 0 (days) 105.5 ² 0 (fays) 0.137 0 (fays) 0.137 0 (fays) 0.137 0 (fit is excellent and χ^2 error is low, however, rate parameter does not differ significantly, from zero 0 (fit or metabolite acceptable) Visual fit is pool, fit for pretabolite acceptable? SFO is not considered acceptable? SFO is nodel ling endpoints 0 (fit or metabolite acceptable? SFO is nodel ling endpoints in model led formation fraction of 0.08 as a realistic worst case investigated.	Plot	() () () () () () () () () ()	
Visual fitExcellent, residerls show no systematic error $\frac{2}{2}$ error (%)62 $\frac{2}{2}$ error (%)62 $\frac{2}{1}$ test $k: p \ge 0.1$ OT_{50} (days) 167^1 OT_{90} (days) 167^1 OT_{90} (days) 105.5^2 DT_{50} (days) 105.5^2 DT_{50} (days) 105.5^2 OT_{50} (days) 105.5^2 OT_{50} (days) 105.5^2 OT_{50} (days) 0.137 $O.08$ Formation fraction 0.137 $O.08$ T_{50} (days) OT_{50} (days)<	Residuals		Time (days)
D1s0 (days) 10 101 4,880° DTs0 (days) 5541 >10,0001 Modelling 105.5 n.a. OTs0 (days) 0.08 Formation 0.137 0.08 Frit acceptable Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero iii) SFO fit for metabolite acceptable? SFO is not considered acceptable? SFO is considered acceptable? SFO is considered acceptable? SFO is modelling endpoints Discussion Considered acceptable and should be used for modelling endpoints Considered acceptable Thereafter, decline after max should be assessed. However, these models will not improve the fit Thereafter, decline after max should be assessed. However, this was not possible as there is limited decline data to clearly establish the dissipation pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.	Visual fit	Excellent, residuals show to systematic effor	Excellent, residuals show no systematic error
D1s0 (days) 10 101 4,880° DTs0 (days) 5541 >10,0001 Modelling 105.5 n.a. OTs0 (days) 0.08 Formation 0.137 0.08 Frit acceptable Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero iii) SFO fit for metabolite acceptable? SFO is not considered acceptable? SFO is considered acceptable? SFO is considered acceptable? SFO is modelling endpoints Discussion Considered acceptable and should be used for modelling endpoints Considered acceptable Thereafter, decline after max should be assessed. However, these models will not improve the fit Thereafter, decline after max should be assessed. However, this was not possible as there is limited decline data to clearly establish the dissipation pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.	$\chi^2 \operatorname{error}(\%)$	<u> </u>	
D1s0 (days) 10 101 4,880° DTs0 (days) 5541 >10,0001 Modelling 105.5 n.a. OTs0 (days) 0.08 Formation 0.137 0.08 Frit acceptable Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero Fit not acceptable Visual fit is cood, perror is low and rate nor rameter differs significantly from zero iii) SFO fit for metabolite acceptable? SFO is not considered acceptable? SFO is considered acceptable? SFO is considered acceptable? SFO is modelling endpoints Discussion Considered acceptable and should be used for modelling endpoints Considered acceptable Thereafter, decline after max should be assessed. However, these models will not improve the fit Thereafter, decline after max should be assessed. However, this was not possible as there is limited decline data to clearly establish the dissipation pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.		k: p ⊙0.05 (k ¹)	k: p > 0.1
 In the intermediate of the interm			4,860'
 In the intermediate of the interm		<u> </u>	
 In the intermediate of the interm		, O 105.5 ² , O K	n.a.
 In the intermediate of the interm			
 In (b) of the fit interation ite deceptable. Si of is not considered acceptable. Therefore, DFOP or FOMC should be assessed. However, these models will not improve the fit Thereafter, decline after max should be assessed. However, this was not possible as there is limited decline data to clearly establish the dissipation pattern. Therefore, use of default DT₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated. 		2 (0.137) O	0.08
 In the intermediate of the interm	nuction	A D D D D	Fit not acceptable
 In the intermediate of the interm		CFit acceptable	Visual fit is excellent and χ^2 error is low.
 In the intermediate of the interm	Assessment	v isual fit is good, y error is low and rate in	
 In the intermediate of the interm	<i>A</i>		
or FOMC should be assessed. However, these models will not improve the fit Thereafter, decline after max should be assessed. How- ever, this was not possible as there is limited decline data to clearly establish the dissipa- tion pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.			
Discussion SFO fit for petabolite acceptable? SFO is modelling entpoints modelling entpoints modelling entpoints are investigated.	s de la		
decline after max should be assessed. How- ever, this was not possible as there is limited decline data to clearly establish the dissipa- tion pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.	۳.λ		
Discussion considered acceptable and should be used for modelling endpoints findelling endpoints are acceptable and should be used for the construction of the constru		(M) SFO fit for metabolite accontable? SFO is	
decline data to clearly establish the dissipa- tion pattern. Therefore, use of default DT ₅₀ and modelled formation fraction of 0.08 as a realistic worst case investigated.	Discussion @	considered accentable and should be used for	
realistic worst case investigated.	L.	Anodelling endpoints	
realistic worst case investigated.	a di seconda di second		
realistic worst case investigated.	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
	Å A	A CAN A CAN	
	xerbret will ca	are – extrapolated beyond experimental period	Toundue worst cube investigated.

Appendix 3.2.2.2. Metabolite kinetics (M01 and M02)

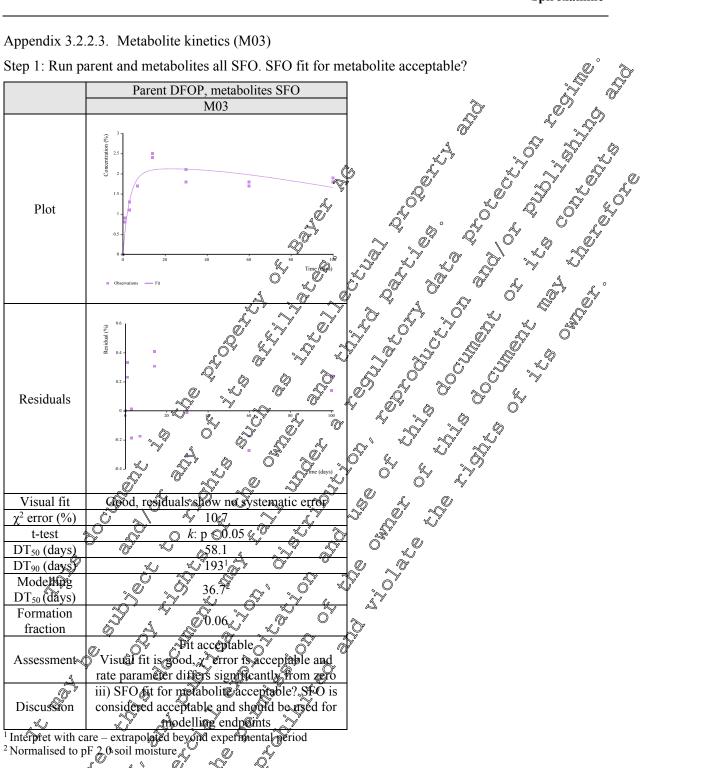


Step 2: Run parent best-fit and metabolite SFO, DT50 fixed to default value. SFO fit for metabolite acceptable?





Appendix 3.2.2.3. Metabolite kinetics (M03)



Step 1: Run parent and metabolites all SFO. SFO fit for metabolite acceptable?

Summary:

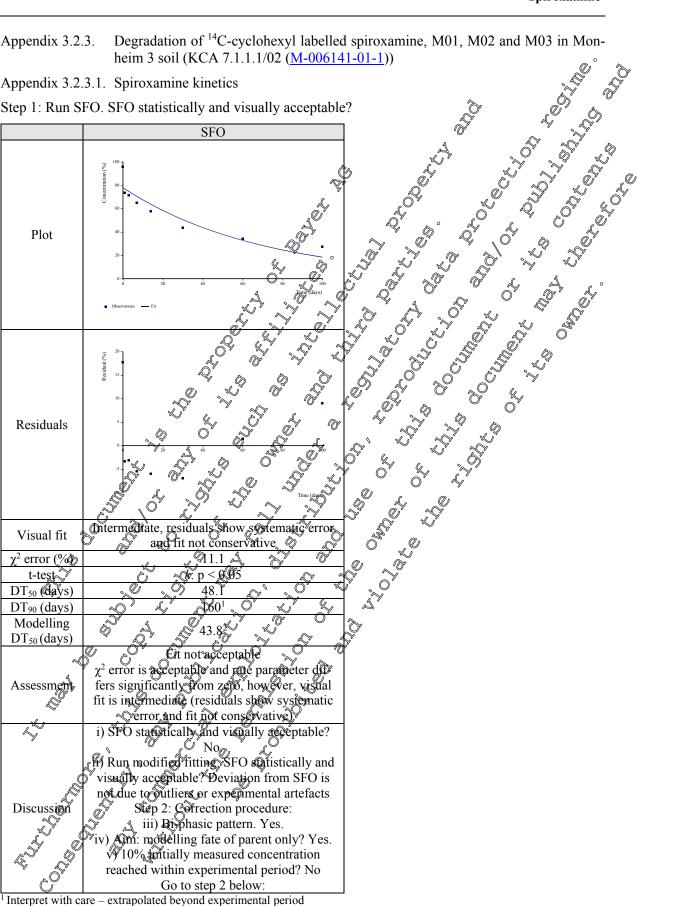
For MO use DDOP/SFO DTG mod = 105.5 (from a non-normalised DT50 of 167 days), f.f. from parent = 0.137 For M02 use DFOP/SFO using conservative parameters). $DT_{50 \text{ mod}} = 1000 \text{ days}, \text{ f.f.}_{\text{from parent}} = 0.08.$ For M@Spuse DFOP/SFO. DT_{50mod} = 36.7 days (from a non-normalised DT50 of 58.1 days), f.f._{from parent} = 0.06.



Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Mon-Appendix 3.2.3. heim 3 soil (KCA 7.1.1.1/02 (M-006141-01-1))

Appendix 3.2.3.1. Spiroxamine kinetics

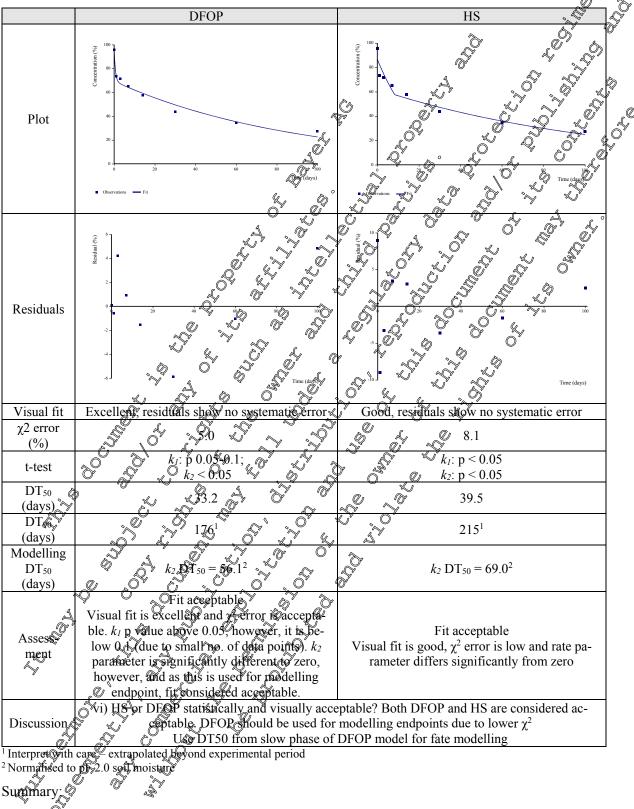
Step 1: Run SFO. SFO statistically and visually acceptable?



² Normalised to pF 2.0 soil moisture



Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually acceptable?



For spiroxamine use DFOP. $DT_{50 \text{ mod}} = 56.1$ days (based on k₂ DFOP 61.7 days normalised to pF 2.0).



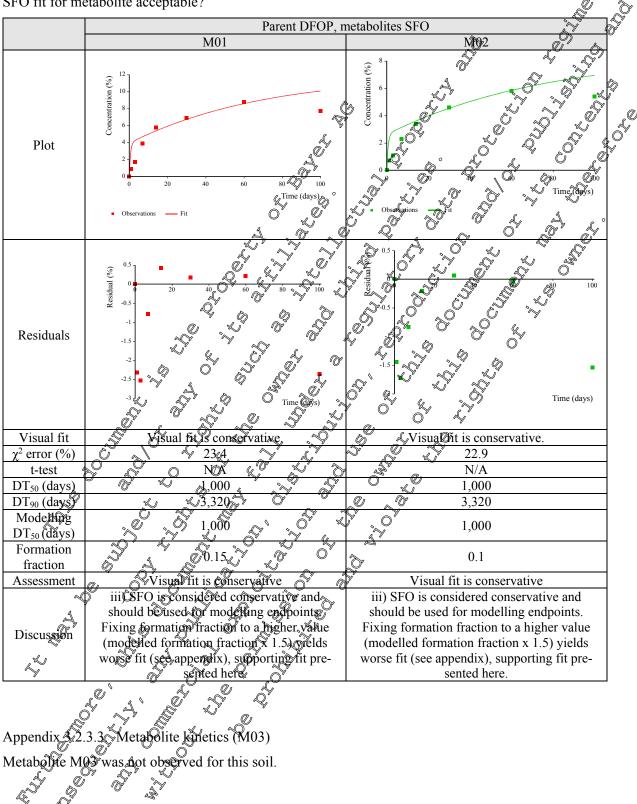
tep 1: Run pa	arent and metabolites all SFO. SFO fit for me	etabolite acceptable?
	Parent DFOP, n	netabolites SFO
	M01	MO2
Plot	Countrations - Fie	etabolite acceptable?
Residuals	1 − 20	y y y y y y y y y y y y y y y y y y y
Visual fit	error	k: p > 0.1
χ^2 error (%)	$\frac{201}{6} \frac{201}{10} \frac{100}{10} \frac{100}{10}$	19.4
t-test		$ \begin{array}{c} 17.4 \\ \hline \\ \hline$
DT ₅₀ (days)		
DT ₉₀ (days)		>10,0001
Modelling DT ₅₀ (days)	\sim	ے × × × × × × × × × × × × × × × × × × ×
Formation		0.001
fraction		0.081
Â		Fit not acceptable
Assessment	Visual fit ionternodiate, Perror shigh and	Visual fit is intermediate, χ^2 error is high and
	rate parameter does not differ significantly	rate parameter does not differ significantly
Ŵ	from zero	from zero
	iii) SFO fit for metabolite a ceptable? SFO is	iii) SFO fit for metabolite acceptable?. SFO is
¥	not considered acceptable. Therefore, DFOP	not considered acceptable. Therefore, DFOP
	or FOMC should be assessed. However, these	or FOMC should be assessed. However, these
C	models will not improve the fir. Thereafter,	models will not improve the fit Thereafter,
Discussion	decline after max should be assessed. How- ever, this was not possible as there is limited	decline after max should be assessed. How- ever, this was not possible as there is limited
Ő	Decline data toolearly establish the dissipa-	decline data to clearly establish the dissipa-
Ţ,	\gtrsim tion pattern, Therefore, use of default DT ₅₀	tion pattern. Therefore, use of default DT_{50}
Discussion	and an increased formation fraction of 0.15	and formation fraction of 0.1 inestigated as a
LAN Q	investigated as a realistic worst case.	realistic worst case.
nterpret with c	are – extrapolated beyond experimental period	

Appendix 3.2.3.2. Metabolite kinetics (M01 and M02)

² Normalised to pF 2.0 soil moisture



Step 2: Case-by-case decision (alternative – but conservative – estimates).



SFO fit for metabolite acceptable?

Summarg

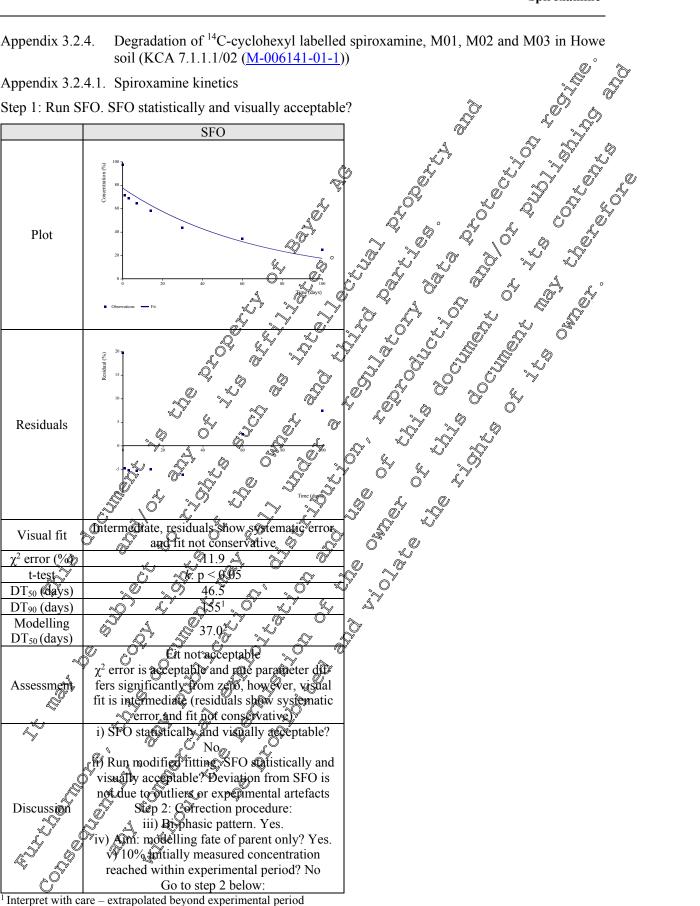
For M01 use DFOP/SFO (using conservative parameters). $DT_{50 \text{ mod}} = 1,000 \text{ days}$, f.f._{from parent} = 0.15. For M02 use DFOP/SFO (using conservative parameters). $DT_{50 \text{ mod}} = 1,000 \text{ days}$, f.f._{from parent} = 0.1. M03 was not observed for this soil.



Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Howe Appendix 3.2.4. soil (KCA 7.1.1.1/02 (M-006141-01-1))



Step 1: Run SFO. SFO statistically and visually acceptable?



² Normalised to pF 2.0 soil moisture



	DFOP	Hor with the statistically and visually
Plot	Observations - Fit	
Residuals		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Visual fit	Excellent, residuals show no systematic error	Bacellent, residuats show no systematic error
χ2 error (%)	Excellent, residuals show no systematic erfor 3.8 k_1 : p = 0.05-0.1 k_2 sp < 0.05	Excellent, residuals show no systematic error 9.7 k_1 : p < 0.05 k_2 = k_1 : p < 0.05
	$\begin{array}{c} 3.8 \times 0^{-1} \times 7^{-1} \\ \hline & & & & & & & \\ \hline & & & & & & \\ \hline & & & &$	k_{l} k_{l} $p < 0.05$
t-test	$k_{2} \neq 0.0 $	$k_1 \cdot p < 0.05$ $k_2 \cdot p < 0.05$
DT ₅₀ (days)		
DT ₉₀ (days)		ک به 197 ¹
	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $	$k_2 DT_{50} = 54.3^2$
<i>(</i>	Eitercentable w	Fit acceptable
Assess	Visual fit is excellent, χ^2 error is fow and rate	Visual fit is excellent, χ^2 error is low and rate
ment	parameters affer significantly from zero	parameters differ significantly from zero
Discus-		ptable? Both DFOP and HS are considered ac-
sion	ceptable. DFOP should be used for the source of I s	modelling endpoints (lower χ^2 error)
		Dr Or model for fate modelling

Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually 🔊

Summary: For spiroxardine use DFQP, $DT_{50 \text{ mod}} = 47.0$ days (based on k₂ DFOP 59.5 days normalised to pF 2.0).



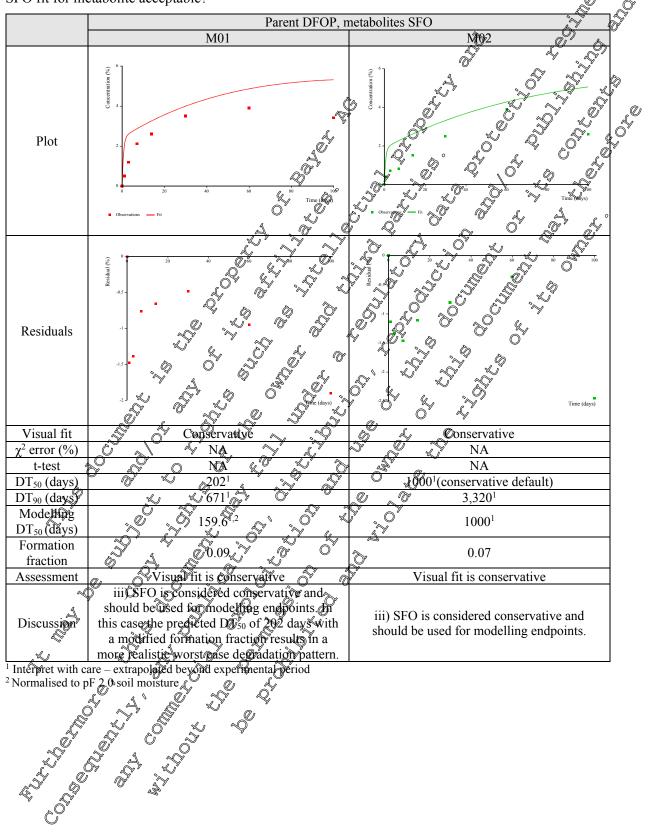
Step 1: Run pa	arent and metabolites all SFO. SFO fit for me	etabolite acceptable?
	Parent DFOP, n	netabolites SFO
	M01	M62
Plot	Peddual (4) (4) (5) (6) (7) (6) (7) (7) (7) (7) (7) (7) (7) (7	etabolite acceptable?
Residuals		y y y y y y y y y y
Visual fit	Intermediate, residuals show systematic effor	Poor residuals show systematic error
χ^2 error (%)	Č 🔊 🔶 1767 🔷 💭	29.5
t-test	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	<i>k</i> : p > 0.1
DT ₅₀ (days)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
DT ₉₀ (days)	√, √ ³ 672 ¹ 0 0	
Model ug DT ₅₀ (days)	159.6 ²	>10,000 ¹
Formation fraction		<u>م</u> ٥.043
fraction	Entrot acceptable	
	Visual fit is intermediate, 2 pror is plightly	Fit not acceptable
Assessment	high and rate parameter do not differ signifi-	Visual fit is poor, χ^2 error is high and rate pa-
A		rameters do not differ significantly from zero
Q^.	capity from zero	:::) SEO 64 for model ality accordable 9 SEO is
	iii) SFO fit for metabolite acceptable of FO is	iii) SFO fit for metabolite acceptable? SFO is
L.	not considered acceptable. Werefore, DFOP	not considered acceptable. Therefore, DFOP
¥	or FOMC abould be assessed. However, these	or FOMC should be assessed. However, these
	models are not appropriate for metabolites	models are not appropriate for metabolites
	Swhich are formed gradually. Thereafter, de-	which are formed gradually. Thereafter, de-
Discussion	cline after now should be a sessed. However,	cline after max should be assessed. However,
Ś	this was not possible as there is limited de-	this was not possible as there is limited de-
	Quine data to cloarly establish the dissipation	cline data to clearly establish the dissipation
S a	pattern. Therefore, use of the estimated DT ₅₀	pattern. Therefore, use of default DT_{50} and
	and a refined formation fraction of 0.09 in-	formation fraction of 0.07 proposed as a
	vestigated as a realistic worst case.	worst case.
Internret with c	are – extrapolated beyond experimental period	

Appendix 3.2.4.2. Metabolite kinetics (M01 and M02)

² Normalised to pF 2.0 soil moisture



Step 2: Case-by-case decision (alternative - but conservative - estimates).



SFO fit for metabolite acceptable?



Appendix 3.2.4.3. Metabolite kinetics (M03)

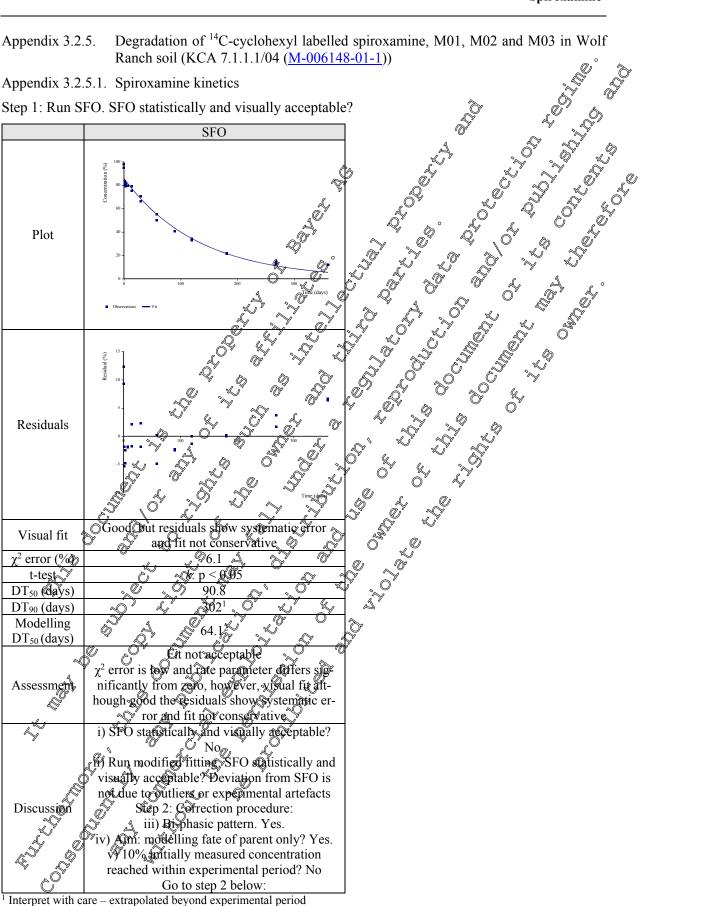
Matabilite M3 was not observed for this soil.



Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02 and M03 in Wolf Appendix 3.2.5. Ranch soil (KCA 7.1.1.1/04 (M-006148-01-1))

Appendix 3.2.5.1. Spiroxamine kinetics

Step 1: Run SFO. SFO statistically and visually acceptable?



² Normalised to pF 2.0 soil moisture



cceptable?	cetion procedure (continued). Run 115 of D1	OP. vi) HS or DFOP statistically and visually
	DFOP	Ho a h
Plot	du du du du du du du du du du	How we have a second se
Residuals		
Visual fit	Gard, residuals show no systematic errors	Good and residuals show no systematic error,
$\chi^2 \text{ error}$ (%)		3 .6
t-test	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \end{array} \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
DT ₅₀ (days)	<u>~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~</u>	
T_{90} (days)	$\frac{1}{\sqrt{2}} \frac{1}{\sqrt{2}} \frac{1}{\sqrt{2}$	2991
Modelling	$k_{2} \stackrel{\text{off}}{\Rightarrow} k_{2} \stackrel{\text{off}}{\Rightarrow} f_{50} = \stackrel{\text{off}}{\otimes} 8.0^{2} \stackrel{\text{off}}{\Rightarrow} $	$k_2 DT_{50} = 68.0^2$
DT_{50} (days)		Fit acceptable
Assessment	Visual fit is good and χ^2 error is low? k_1 rate parameter does not diffe significantly from zero, however, ky parameter is significantly	Visual fit is good and χ^2 error is low. k_1 rate parameter does not differ significantly from zero, however, k_2 parameter is significantly different
L.	different to zero, and os this is used for mod- elling endpont, fit is considered acceptable.	to zero, and as this is used for modelling end- point, fit is considered acceptable
V	will HS or DFOP statistically and visually and	eptable? Both DFOP and HS are considered ac-
Discussion	Ceptable. DPOP should be	used for modelling endpoints
Å	Use DT50 from slow phase of	DFOP model for fate modelling
nterpret with	care extrapolated beyond experimental period	
vormalised to	pr w son monsture	
unamary	pr w soil moisture	

Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually

Summary:

For spice xamine use DFOP. $DT_{50 \text{ mod}} = 68.0$ days (based on k₂ DFOP 96.3 days normalised to pF 2.0).



		notoholitos SEO
	M01	netabolites SFO
Plot	Concentration (%)	netabolites SFO Mto2
Residuals		
Visual fit		& Cood RA sustamentia arrang
$\chi^2 \text{ error (\%)}$ t-test		$\frac{2}{\sqrt{3}} \frac{19.0}{k: p < 0.05}$
DT ₅₀ (days)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
DT ₉₀ (days)	278.2 260 ¹ 0 0	<i>∞ ∞</i> 317 ¹
Modelting DT ₅₀ (days)		67.4 ²
Formation fraction		0.113
nuction	Dit acceptable	Fit acceptable
\sim	visual in is good and rate parameters unless	Visual fit is good and rate parameter differs
Assessment	significantly from ero, however rerors	significantly from zero, however, χ^2 error is
	a stightly by gh. and a start	slightly high.
Ŵ.	Nevertheless, residuals show no large sys-	Nevertheless, residuals show no large, sys-
	tematic error y	tematic error
∛ Discussion	iii) SFO fig for metabolite acceptable? SFO is considered acceptable and should be used for	iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for
		modelling endpoints
nterpret with	re – extrapolated beyond experimental period	
normanseq.to [*] p		
	F 2. Colling endpoints	
v Av		

Appendix 3.2.5.2. Metabolite kinetics (M01 and M02)



A CONTRACTION OF THE OWNER OWNE Appendix 3.2.5.3. Metabolite kinetics (M03) Step 1: Run parent and metabolites all SFO. SFO fit for metabolite acceptable? SFO fit for metabolite acceptable? Parent DFOP, metabolites SFO M03 Concentration (%) Plot Residual (%) Residuals Ő Visual fit Good no systematic or ors χ^2 error (%) t-test < 0.03 Ô DT₅₀ (days) DT₉₀ (days) Modelling DT₅₀ (days) Formation 0. IOI 0 fraction Fit acceptable Ş. Visual fit is good and rate parameter differs significantly from zero, however, χ^2 error is Assessment slightly high ~ Nevertheless, residuals show no large, systernatic error (H) SFQ fit for metabolite acceptable? SFO is Discussion O considered acceptable and should be used for Smodelling empoints ¹ Interpret with care extrapolated beyond experimental period ² Normalised to pp.0.0 soil moisture Summary:

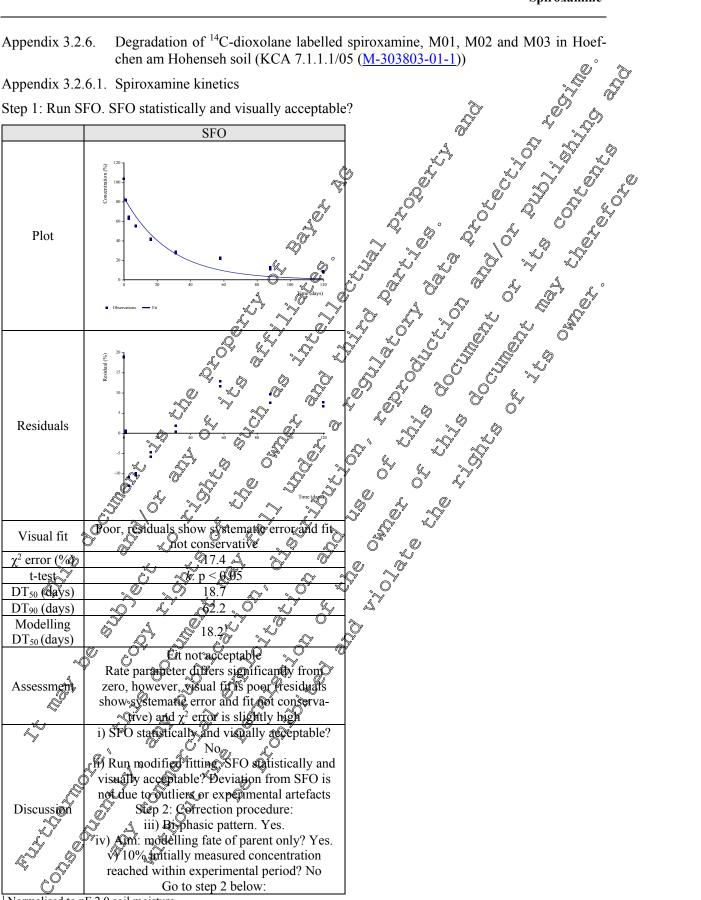
For M01 use DFOP/SFO. $DT_{50 \text{ mod}} = 55.3 \text{ days}, \text{ f.f.}_{\text{from parent}} = 0.182.$ For M02 use DFOP/SFO. $DT_{50 \text{ mod}} = 67.4 \text{ days}, \text{ f.f.}_{\text{from parent}} = 0.113.$ M03 use DFOP/SFO. $DT_{50 \text{ mod}} = 107 \text{ days}, \text{ f.f.}_{\text{from parent}} = 0.171.$



Degradation of ¹⁴C-dioxolane labelled spiroxamine, M01, M02 and M03 in Hoef-Appendix 3.2.6. chen am Hohenseh soil (KCA 7.1.1.1/05 (<u>M-303803-01-1</u>))

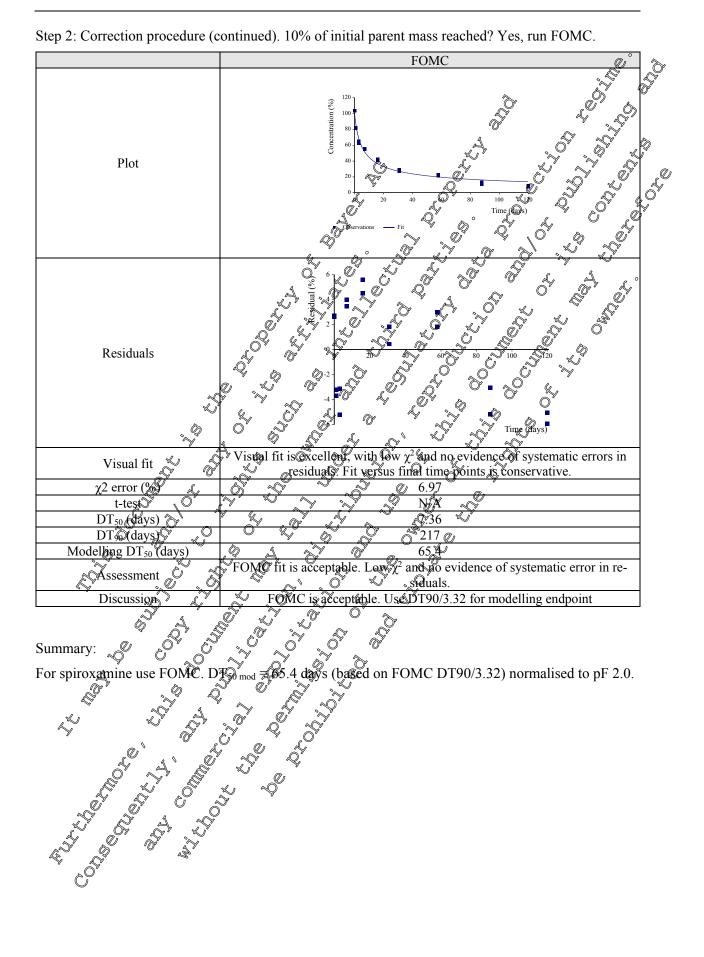
Appendix 3.2.6.1. Spiroxamine kinetics

Step 1: Run SFO. SFO statistically and visually acceptable?



¹Normalised to pF 2.0 soil moisture







	Parent FOMC, n	netabolites SFO
	M01	<u>M092</u>
Plot	(0)	netabolites SFO
Residuals	0 20 20 20 20 20 20 20 20 20 20 20 20 20 2	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} $ \left \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \end{array} \left \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \end{array} \left \\ \end{array} \\ \left \\ \end{array} \\ \left \\ \\ \\ \\ \\ \\ } \\) \\ } \\) \\) } \\) \\) \\) } \\) \\) } \\) \\) } \\) \\) \\) \\) \\) \\) \\) \\) \\) \\) \\) \\) \\) \\
Visual fit	Good, residuals show no systematic error	Good residual show no systematic error
χ^2 error (%)	Č , ~ 7.54 ~ (~	× 821
t-test 4	k: p ⊙0.05 (1 < 0.05
DT ₅₀ (days)		75.9
DT ₉₀ (days)		K: p < 0.05 Ø 75.9 Ø 252
Modelhurg DT ₅₀ (days)		75.9
Formation		A 0 147
fraction	2 A 0.1336 C O	0.147
Assessment	a, or pit accoptable or or o	Fit acceptable Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero
<u>A</u>		iii) SFO fit for metabolite acceptable? SFO is
Discussion	considered acceptable and should be used for	considered acceptable and should be used for
, K	The modelling endpoints	modelling endpoints
, ~		

Appendix 3.2.6.2. Metabolite kinetics (M01 and M02)

Appendix 3, 26.3. Metabolite kinetics (2003) Metabolite M03 vas not observed for this soil. Summary:

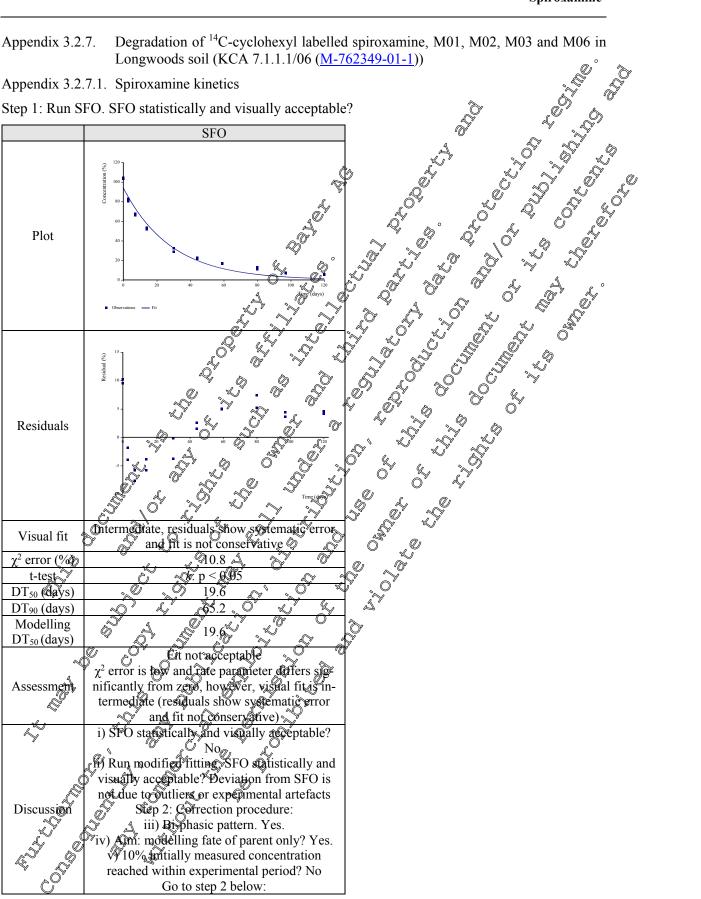
For M02 use FOMC/SFO: $DT_{50 \text{ mod}} = 78.0 \text{ days}$, f.f._{from parent} = 0.1336. For M02 use FOMC/SFO. $DT_{50 \text{ mod}} = 75.9 \text{ days}$, f.f._{from parent} = 0.147. M03 was not observed for this soil.



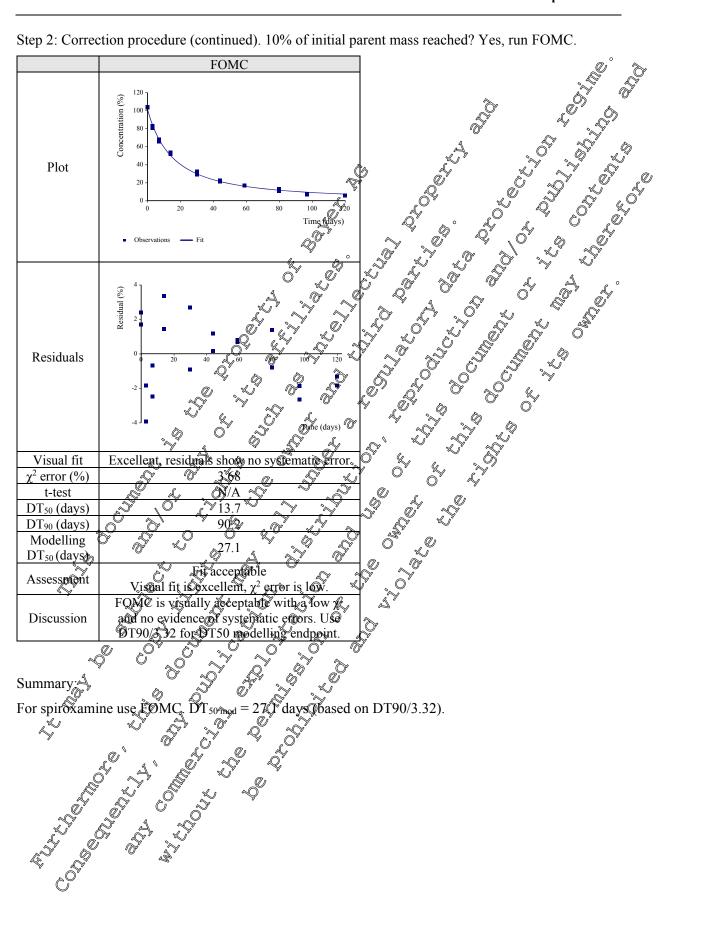
Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Appendix 3.2.7. Longwoods soil (KCA 7.1.1.1/06 (M-762349-01-1))

Appendix 3.2.7.1. Spiroxamine kinetics

Step 1: Run SFO. SFO statistically and visually acceptable?

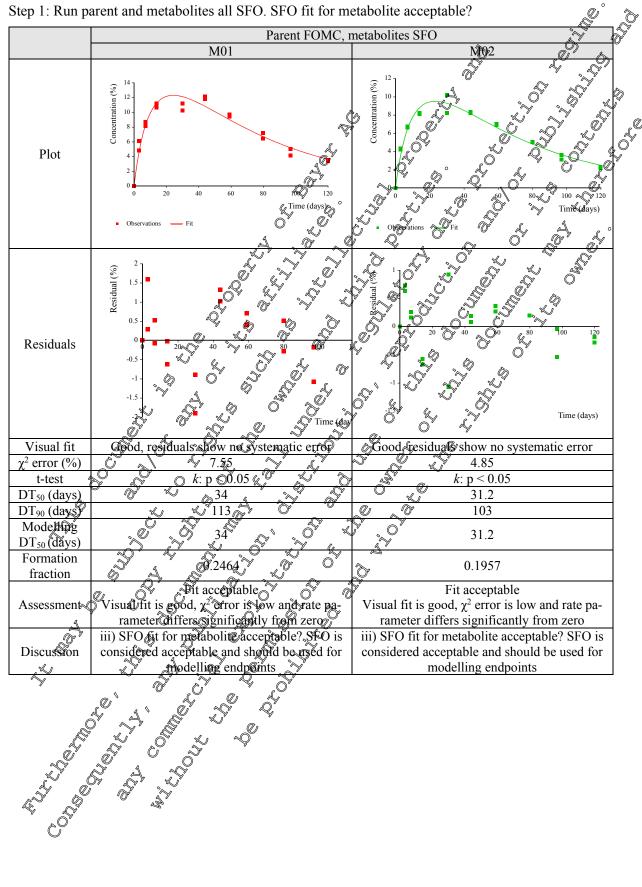






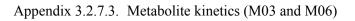
Step 2: Correction procedure (continued). 10% of initial parent mass reached? Yes, run FOMC.





Appendix 3.2.7.2. Metabolite kinetics (M01 and M02)





	Parent FOMC, r	netabolites SFO
	M03	M06
Plot	Concentration (%) Concentration	netabolites SFO
Residuals	$\begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $	1.5 1.5 1.5 1.5 1.5 1.5 1.5 1.5
Visual fit	Excellent, Pesidual's show no systematic error	Antermediate, reviduals show no systematic
$\chi^2 \operatorname{error}(\%)$	$\frac{1}{6}$	19.1
t-test		
DT ₅₀ (days)	L L 19.8 V V	32.)
DT ₉₀ (days)	C & 65.4 S	× 176
Modelling		<u>ک</u> 52.9
DT ₅₀ (days)	30 49.8 0 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	All 32.7
Formation	4 19.8 5 65 65 65 65 65 65 65 65 65 65 65 65 6	0.05855
fraction		0.05855
\sim	Fit acceptable in a	Fit acceptable
Assessment	Visual fit good rerrors acceptable and	Visual fit is good, χ^2 error is slightly high and
à	rate parameter differs significantly from zero	rate parameter differs significantly from zero
J.	iii) SFO/iit for metabolite acceptable FO is	iii) SFO fit for metabolite acceptable? SFO is
Discussion	considered acceptable and should be used for	considered acceptable and should be used for

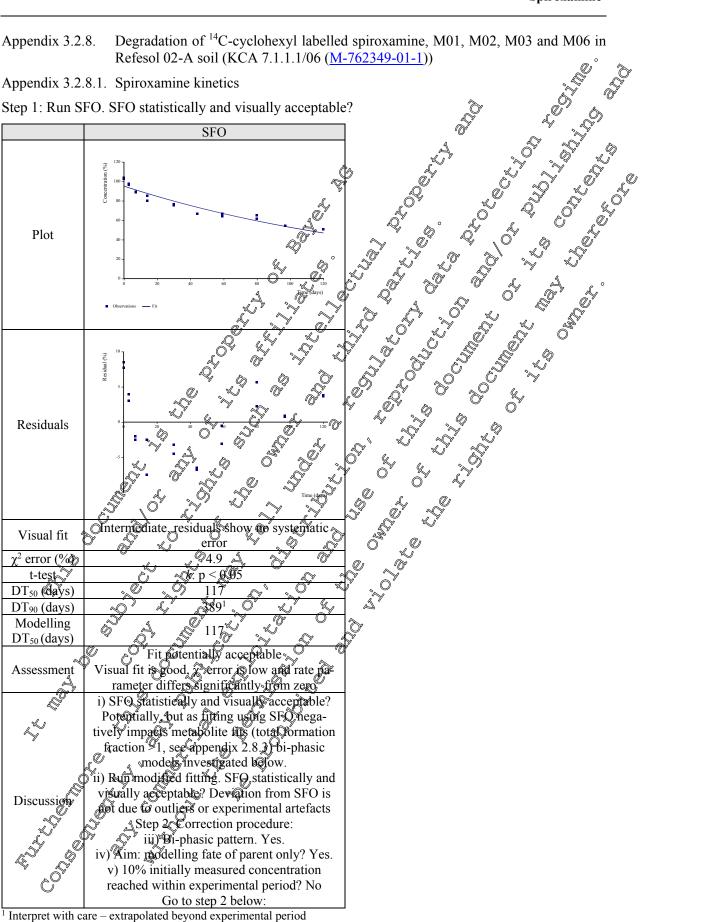
Summary: For M01 (se FOMC/SFO: DT_{50 mod} = 34.0 days, f.f._{from parent} = 0.2464. For M02 use FOMC/SFO: DT_{50 mod} = 31.2 days, f.f._{from parent} = 0.1957. For M03 use FOMC/SFO: DT_{50 mod} = 19.8 days, f.f._{from parent} = 0.199. For M06 use FOMC/SFO: DT_{50 mod} = 52.9 days, f.f._{from parent} = 0.0586.



Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Appendix 3.2.8. Refesol 02-A soil (KCA 7.1.1.1/06 (M-762349-01-1))



Step 1: Run SFO. SFO statistically and visually acceptable?





	DECD	
	DFOP	ØHS
Plot	Computing - Fr	PP. vi) HS or DFOP statistically and visually
Residuals		By a
Visual fit	Axcellent residuals show no systematic error	Good. resideals snow no systematic error
² error (%)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
t-test 🔊	$k_{1}: p \neq 0.05 \neq 0.1$	$k_1: p < 0.05$ $k_2: p > 0.1$
T ₅₀ (days)		
T ₉₀ (days)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	$2 > 10,000^{1}$
Iodelling	$\frac{116}{5}$	$k_2 \mathrm{DT}_{50} = > 10,000^1$
T_{50} (days)	Fit acceptable Visual fit iδexcellent, χ ² error is low and rate	Fit not acceptable
\sim	Viewal fit i Fit acceptable	Visual fit is good, χ^2 error is low, however k ₂
ssessment	parameters differ significantly from zero	rate parameter not significantly different to
	wi) HS or DEOD settion 200 and vie	zero sually acceptable? DFOP acceptable.
iseussion	\sim Use β T50 from skew phase of	DFOP model for fate modelling
terpret with c	are - extrapolated becond experimental period	
nmary:		
mirova	\sim	k DEOD
spirozanii	vi) HS or DFOP statistically and vis Use DT50 from skow phase of are – extrapolated becond experimental period	и к2 Dr OF).

Step 2: Correction procedure (continued). Run HS or DFOP, vi) HS or DFOP statistically and vis



Step 1: Run pa	arent and metabolites all SFO. SFO fit for me	etabolite acceptable?
	Parent DFOP, n	netabolites SFO
	M01	NO2
Plot	(c) ¹² 10 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	netabolites SFO MO2
Residuals	2 1 1 1 1 1 1 1 1 1 1 1 1 1	
Visual fit	Good, residuals show no systematic error	Ontermediate, residuals show no systematic 5.6 k: p < 0.05
χ^2 error (%)		5.6
t-test		
DT ₅₀ (days)		204 ¹
DT ₉₀ (days)	0 5 72 F	6781
Modelling		ک ^۲ 204 ¹
DT ₅₀ (days)		
Formation		0.166
fraction	a $o^{\gamma} \sim 0$ $o' o' n$	9 ⁹
A	Fit acceptable Y	Fit acceptable
Assessment	Visual fit is good of error is low, and rate pa-	Visual fit is intermediate, χ^2 error is low and
	rameter differs significantly from zero	rate parameter differs significantly from zero
	iii) SFO/lit for metabolite acceptable SFO is	iii) SFO fit for metabolite acceptable? SFO is
Discussion	considered acceptable and skould bevised for	considered acceptable and should be used for modelling endpoints
//	are extrapolated beyond experimental period	modening endpoints

Appendix 3.2.8.2. Metabolite kinetics (M01 and M02)

extrapolated beyond experimental



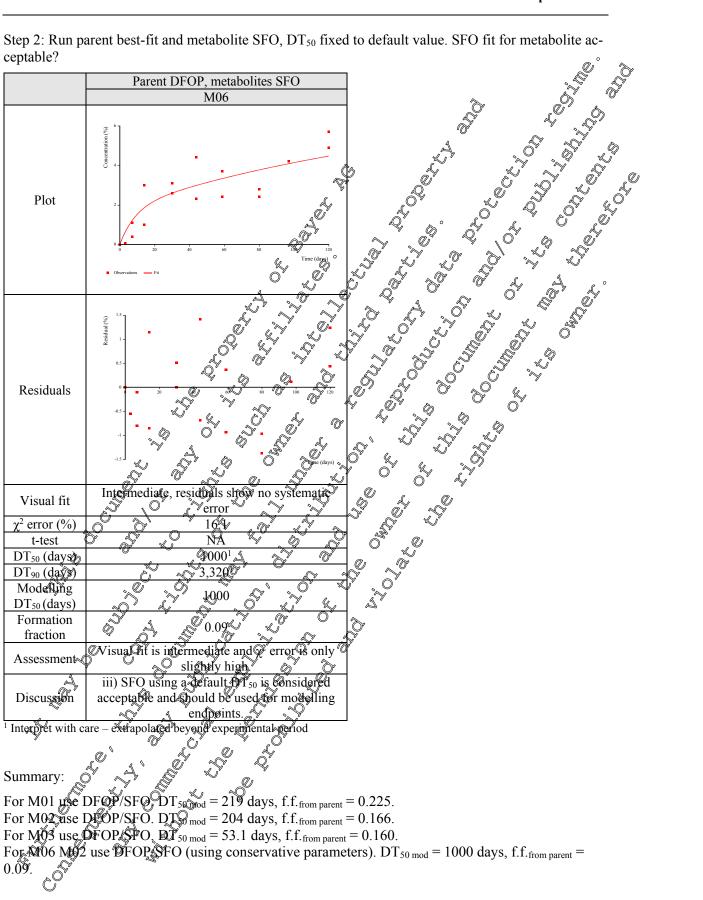
		notoholitos SEO
	Parent DFOP, n M03	Nitho and Andrews
Plot	Concentrations — Fit	netabolites SFO M06
Residuals		Constrained in the second seco
Visual fit	Intermediate, residuals show no systematic	Antermediate, residuals show no systematic $\frac{1}{2}$ error 16.6 k, $p > 0.1$
$\chi^2 \operatorname{error}(\%)$	$\frac{10^2}{k} = 0.05$	16.6
t-test DT ₅₀ (days)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
DT_{50} (days) DT_{90} (days)	\$3.1 0 \$3.1 00\$\$	>10,000 >>10,000
Modelling		
DT ₅₀ (days)	27 £3.1 7 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	گ ^۳ >10,000 ¹
Formation fraction		0.087
naction		Fit not acceptable
Assessment	Visual fit is good χ^2 error is acceptable and rate parameter offers significantly from zero	Visual fit is intermediate and χ^2 error is only slightly high, however rate parameter differs significantly from zero.
L.	iii) SFO fit for metabolite acceptable? SFO is	iii) SFO fit for metabolite acceptable? SFO is not considered acceptable. Therefore, DFOP or FOMC should be assessed. However, these models are not appropriate for metabolites
Discussion	111) Sty tit for metabolite acceptable? SFO is	which are formed gradually. Thereafter, de-
	considered acceptable and should be used for	cline after max should be assessed. However,
Discussion	considered acceptable and should be used for modelling endpoints	this was not possible as there is no decline data to clearly establish the dissipation pat- tern. Therefore, use of default DT ₅₀ and for- mation fraction of 0.09 proposed as a worst

Appendix 3.2.8.3. Metabolite kinetics (M03 and M06)

¹ Interpret with care – extrapolated beyond experimental period



Step 2: Run parent best-fit and metabolite SFO, DT₅₀ fixed to default value. SFO fit for metabolite acceptable?

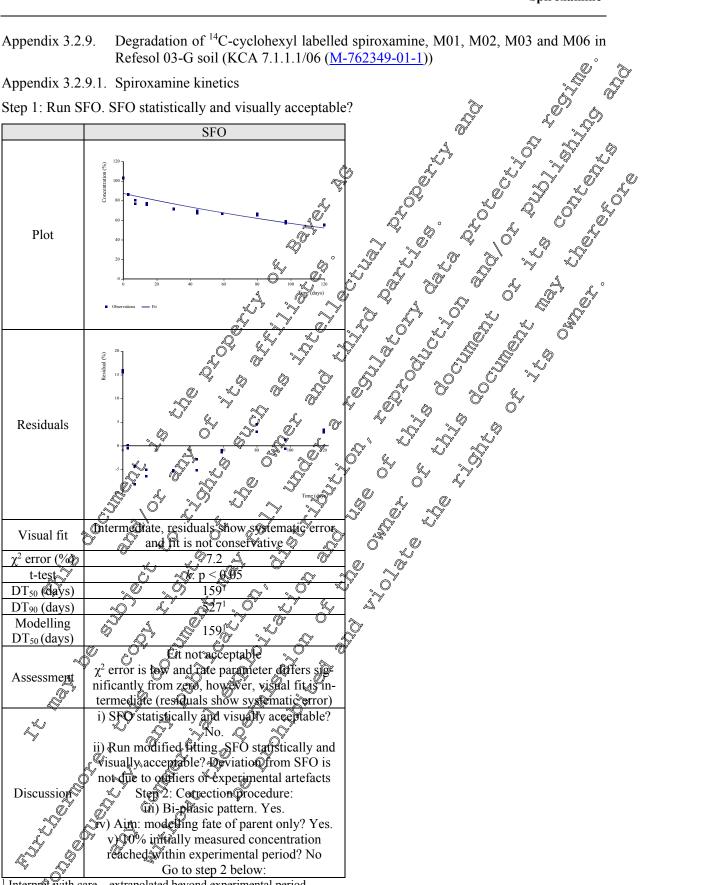




Appendix 3.2.9. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Refesol 03-G soil (KCA 7.1.1.1/06 (M-762349-01-1))



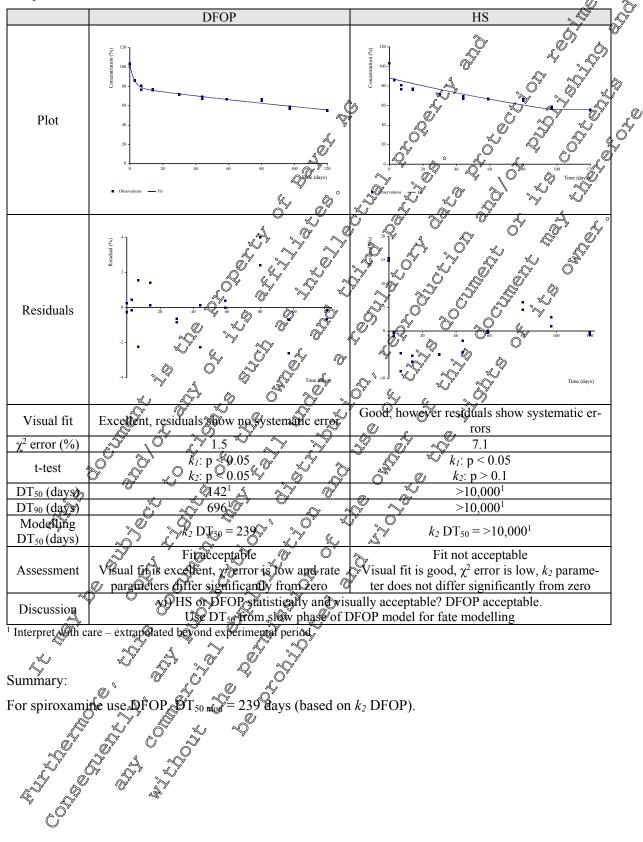
Step 1: Run SFO. SFO statistically and visually acceptable?



Interpret with care – extrapolated beyond experimental period

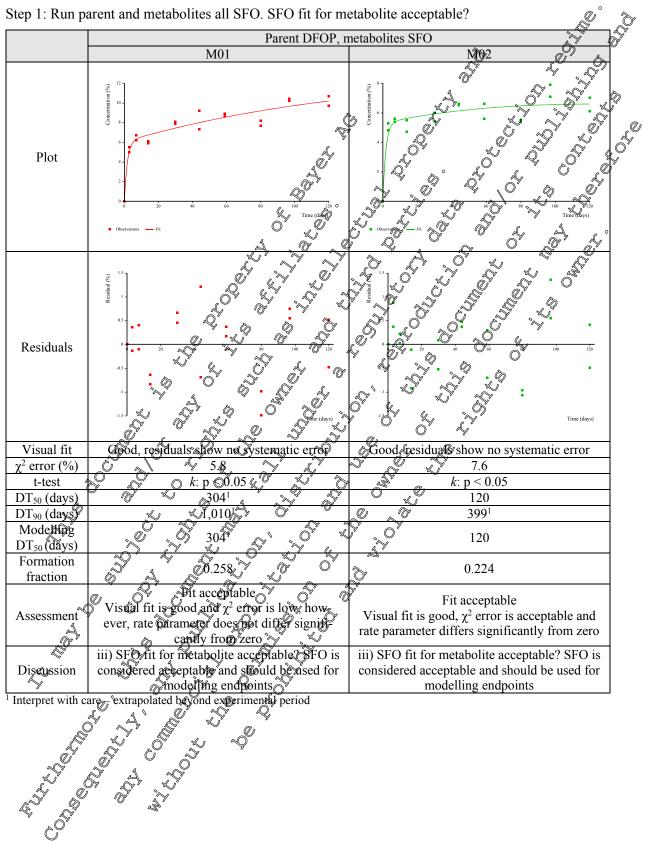


Step 2: Correction procedure (continued). Run HS or DFOP. vi) HS or DFOP statistically and visually acceptable?



239 days (based on k_2 DFOP).





Appendix 3.2.9.2. Metabolite kinetics (M01 and M02)



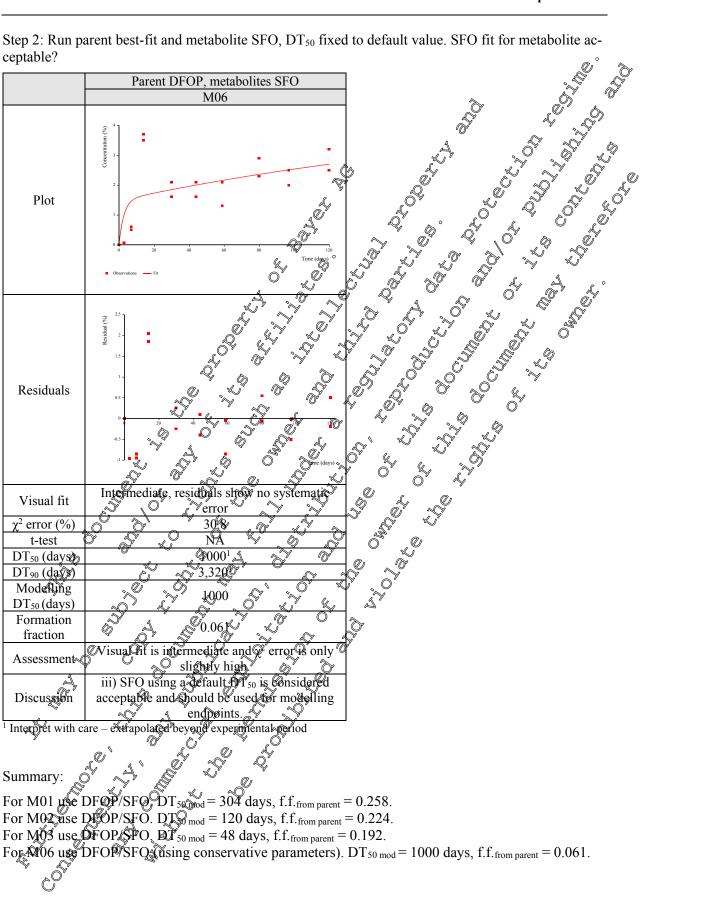
	arent and metabolites all SFO. SFO fit for m	notoholitas SEO
	M03	netabolites SFO
Plot	Correntions — Fi	netabolites SFO Moo Moo Moo Moo Moo Moo Moo Mo
Residuals	Observations — Fit	A A A A A A A A A A A A A A A A A A A
Visual fit	Good, residuals show no systematic error	Antermediate, residuals show no systematic error 33.9 k; p > 0.1
χ^2 error (%)		33.9
t-test	$\sqrt{0}$ $\sqrt{0}$ $\sqrt{10}$ $\sqrt{10}$	
DT ₅₀ (days)		1,380
DT ₉₀ (chay's)	<u> </u>	4,570 ¹
Modelling	248 0 27 47 27 27 27 27 27 27 27 27 27 27 27 27	1,380 ¹
DT ₅₀ (days) Formation	48 0 48 0	0.061
fraction		0.001
Assessment	Fit acceptable Visual fit is good χ^2 error is acceptable and rate parameter differs significantly from zero	Visual fit is intermediate, χ^2 error is high and rate parameter does not differ significantly from zero
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	iii) Sto fit for metabolite acceptable? SFO is	iii) SFO fit for metabolite acceptable? SFO is not considered acceptable. Therefore, DFOP or FOMC should be assessed. However, these models are not appropriate for metabolites which are formed gradually. Thereafter, de-
Discussion	considered acceptable and should be used for modelling endpoints	which are formed gradually. Thereafter, de- cline after max should be assessed. However, this was not possible as there is no decline data to clearly establish the dissipation pat-
		tern. Therefore, use of default $DT_{50}$ and mod- elled formation fraction of 0.061 investigated as a realistic worst case.

Appendix 3.2.9.3. Metabolite kinetics (M03 and M06)

¹ Interpret with care – extrapolated beyond experimental period

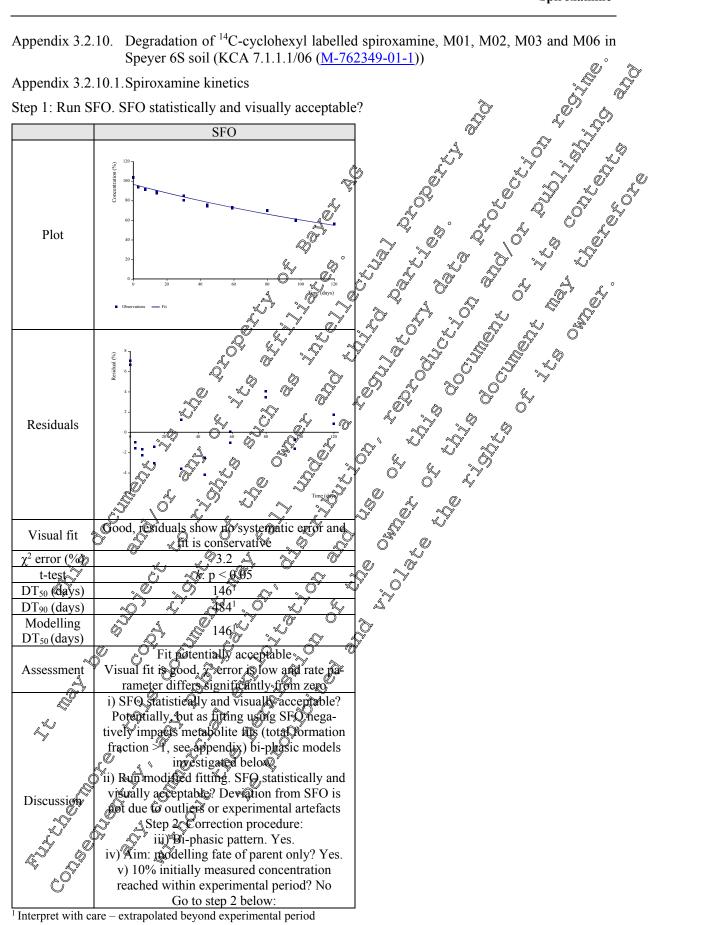


Step 2: Run parent best-fit and metabolite SFO, DT₅₀ fixed to default value. SFO fit for metabolite acceptable?





Appendix 3.2.10. Degradation of ¹⁴C-cyclohexyl labelled spiroxamine, M01, M02, M03 and M06 in Speyer 6S soil (KCA 7.1.1.1/06 (M-762349-01-1))





	DFOP	DP. vi) HS or DFOP statistically and visually
Plot	Operations — Fit	
Residuals	$\begin{array}{c c} & & & & & & & & & & & & & & & & & & &$	
Visual fit	Excellent, residuals, show to systematic error	Excellent, residerals show no systematic error
error (%)	$\sim$	3.7
t-test	$\sum_{i=1}^{n} \sum_{j=1}^{n} \frac{k_{1} \cdot p \otimes 0.05}{k_{2} \cdot p} < 0.05$	$\begin{array}{c} 3.7 \\ \hline \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ &$
T ₅₀ (days)	$\sqrt{\sqrt{127}}$	$\begin{array}{c c} & & & \\ & & & \\ \hline & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$
T ₉₀ (days)	<u> </u>	
Aodelling	$k_2 D k_3 = 160^{\circ}$	No.
T., (dava)	$k_2 D k_0 = 160$	$k_2 \mathrm{DT}_{50} = > 10,000^1$
50( )/	Wisual Ait is excellent X error is low and rate	Fit not acceptable
~~~~~	Time acceptable where a second large of the second se	Visual fit is good, $\chi^2$ error is low, however $k_2$
ssessment	parameters differ significantly from zero	rate parameter is not significantly different to
.1		zero
J.	vi) HS or DFOP statistically and visually accept	otable? DFOP acceptable. DFOP should be used
iscussion		nts best acceptable fit)
N.	Use of 150 from slow phase of	DFOP model for fate modelling
terpret with c	are – extrapolated beyond experimental period	
nmary:	are – extrapolated beyond experimental veriod $\int_{0}^{1} \int_{0}^{1} \int_{0}^{$	n <i>k</i> 2 DFOP).

Step 2: Correction procedure (continued). Run HS or DFOP, vi) HS or DFOP statistically and visually

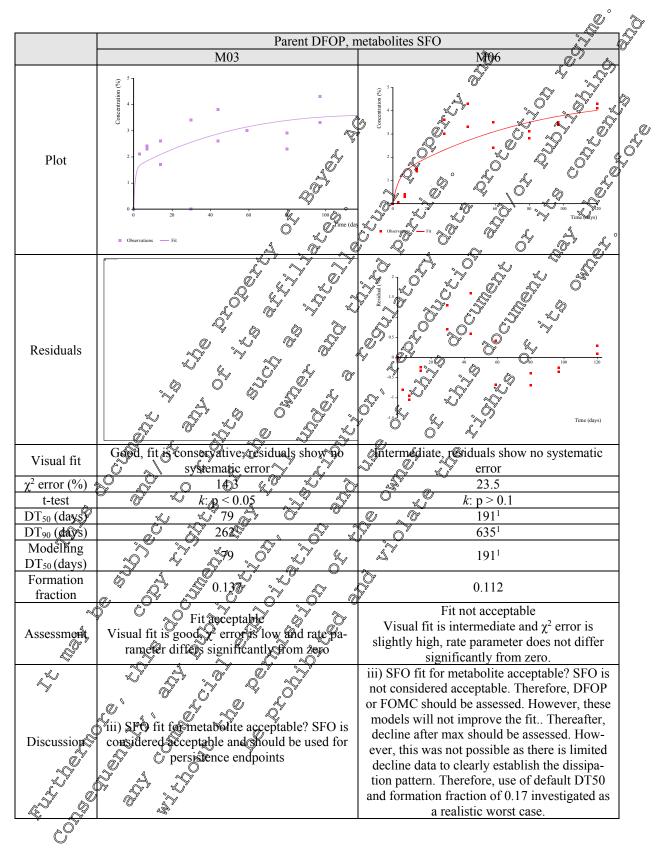


Step 1: Run p	arent and metabolites all SFO. SFO fit for me	etabolite acceptable?
	Parent DFOP, n	netabolites SFO
	M01	<u>N692</u>
Plot	Requiring (a) (b) Revalues - Fa (b)	$\frac{1}{2} + \frac{1}{2} + \frac{1}$
Residuals		1 1 1 1 1 1 1 1 1 1 1 1 1 1
Visual fit	Good, residuals show no systematic error	Good residuals show no systematic error
$\chi^2 \operatorname{error}(\%)$		
t-test	k: p ⊙0.05 ¢	$\frac{11.4}{11.4}$ $\frac{11.4}{65.2}$ $\frac{65.2}{217^{1}}$
DT ₅₀ (days)		$\begin{array}{c} & & & \\ & & & \\ \hline \\ & & & \\ \hline & & \\ \hline & & & \\ \hline \\ \hline$
DT ₉₀ (days)		
DT ₅₀ (days)	70.7 70.7	65.2
Formation	3	0.183
fraction		
	Pit acceptable	Fit acceptable
Assessment	Visual fit is good, χ^2 or for is yow and rate pa-	Visual fit is good, χ^2 error is low and rate pa-
<u> </u>		rameter differs significantly from zero
Discussion	iii) SFO fit for metabolite acceptable? SFO is	iii) SFO fit for metabolite acceptable? SFO is
Discussion	considered acceptable and should be used for	considered acceptable and should be used for
Int Strat with a	are autronale d have d automatal mind	persistence endpoints
	III) SFO at for metabolite acceptable? SFO is considered acceptable and should be used for persistence endpoints are – extrapolated beyond experimental period	

Appendix 3.2.10.2. Metabolite kinetics (M01 and M02)

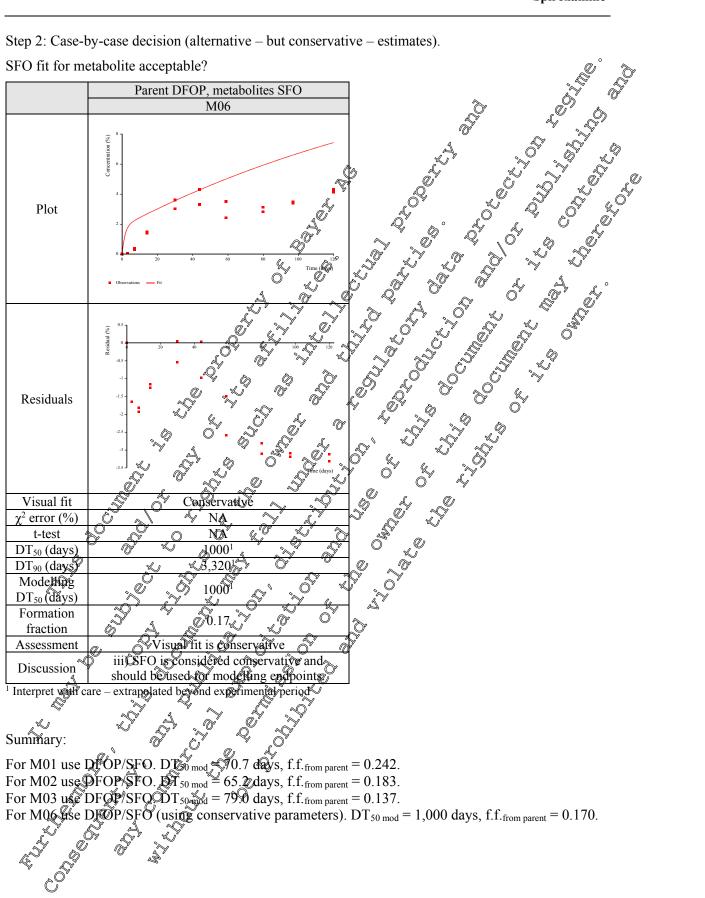


Appendix 3.2.10.3. Metabolite kinetics (M03 and M06)





Step 2: Case-by-case decision (alternative – but conservative – estimates).

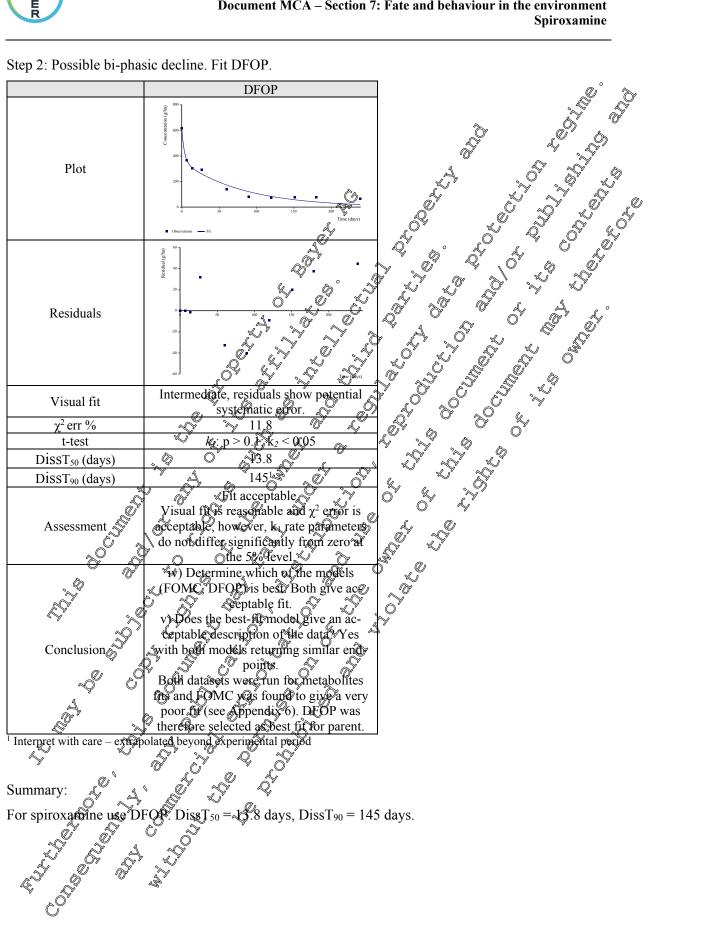


SFO fit for metabolite acceptable?



Appendix 4: Kinetic evaluation of field soil studies **Appendix 4.1:** Kinetic evaluation for persistence/trigger endpoints Dissipation of spiroxamine in Höfchen soil trial no. 30122/1 (KCA 7.1.2.2. Appendix 4.1.1. 006116-01-1)) Appendix 4.1.1.1. Parent Fitting Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit? SFO Plot Residuals Poor, residuals show systematic error Excellent residuals show no potential Visual fit and fit not conservative systematic error. 10.7) N P err ¥0.05% NA p 31.9 14.3 DissT₃(days) Ø. 230¹ Dissign (days) 106 «Fit not acceptable. Fit acceptable. Rate parameter differs significantly Visual fit is excellent and χ^2 error is ac-Assessment from zero, however, visual fit is poor ceptable. and xerror is light high. SFO more appropriate than FQMC and gives acceptable fit? SFO is not more appropriate than FOMC. Ryp modified fitting. SFQ more appropriate than FOMC & fit acceptable (modi-....n cate – extrapolated beyond experimental period fied (foting)? Modified fitting not needed. Deviation from SFQ due to experimental artefact/decline in microbial activity? No. Go to step 2 below. ¹ Interpret with case





Step 2: Possible bi-phasic decline. Fit DFOP.

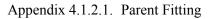


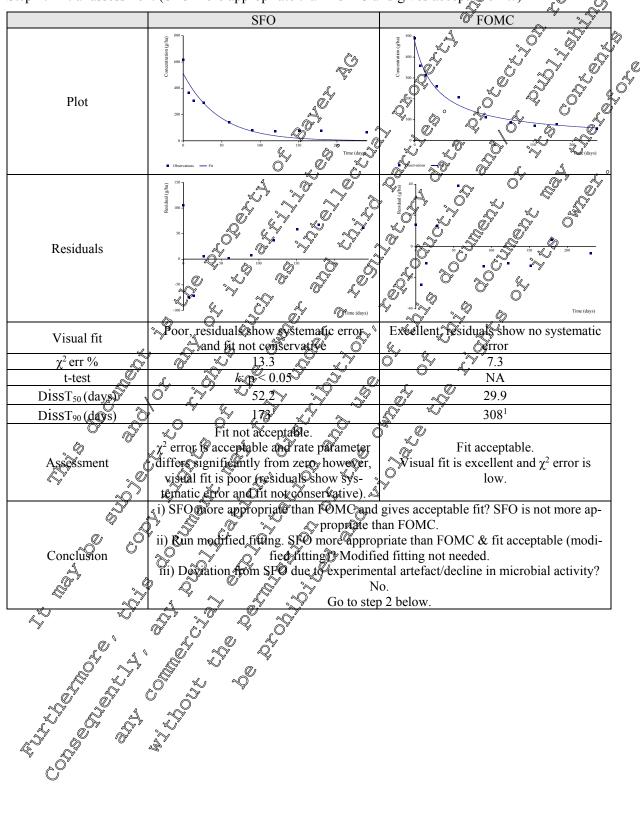
tep 4. Kull parent best-	fit and metabolite SFO. iii) SFO fit for	
	Parent DFOP, 1	metabolite SFO
	M01	M02
Plot	Constructions - Fit	
Residuals	restant (g has a second	
Visual fit	Intermediate, final time points underes-	Intermediate, Anal time points underes-
$\chi^2 \mathrm{err} \%$	<u>~</u> <u></u>	×
t-test 🔬	<i>Qk</i> : p < 0 .05	\$\$ & \$k^2 < 0.05
DissT ₅₀ (days)	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
DissT ₉₀ (days)	Fit acceptable. Rate parameter differs significantly from zero, χ^2 error is slightly high and visual fit is intermediate Residuals at fi-	Kate parameter uniters significantly
	nal three timepoints are considered to be due to data scatter rathe Ohan the ki- netter to be in propriorite.	That three time points are considered to be due to data scatter rather than the ki- netic fit being inappropriate.
Discussion	considered acceptable and should be oused for persistence endpoints	iii) SFO fit for metabolite acceptable? is considered acceptable and should be used for persistence endpoints.
ummarx or metabolite M0k use or metabolite M02 use	DEOP/SFO Diss ¹⁵ ⁵⁰ = 18.1 days, DissT ₉₀	$\Gamma_{90} = 60.2 \text{ days.}$ $\sigma = 69.6 \text{ days.}$

Appendix 4.1.1.2. Metabolite fitting (M01 and M02)

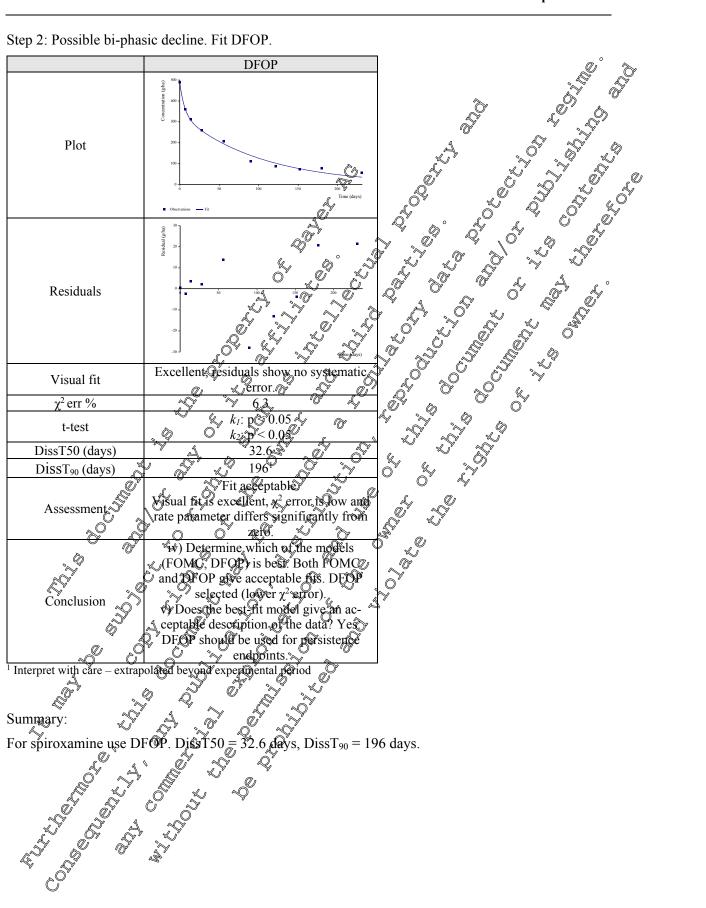


Appendix 4.1.2. Dissipation of spiroxamine in Laacher Hof soil trial no. 30124/8 (KCA 7.1.2.2.1/01 (M-006116-01-1))









Step 2: Possible bi-phasic decline. Fit DFOP.

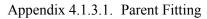


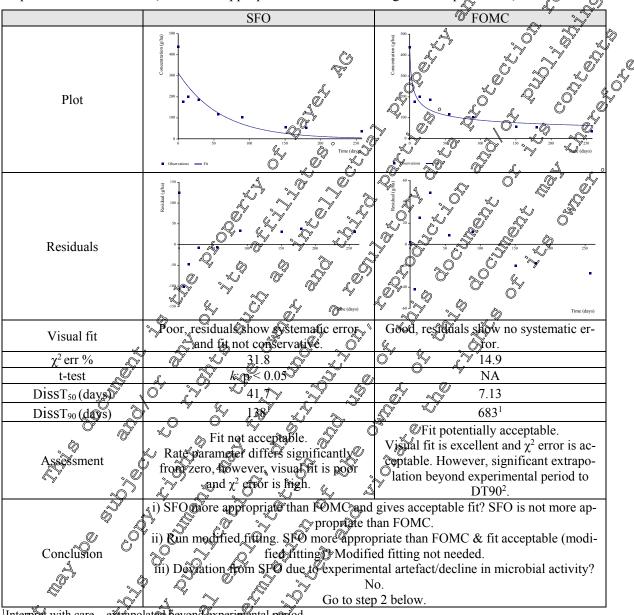
Step 4: Run parent best-	fit and metabolite SFO. iii) SFO fit for me	etabolite acceptable?	ð
	Parent DFOP, met	tabolite SFO	6
	M01	M02	
Plot	a - - - - - - - - - - - - -		
Residuals			0
Visual fit	Excellent residuals show no systematic (E	Excellent, residuals show no systematic	
$\chi^2 \mathrm{err} \%$	N Q11.9 N Q	<u> </u>	
t-test 🛒	, @k: p < 0 .05	<u>√ k</u> k.	
DissT50 (days)	59.3 ST L	<u>م</u> الم 48.3	
Assessment		 160 Fit acceptable. Visual fit is excellent, χ² error is acceptable and rate parameter differs significantly from zero. SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- 	-
¹ Interpret with care ©extrap	should be used for persistence end-	points.	
Summary: A For metabolite M01 use	DFOP/SFQ DissTer = 563 days, DissT ₉₀	$_{0} = 167 \text{ days.}$	
For metabolite M02 use	DPOP/SEO DisoT50 48.3 days, DissT ₉₀	0 = 160 days.	
	ceptable and rate parameter differs sig- iii) SFO fit for metabolite acceptable SPO is considered acceptable and should be used or persistence end- points DFOP/SFQ Diss T50 = 563 days, Diss T ₉₀ DFOP/SFQ Diss T50 = 48.3 days, Diss T ₉₀		

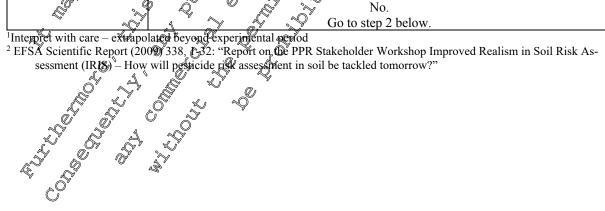
Appendix 4.1.2.2. Metabolite fitting (M01 and M02)



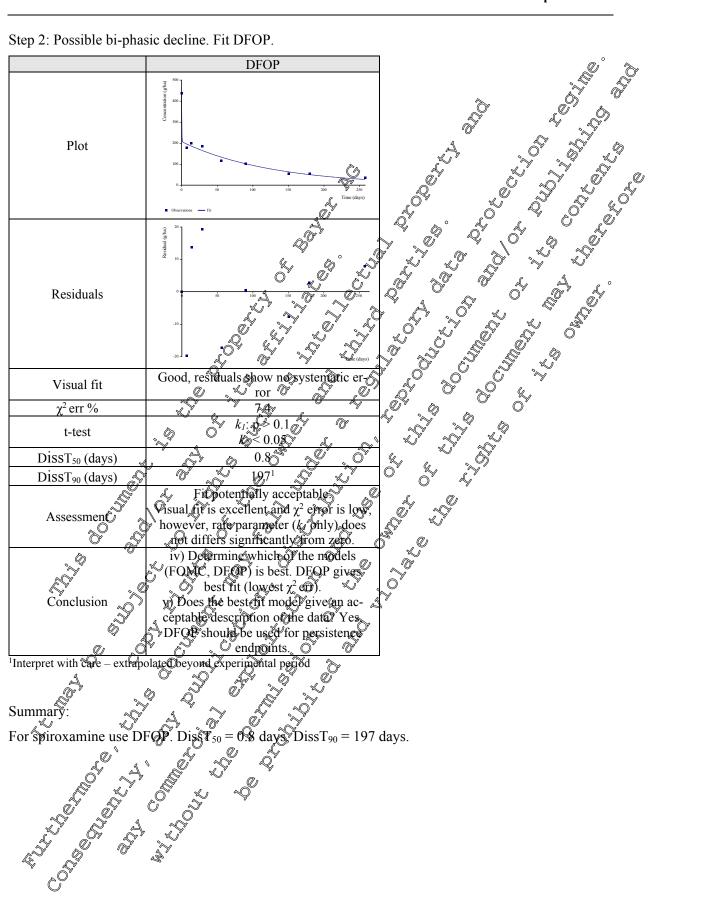
Dissipation of spiroxamine in Elm Farm/Thurston soil trial no. 30262/7 (KCA Appendix 4.1.3. 7.1.2.2.1/01 (M-006116-01-1))











Step 2: Possible bi-phasic decline. Fit DFOP.

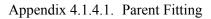


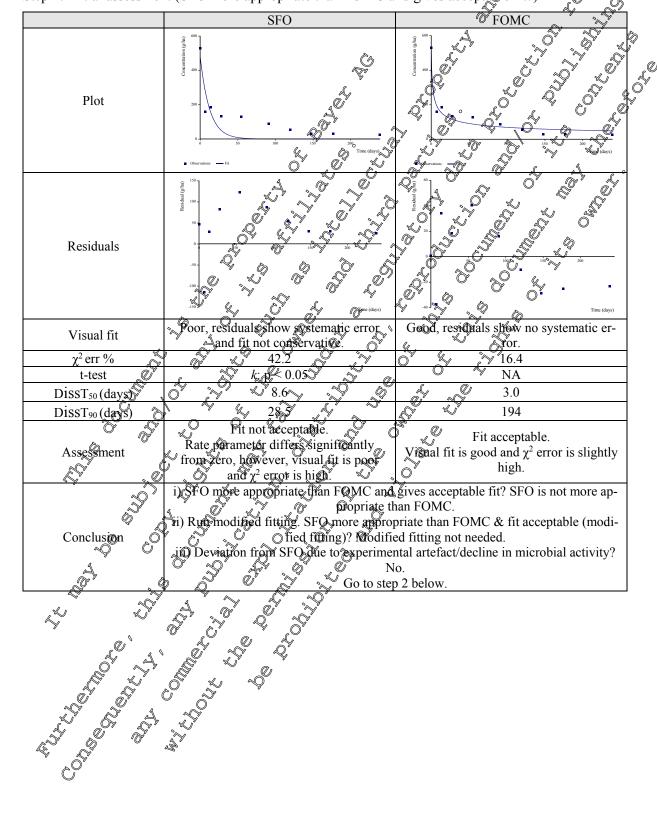
Step 4: Run parent best-	fit and metabolite SFO. iii) SFO fit for metabolite acceptable?
	Parent DFOP, metabolite SFO
	M01
Plot	Parent DFOP, metabolite SFO M01 u_{0} $u_{$
Residuals	
Visual fit	Good, residuals show no systematic er-
$\chi^2 \mathrm{err} \%$	<u>~</u>
t-test 🔬	$k = \sqrt{k} + \frac{1}{2} = $
DissT ₅₀ (days)	
DissT ₉₀ (days)	4 5 7 171 6 1924 Fit acceptable. 5 7 7 Fit acceptable.
Assessment	Visual fit is good γ^2 error is acceptable Visual fit is good, γ^2 error is acceptable
Discussion	should be used for persistence end- points.
Interpret with care – extrand Summary For metabolite M01 nse For metabolite M02 use	and rate parameter differs significantly from zero. iii) SPO fit for metabolite acceptable? SPO is considered acceptable and should be used for persistence end- points the beyond exterimental period FOMC/SFQ Diss $f_{50} = 5$, 4 days, Diss $T_{90} = 171$ days. FOMC/SFQ Diss $f_{50} = 5$, 7 days, Diss $T_{90} = 192$ days.

Appendix 4.1.3.2. Metabolite fitting (M01 and M02)

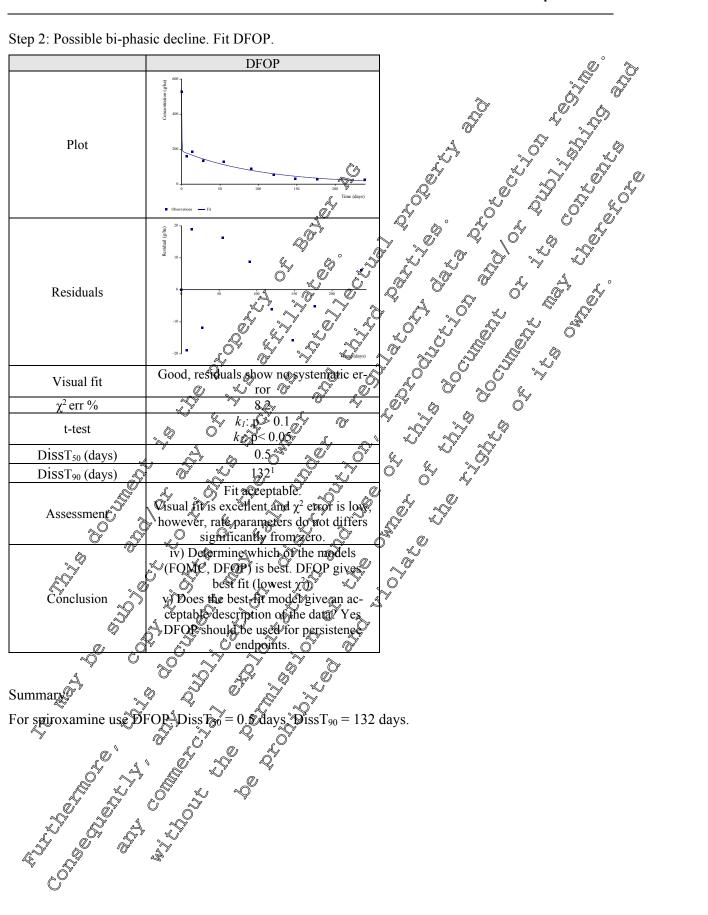


Appendix 4.1.4. Dissipation of spiroxamine in Pakenham soil trial no. 30263/5 (KCA 7.1.2.2.1/01 (M-006116-01-1))



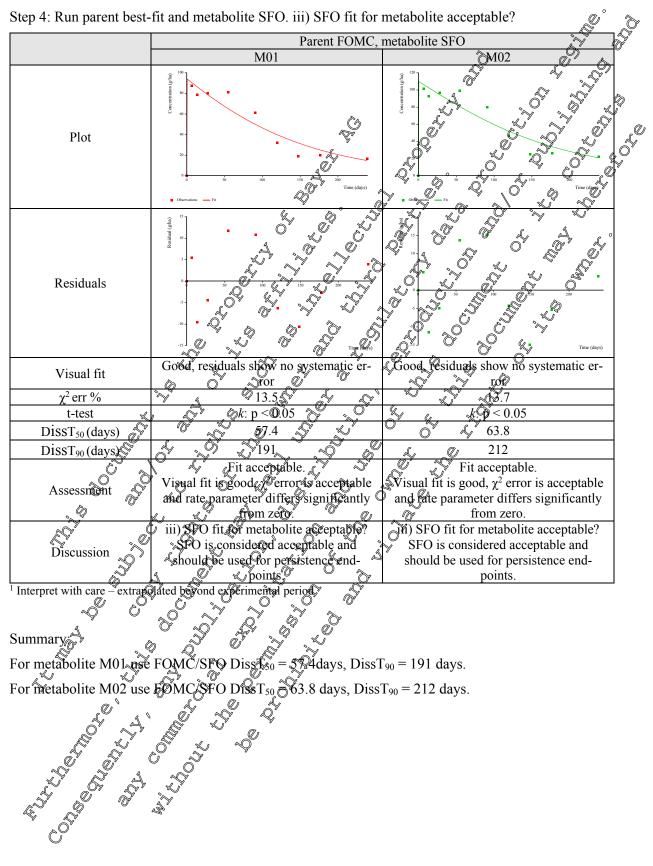






Step 2: Possible bi-phasic decline. Fit DFOP.

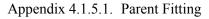


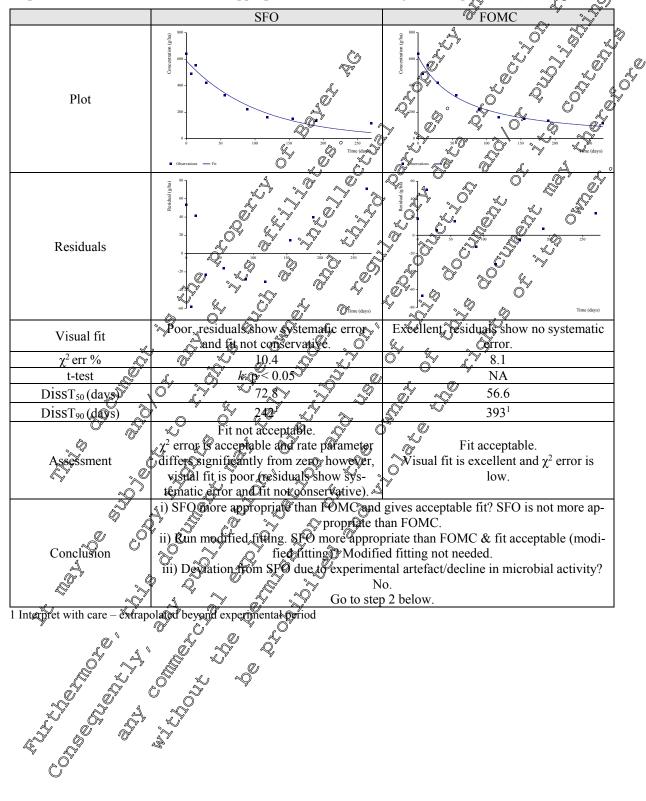


Appendix 4.1.4.2. Metabolite fitting (M01 and M02)

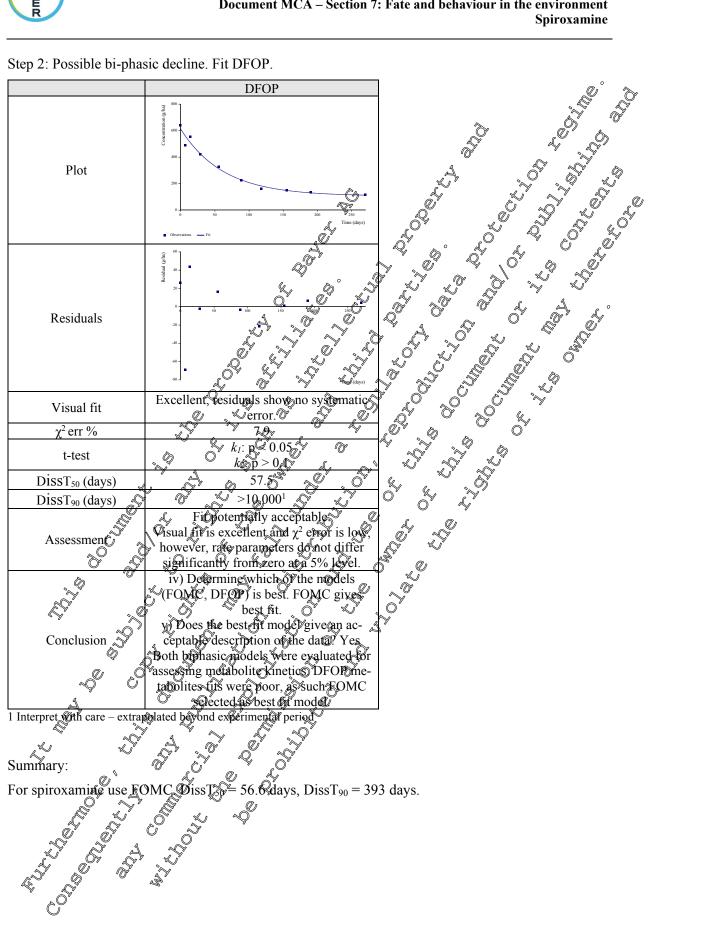


Appendix 4.1.5. Dissipation of spiroxamine in Höfchen trial no. 40006/8 (KCA 7.1.2.2.1/02 (\underline{M} -<u>006126-01-1</u>))









Step 2: Possible bi-phasic decline. Fit DFOP.

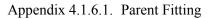


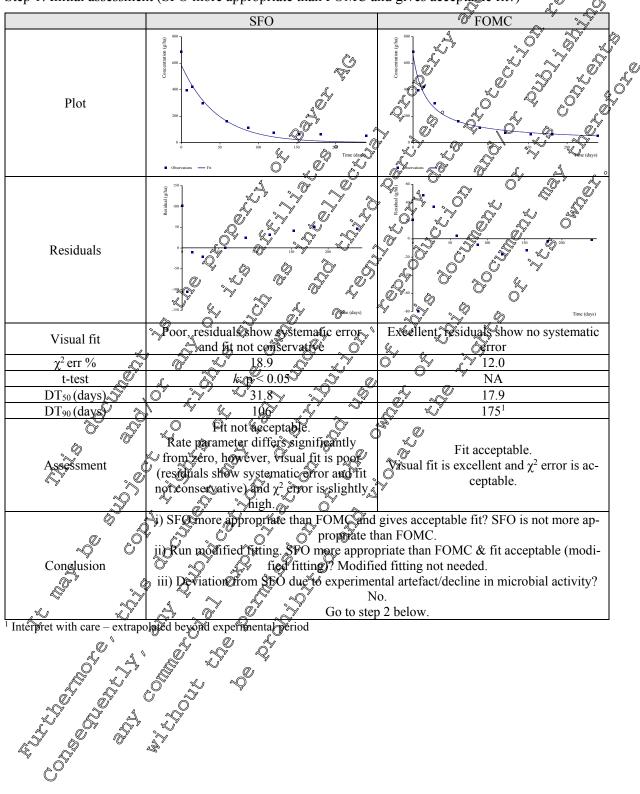
Step 4: Run parent best-	fit and metabolite SFO. iii) SFO fit for	metabolite acceptable?
	Parent FOMC,	metabolite SFO
	M01	€M02
Plot	Concention Fit	metabolite SFO
Residuals	0 50 100 10 <u>10</u> <u>20</u> <u>100</u> <u>1</u>	A A A A A A A A A A A A A A A A A A A
Visual fit	Excellent residuals show to systematic	Excellent, restduals show no systematic
$\chi^2 \text{err} \%$	6.93 × ×	27 207.19
t-test 🚿	v _ Qk: p < 0.05 ℃	k k k k k k k k k k k k k k k k k k k
DissT ₅₀ (days)	0 230 S 2	0 4 135
DissT ₉₀ (days)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	& _@ 447 ¹
	Fit acceptable. Visual fit is excellent. 25 error is how	Fit acceptable. Visual fit is excellent. γ^2 error is low
Discussion	iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end-	 SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- points.
Summary: For metabolite M01 use For metabolite M02 use	and rate parameter differs significantly trom zeto. FO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- points FOMC/SFO Diss Tsp = 130 days, Diss T FOMC/SFO Diss Tsp = 130 days, Diss T FOMC/SFO Diss Tsp = 135 days, Diss T	$\Gamma_{90} = 432 \text{ days.}$ $\Gamma_{90} = 447 \text{ days.}$

Appendix 4.1.5.2. Metabolite fitting (M01 and M02)

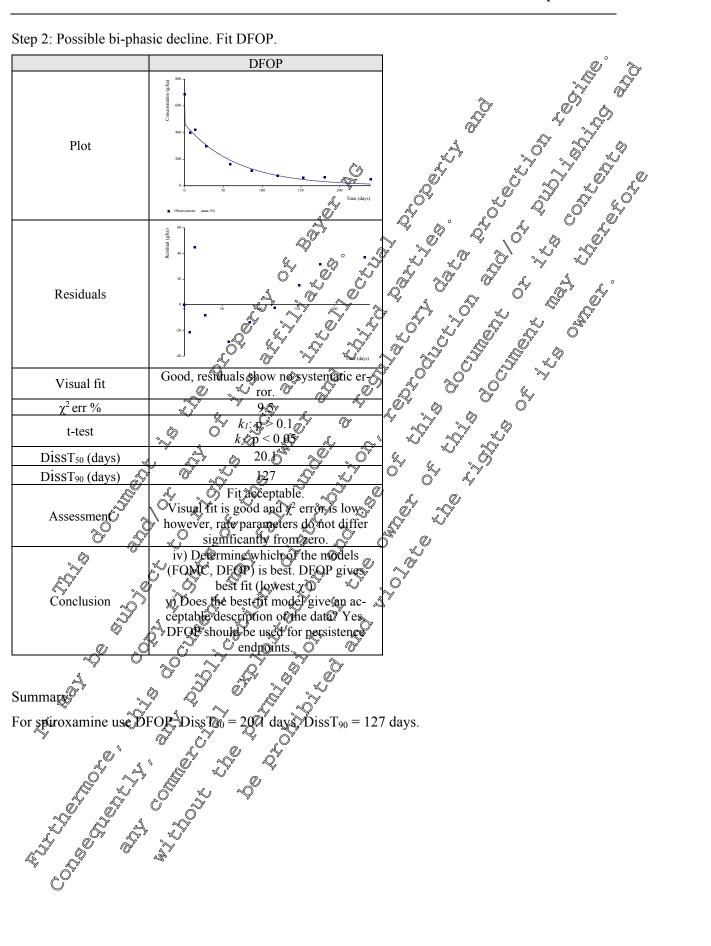


Appendix 4.1.6. Dissipation of spiroxamine in Laacher Hof soil trial no. 40007/6 (KCA 7.1.2.2.1/02 (M-006126-01-1))



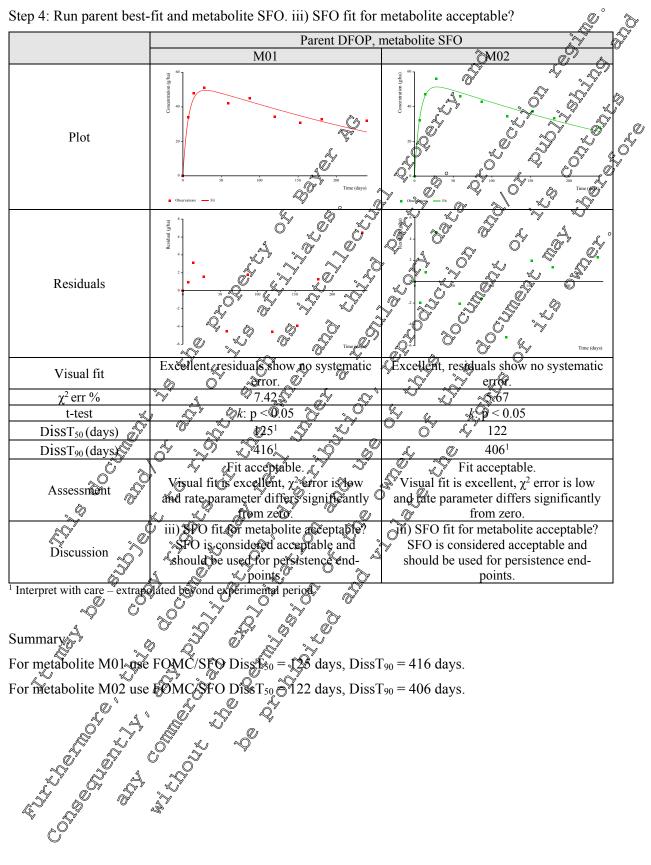






Step 2: Possible bi-phasic decline. Fit DFOP.





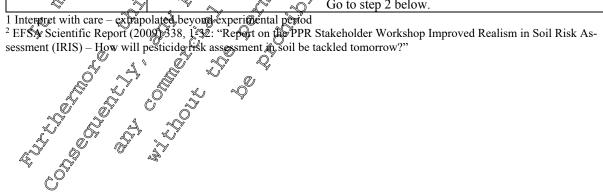
Appendix 4.1.6.2. Metabolite fitting (M01 and M02)



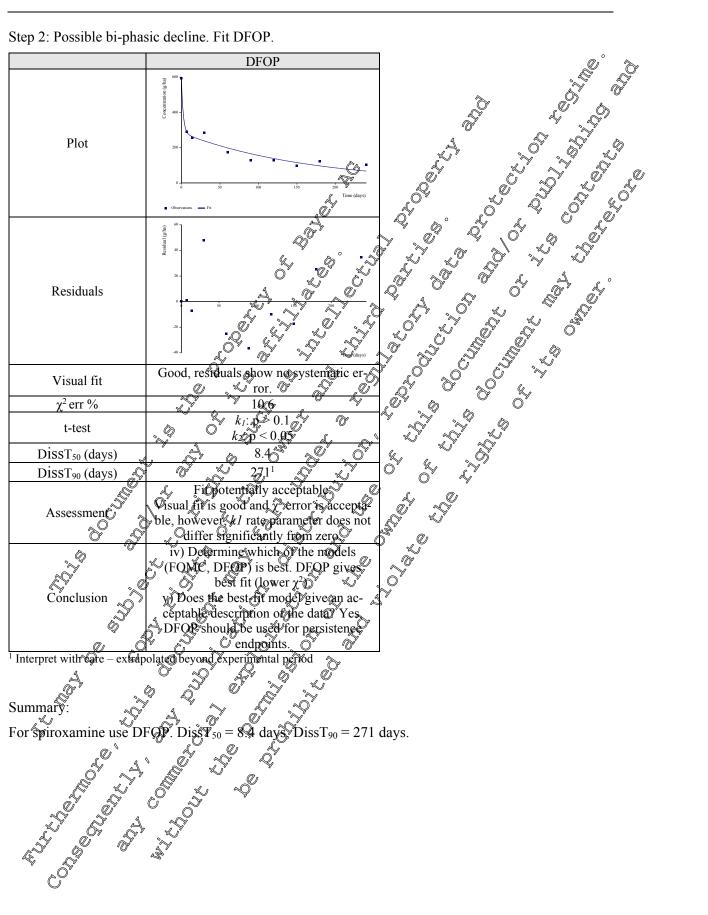
Appendix 4.1.7. Dissipation of spiroxamine in Maasen soil trial no. 40008/4 (KCA 7.1.2.2.1/02 (M-006126-01-1))

Appendix 4.1.7.1. Parent Fitting

	in (SFO more appropriate than FOMC a	
	SFO	FOMC
Plot	Corrections Fit	FOMC FOMC
Residuals	Cherraters = 12	
Visual fit	© oor, residuals show systematic error	Excellent, residuals show no systematic
$\chi^2 \text{err } \%$	26.9 × ×	× × × 11.1
t-test	k: p& 0.05	O S NA
DissT ₅₀ (days)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	L Q 11.3
DissT ₉₀ (days)		1,870 ¹
Assessment	from zero, however, visual fit is poor and χ^2 error is high.	Fit potentially acceptable. Visual fit is excellent and χ^2 error is acceptable. However, significant extrapo- lation beyond experimental period to DT90 ² .
	i) SFO pore appropriate than FOMC and	gives acceptable fit? SFO is not consid-
Q.		
Concluçãon	ii) Run modified fitting. SFO more pprop	priate than FOMC & fit acceptable (modi-
Concluçãon ô	fied fitting 2 Modifie	ed fitting not needed.
4	(I) Descrition from SFG due to experimen	ntal artefact/decline in microbial activity?
	(iii) Devotion from SFS due to experiment Go to step	o. o 2 below.
nterøret with care – extra	polated beyond experimental period	







Step 2: Possible bi-phasic decline. Fit DFOP.

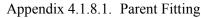


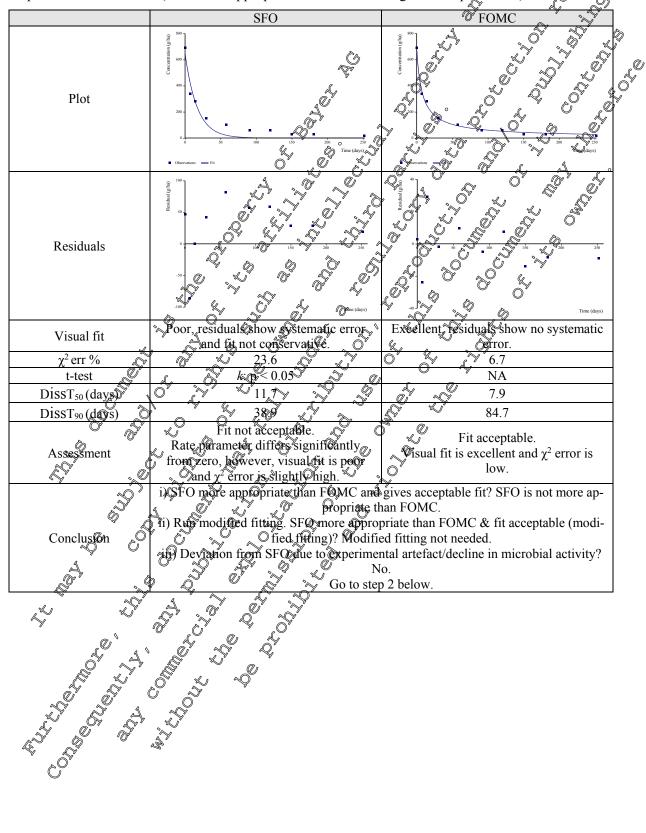
Step 4: Kun parent best-	fit and metabolite SFO. iii) SFO fit for metabolite acceptable?
	Parent DFOP, metabolite SFO
	M01
Plot	Parent DFOP, metabolite SFO M01 $(u_{ij})_{ij}$ (u_{ij}) (u_{ij}) (u_{ij}) (u_{ij}) $(u_{ij}$
Residuals	Time (day)
Visual fit	Excellent residuals show no systematic
$\chi^2 \mathrm{err} \%$	× 8.54 × ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
t-test 🔬	$k = \frac{1}{2} \sum_{k=1}^{\infty} \sum_{k$
DissT ₅₀ (days)	
DissT ₉₀ (days)	
Š Š	Fit acceptable. Fit acceptable. Fit acceptable. Fit acceptable. Visual fit is excellent, χ^2 error is low and rate parameter differs significantly from zero. from zero.
Discussion	iii) SPO fit for metabolite acceptable? SPO is considered acceptable and should be used for persistence end- points.
Interpret with care – extraction	alated beyond experimental period
For metabolite M01 nse	FOMC/SFQ Diss $f_{50} = 223$ days, Diss $T_{90} = 742$ days.
or metabolite M02 use	$pOMCSFO$ Diss $T_{50} = 761$ days, Diss $T_{90} = 533$ days.
	Visual fit is excellent, χ^2 error is low and rate parameter differs significantly from zero. iii) SPO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- points. lated beyond efferimental period FOMC/SFO Diss $f_{50} = 223$ days, Diss $T_{90} = 742$ days. FOMC/SFO Diss $f_{50} = 161$ days, Diss $T_{90} = 533$ days.

Appendix 4.1.7.2. Metabolite fitting (M01 and M02)

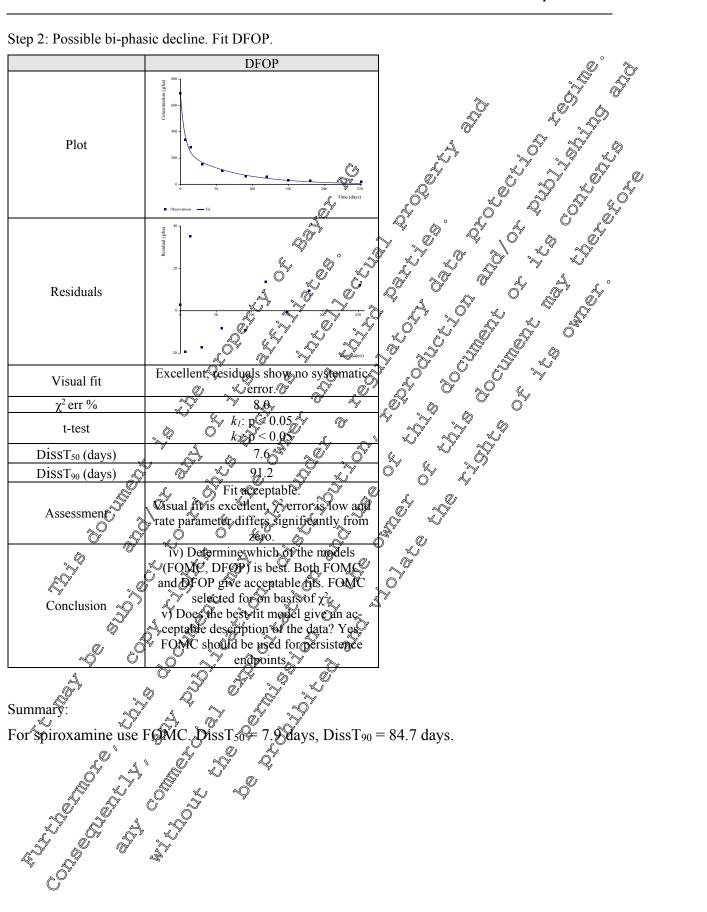


Appendix 4.1.8.Dissipation of spiroxamine in Swisttal-Hohn soil trial no. 40009/2 (KCA
7.1.2.2.1/02 (M-006126-01-1))



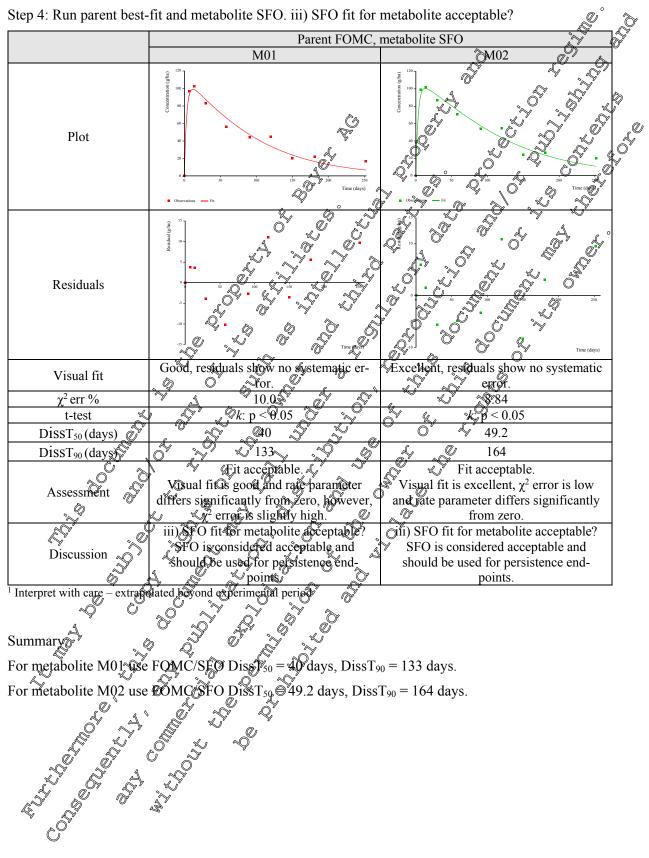






Step 2: Possible bi-phasic decline. Fit DFOP.

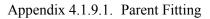


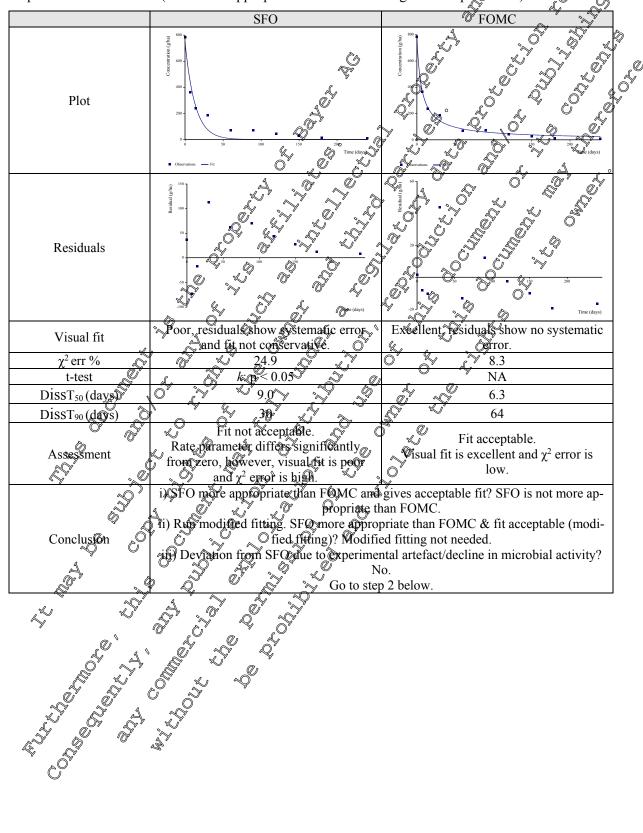


Appendix 4.1.8.2. Metabolite fitting (M01 and M02)

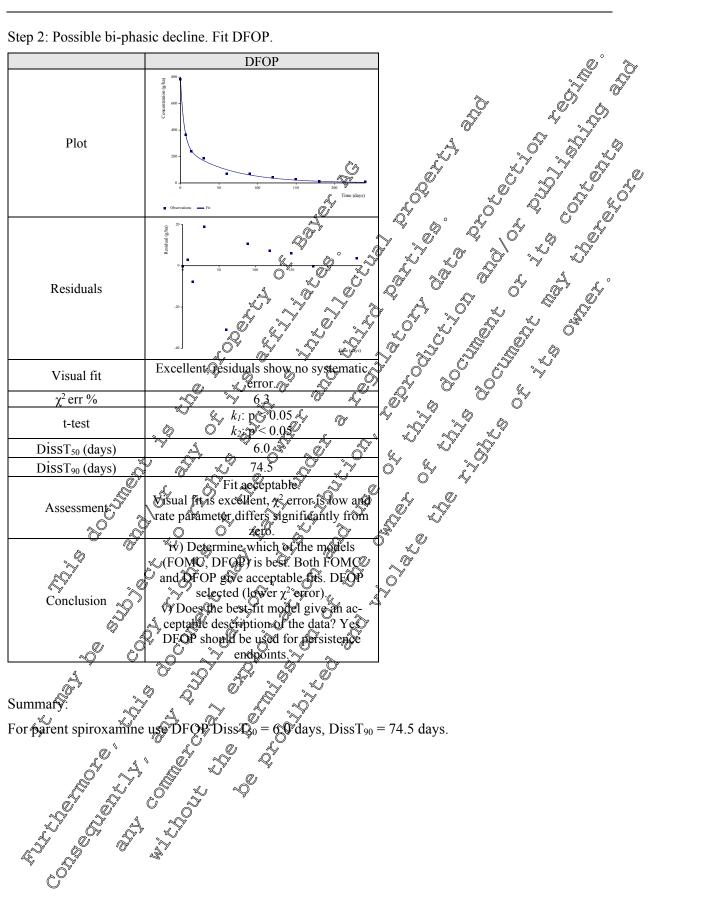


Appendix 4.1.9. Dissipation of spiroxamine in Albig soil trial no. 40010/6 (KCA 7.1.2.2.1/02 (M-006126-01-1))



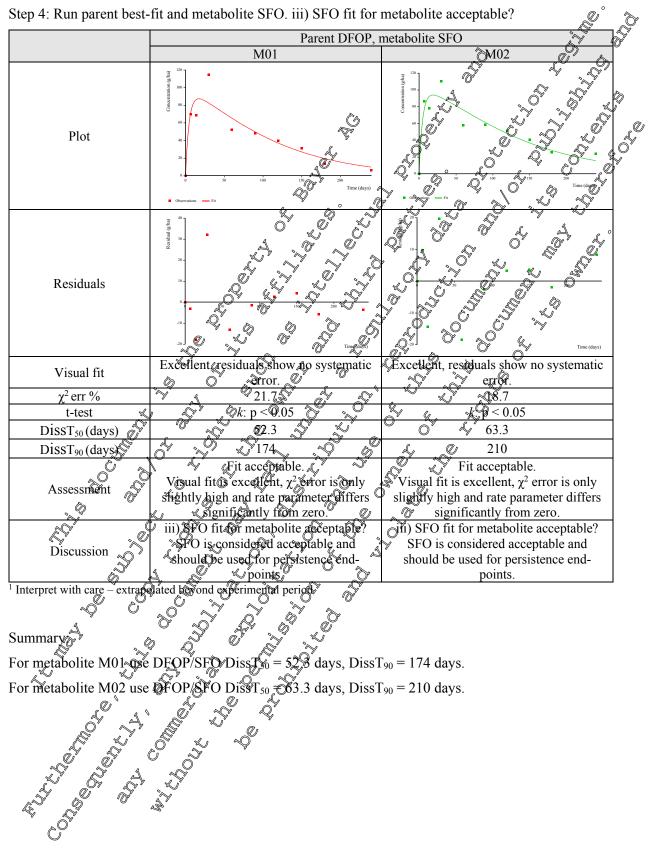






Step 2: Possible bi-phasic decline. Fit DFOP.

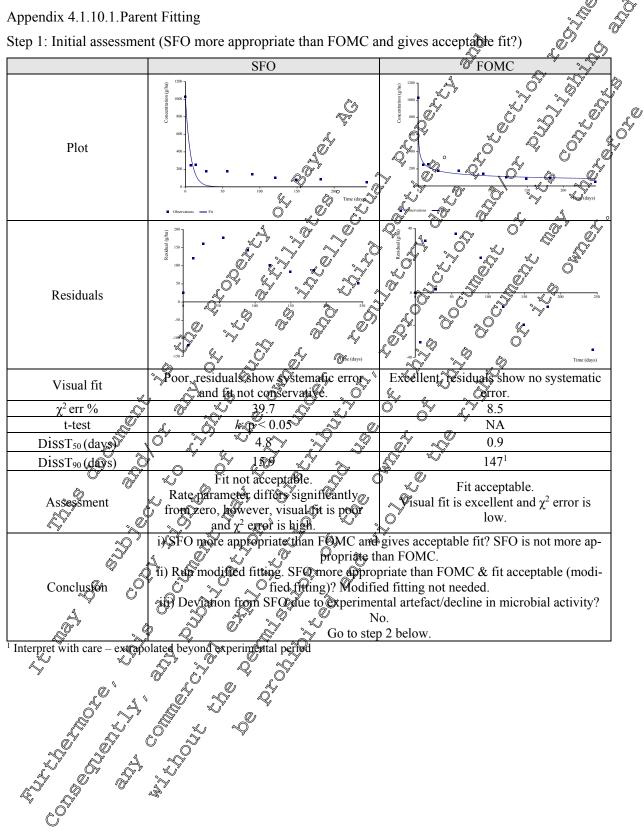




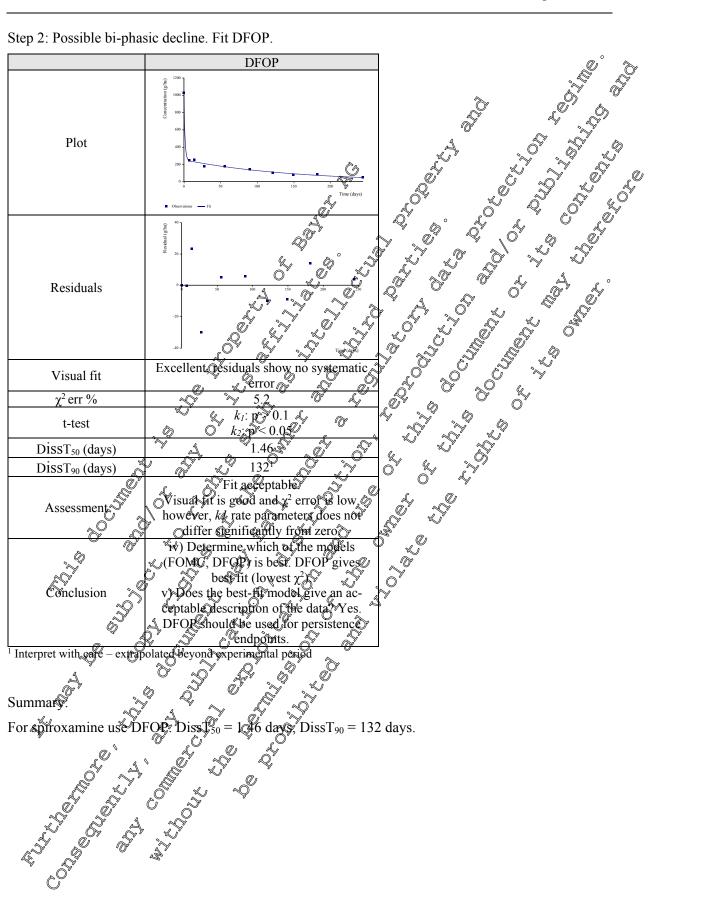
Appendix 4.1.9.2. Metabolite fitting (M01 and M02)



Appendix 4.1.10. Dissipation of spiroxamine in Elm Farm/Thurston soil trial no. 40097/1 (KCA 7.1.2.2.1/03 (M-006127-01-1))

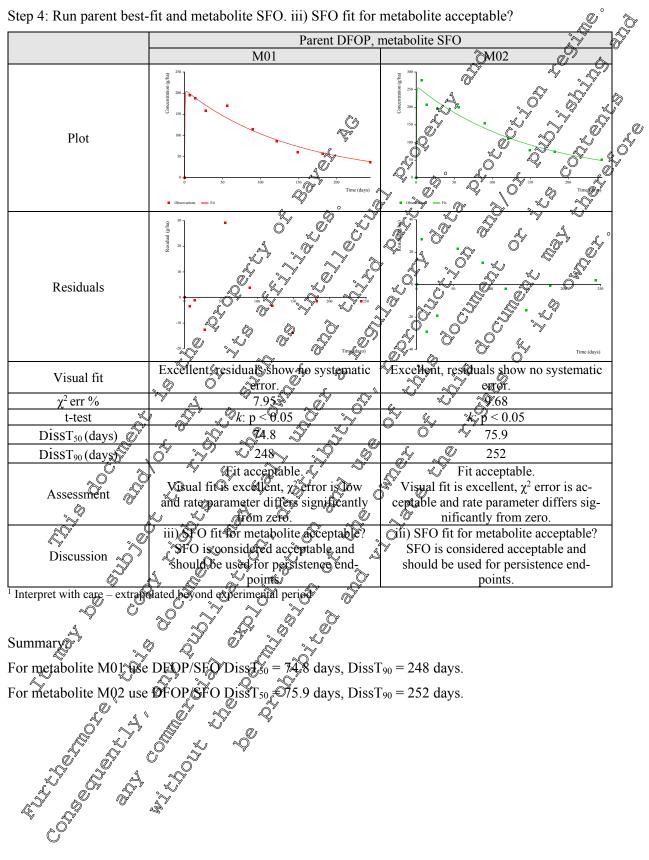






Step 2: Possible bi-phasic decline. Fit DFOP.

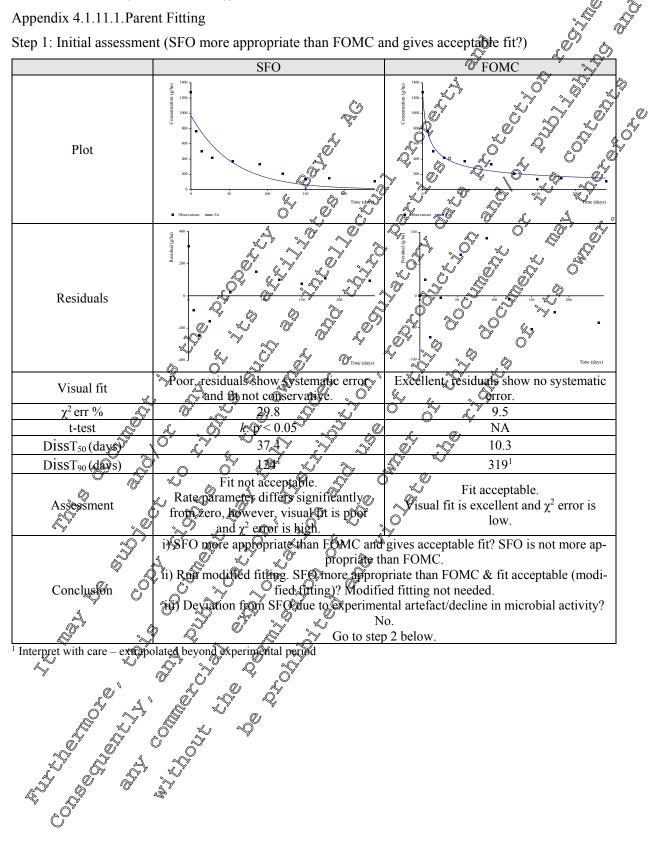




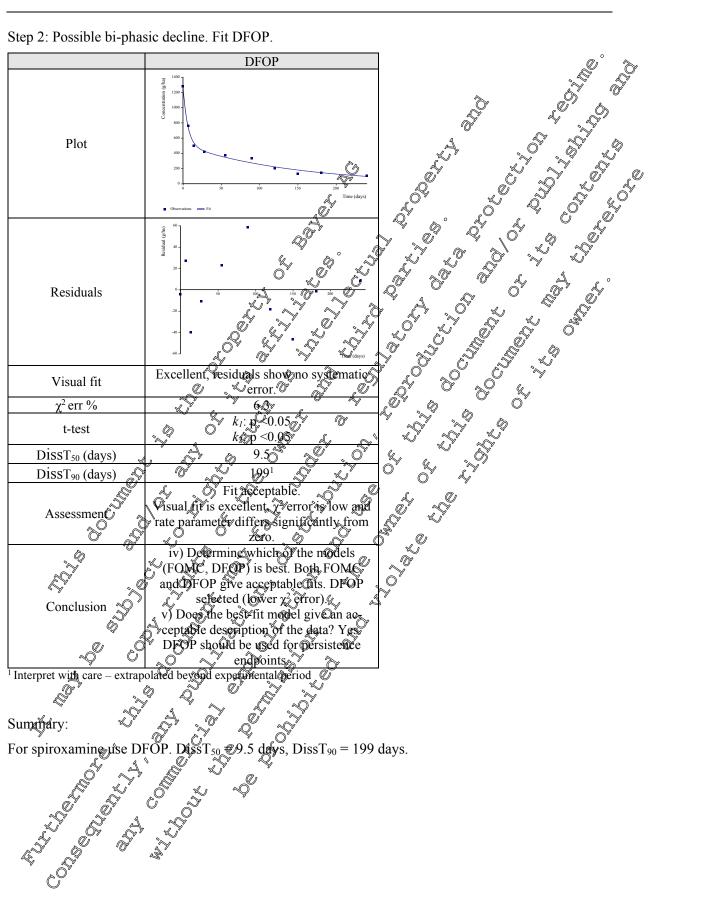
Appendix 4.1.10.2. Metabolite fitting (M01 and M02)



Appendix 4.1.11. Dissipation of spiroxamine in Pakenham soil trial no. 40099/8 (KCA 7.1.2.2.1/03 (M-006127-01-1))

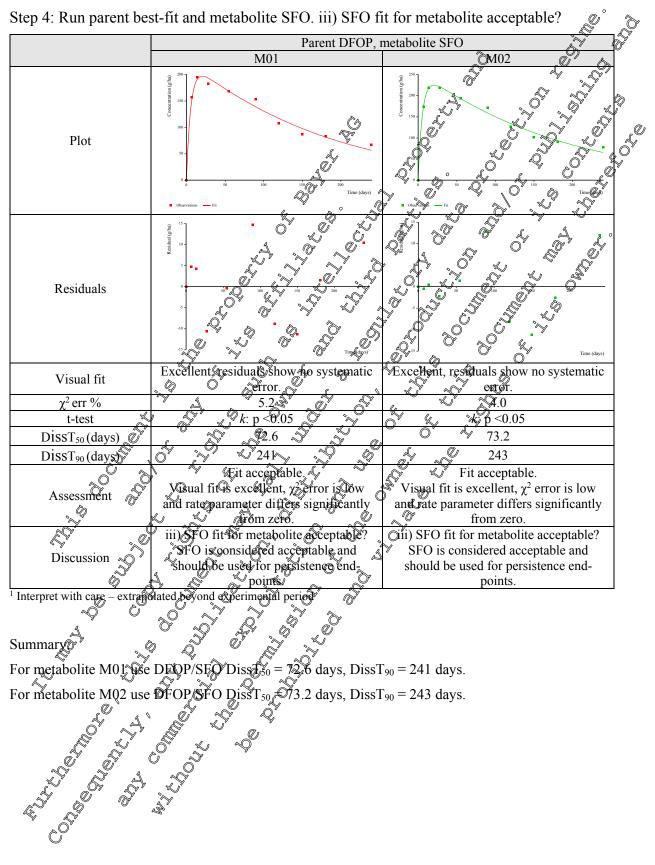






Step 2: Possible bi-phasic decline. Fit DFOP.

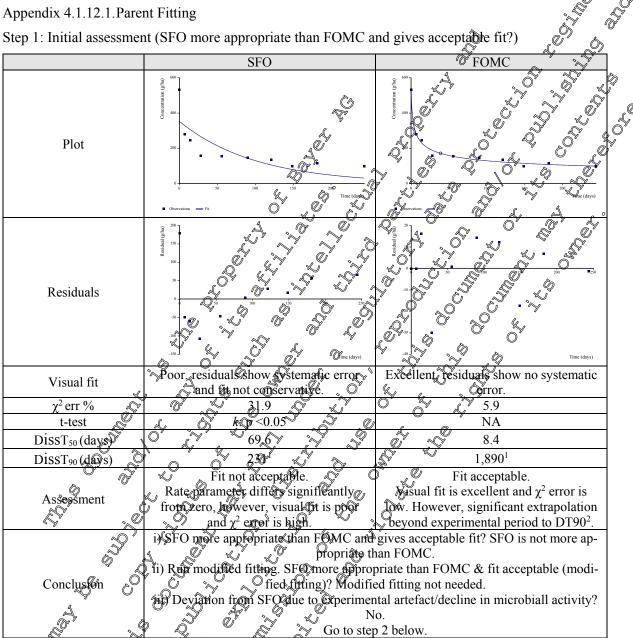


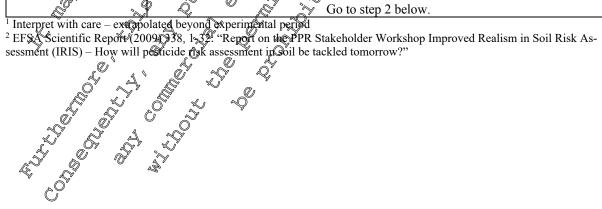


Appendix 4.1.11.2. Metabolite fitting (M01 and M02)

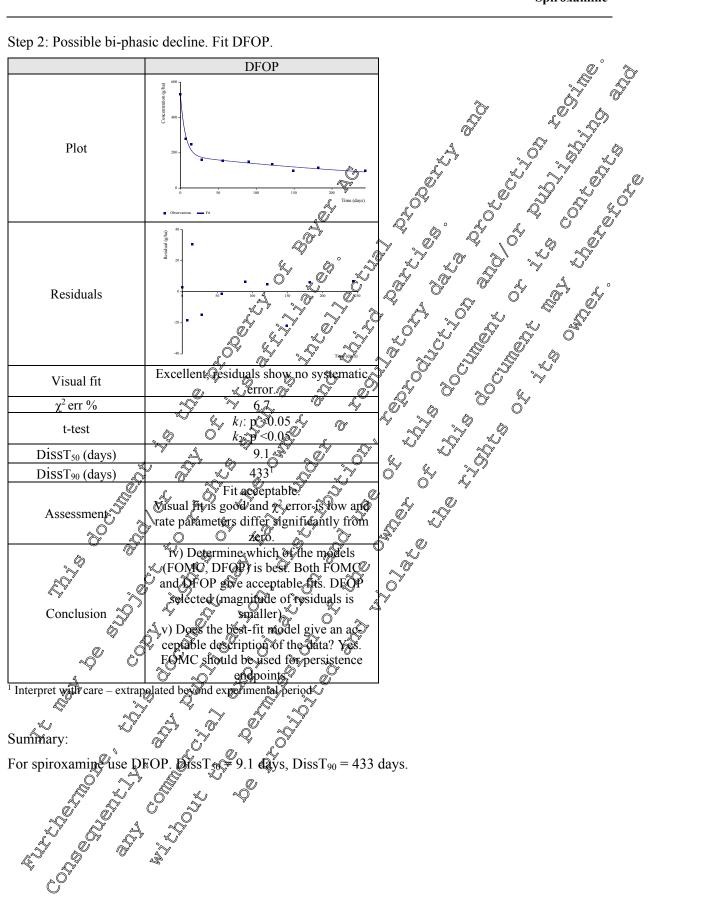


Appendix 4.1.12. Dissipation of spiroxamine in Elm Farm/Thurston soil trial no. 40100/5 (KCA 7.1.2.2.1/03 (M-006127-01-1))



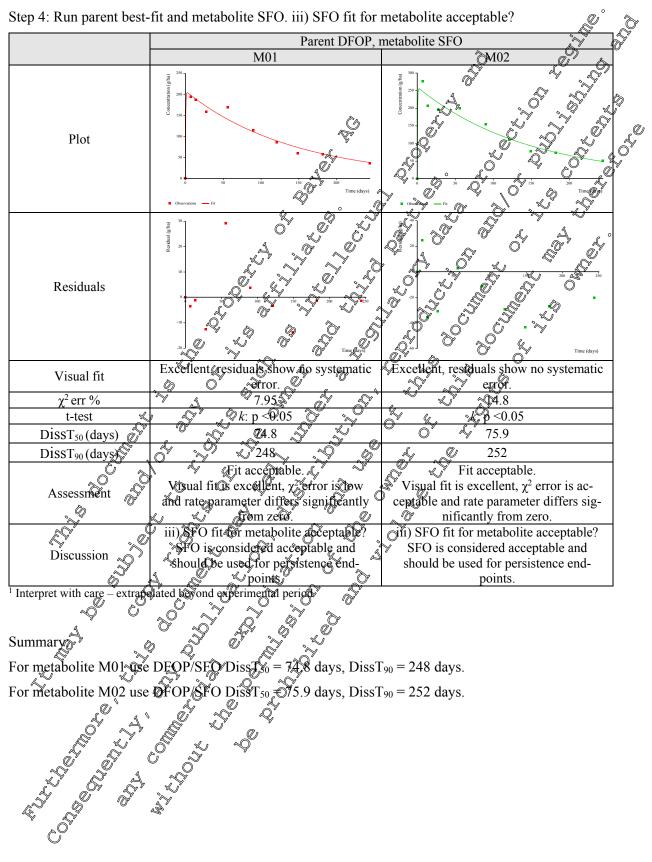






Step 2: Possible bi-phasic decline. Fit DFOP.

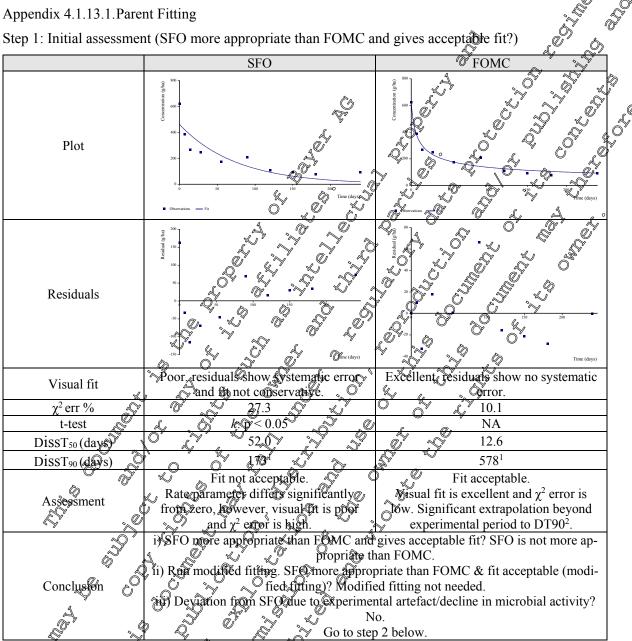


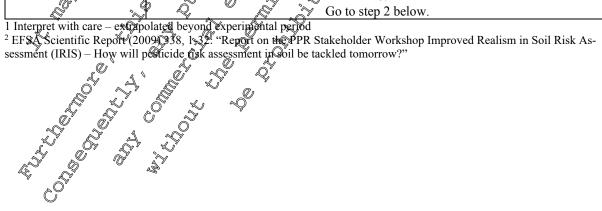


Appendix 4.1.12.2. Metabolite fitting (M01 and M02)

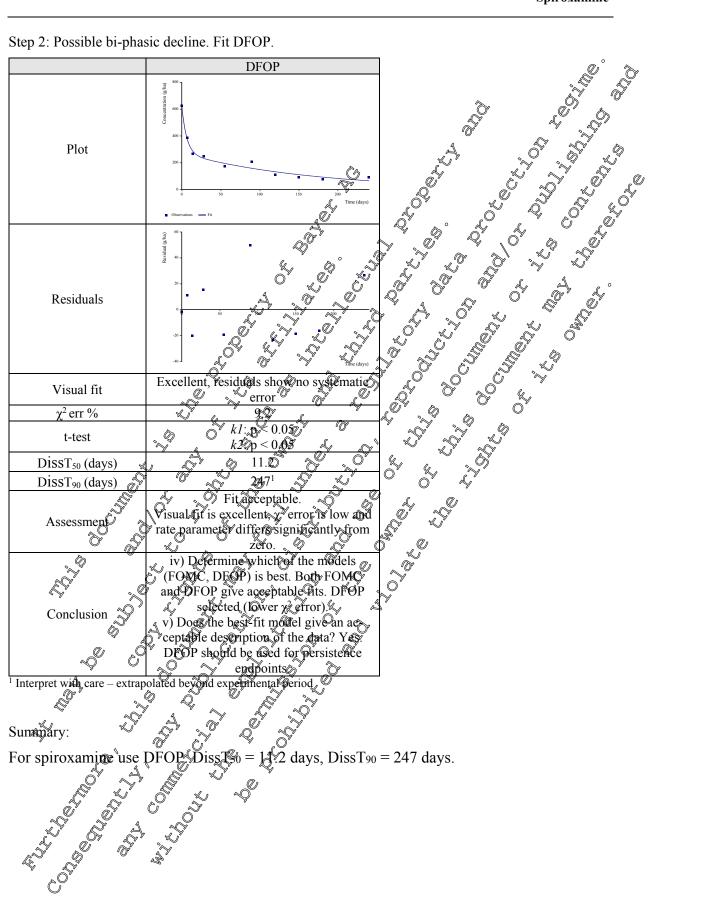


Appendix 4.1.13. Dissipation of spiroxamine in Pakenham soil trial no. 40101/3 (KCA 7.1.2.2.1/03 (M-006127-01-1))









Step 2: Possible bi-phasic decline. Fit DFOP.

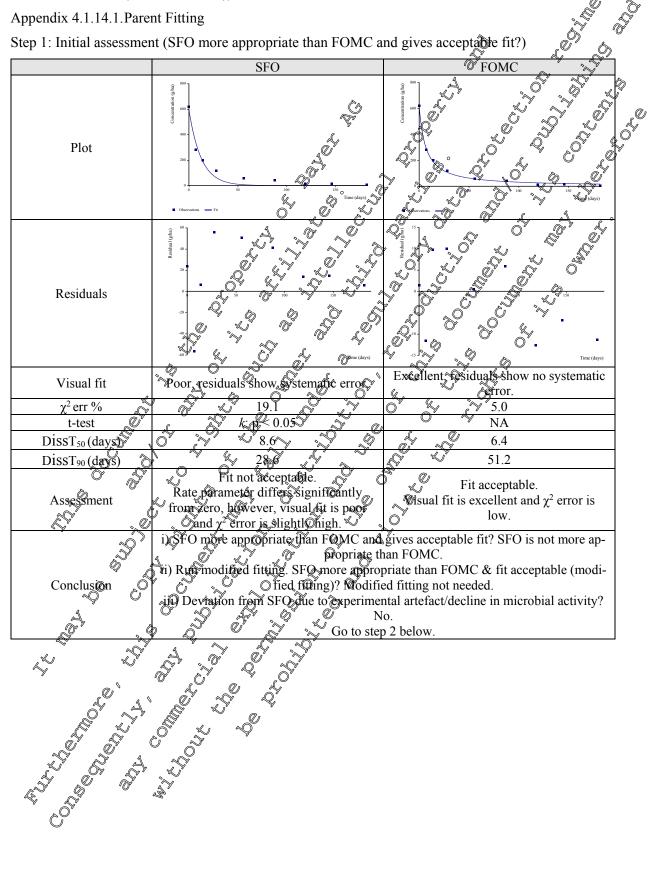


Step 4: Run parent best-	fit and metabolite SFO. iii) SFO fit for	metabolite acceptable?
	Parent DFOP, metabolite SFO	
	M01	M02
Plot	Communications and the second se	
Residuals	Observations - 12 Observations	Q ¹ Q ¹
Visual fit	Good, residuals show no systematic er-	Good residuate show no systematic er-
$\chi^2 \text{err} \%$	× 10.28	L \$ 290.8
t-test 🕺	∞	× (× p < 0.05
DissT ₅₀ (days)	96.8 Å	[♥] [♥] 103
DissT ₉₀ (days)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<i>₹ Q</i> 342 ¹
Assessment	Fit acceptable. Vi@al fit i@good@gerror s acceptable and rate parameter differs significantly from zero.	Fit acceptable. Visual fit is good, χ^2 error is acceptable and rate parameter differs significantly from zero.
Discussion	iii) FO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- points	 SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for persistence end- points.
¹ Interpret with care – extrans	ated by ond experimental period	pomo.
Summary For metabolite M0Que For metabolite M0Que	should be used for persistence end- ated by ond experimental period se DFOP/SFO Diss $P_{0} = 103$ days, I	DissT ₉₀ = 322 days. DissT ₉₀ = 342 days.

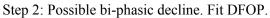
Appendix 4.1.13.2. Metabolite fitting (M01 and M02)

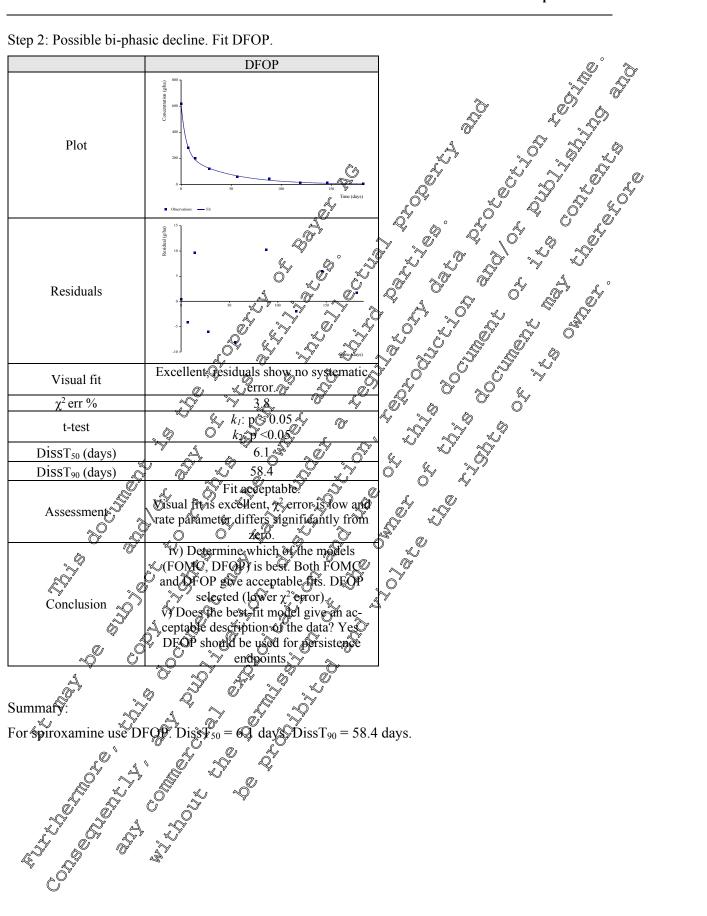


Appendix 4.1.14. Dissipation of spiroxamine in Touffreville soil trial no. 40193/5 (KCA 7.1.2.2.1/03 (M-006127-01-1))









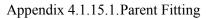


Step 4: Run parent best-	Step 4: Run parent best-fit and metabolite SFO. iii) SFO fit for metabolite acceptable?	
	Parent DFOP, metabolite SFO	
	M01	
Plot	Parent DFOP, metabolite SFO M01 (u) (u) (u) (u) (u) (u) (u) (u) (u) (u	
Residuals	10 10<	
Visual fit	Excellent residuals show no systematic	
$\chi^2 \text{err} \%$	16.4 × × × × × × × × × × × × × × × × × × ×	
t-test 🔬	$ \begin{array}{c} & & & & \\ & & & & \\ & & & & \\ & & & & $	
DissT ₅₀ (days)		
DissT ₉₀ (days)	1 175.2 175.2 TO 1 1 10 70.7	
	Fit acceptable. Fit acceptable. Visual fit is exceptable. Visual fit is exceptable. Visual fit is exceptable. Visual fit is exceptable. visual fit is exceptable. Visual fit is excellent, χ ² error is acceptable and rate parameter differs significantly from zero. visual fit is exceptable. Visual fit is excellent, χ ² error is acceptable and rate parameter differs significantly from zero. visual fit is exceptable. Visual fit is excellent, χ ² error is acceptable and rate parameter differs significantly from zero. visual fit is exceptable. Visual fit is excellent, χ ² error is acceptable and rate parameter differs significantly from zero. visual fit is exceptable. visual fit is exceptable. visual fit is	
Summary:	DFOQSFO DissT $= 22$ 6 days, DissT ₉₀ = 75.2 days.	
For pretabolite M02 ase	Fit acceptable. Visual fit's excellent, χ^2 error is acceptable and rate parameter differs sig- nificantly from zero. iii) SPO fit for metabolite acceptable? SPO is considered acceptable and should be used for persistence end- points. DFOP/SFO DissT ₅ = 22 6 days, DissT ₉₀ = 75.2 days. DFOP/SFO Diss $\Psi_{50} = 2V.3$ days, DissT ₉₀ = 70.7 days.	

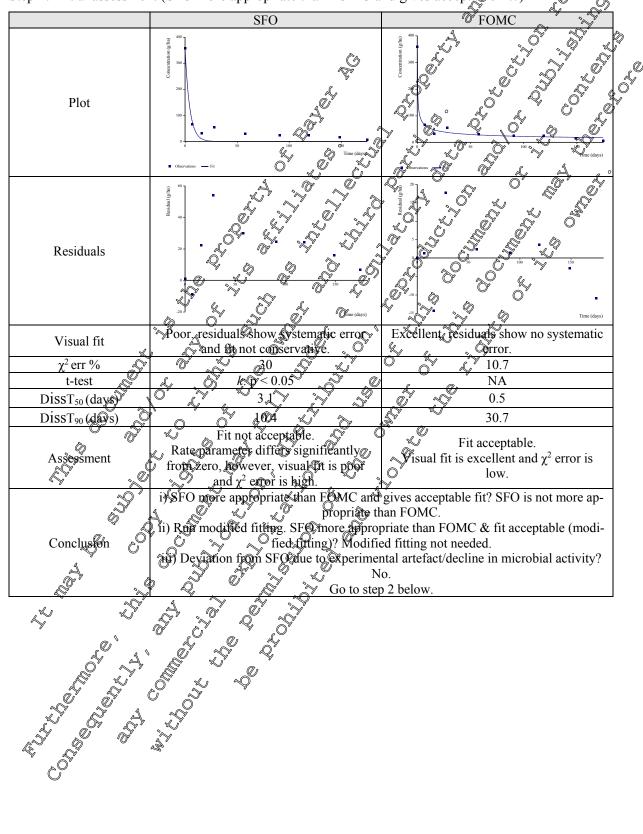
Appendix 4.1.14.2. Metabolite fitting (M01 and M02)



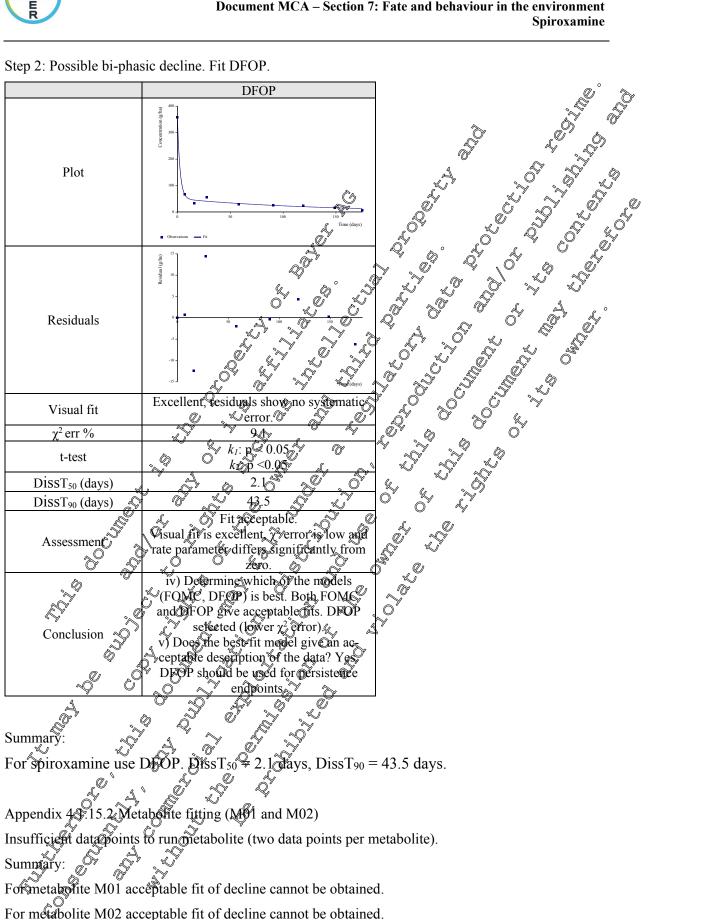
Appendix 4.1.15. Dissipation of spiroxamine in Laudun soil trial no. 40198/6 (KCA 7.1.2.2.1/04 (M-006128-01-1))



Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)



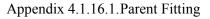




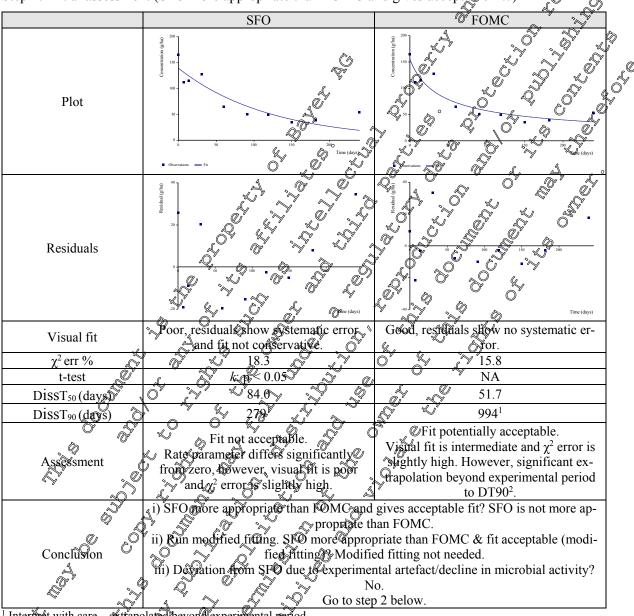
Step 2: Possible bi-phasic decline. Fit DFOP.

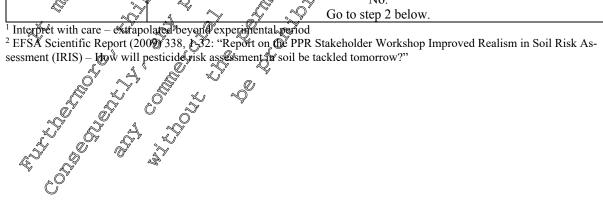


Appendix 4.1.16. Dissipation of spiroxamine in Filetto soil trial no. 40424/1 (KCA 7.1.2.2.1/04 (M-006128-01-1))

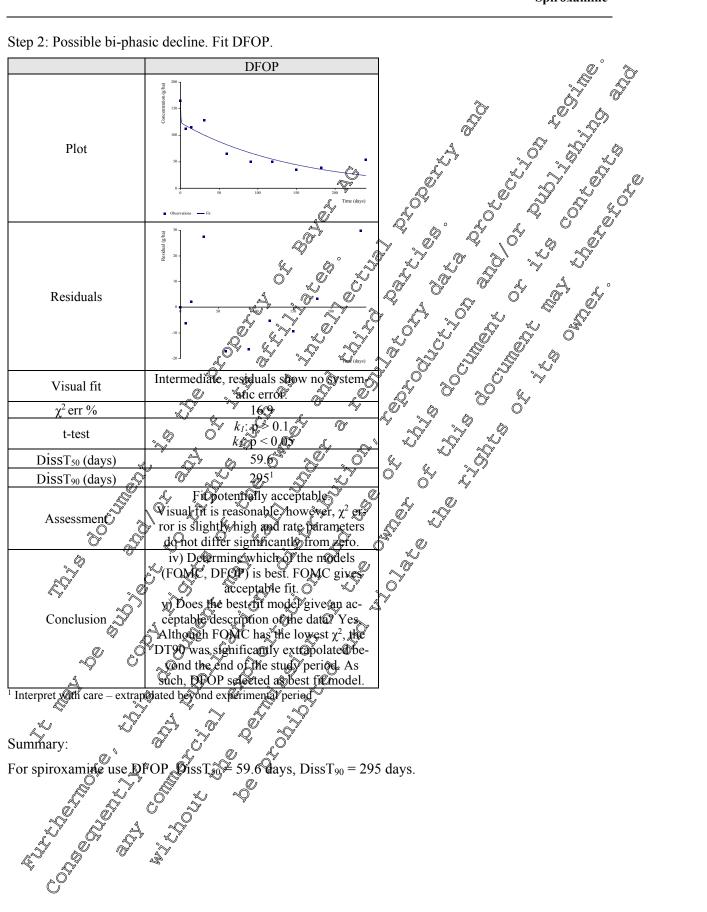


Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)



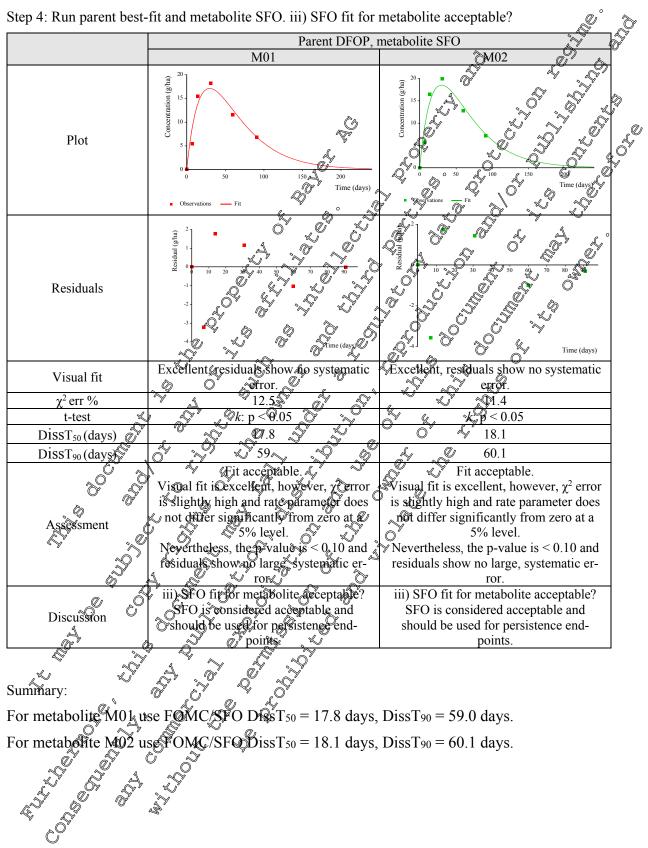






Step 2: Possible bi-phasic decline. Fit DFOP.

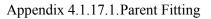




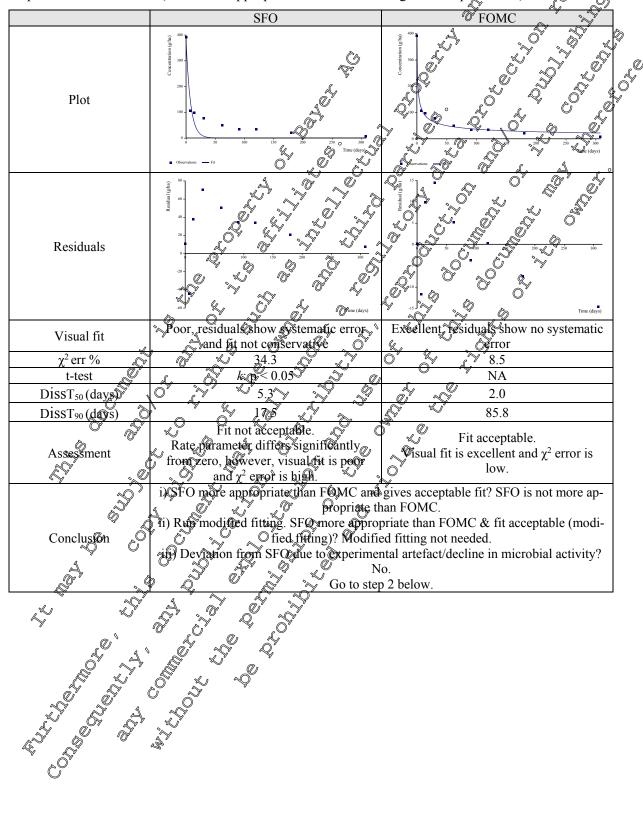
Appendix 4.1.16.2. Metabolite fitting (M01 and M02)



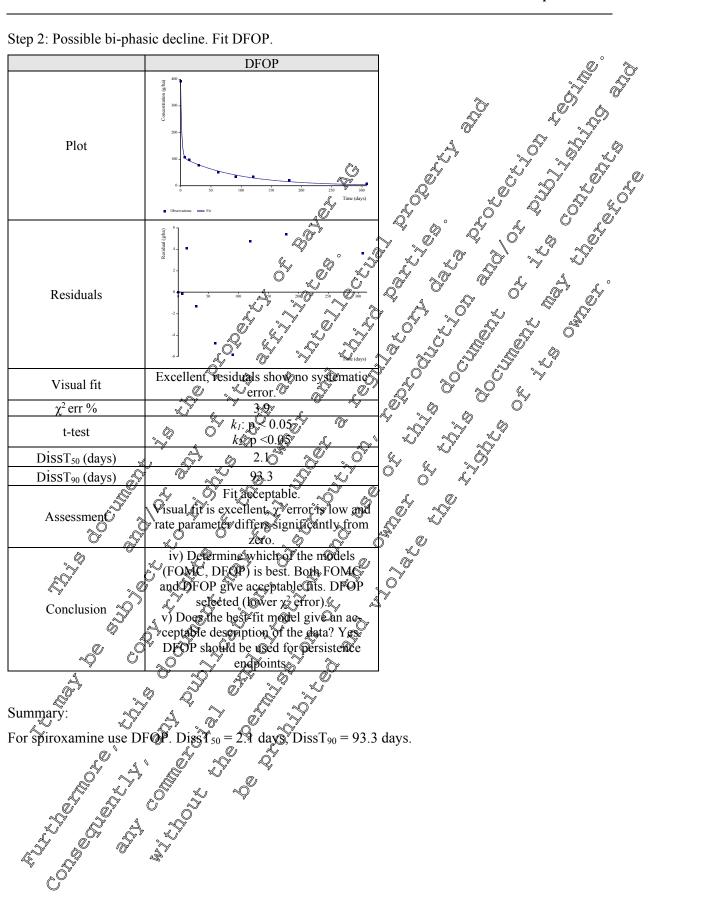
Appendix 4.1.17. Dissipation of spiroxamine in Laudun soil trial no. 50135/2 (KCA 7.1.2.2.1/05 (M-006129-01-1))



Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)

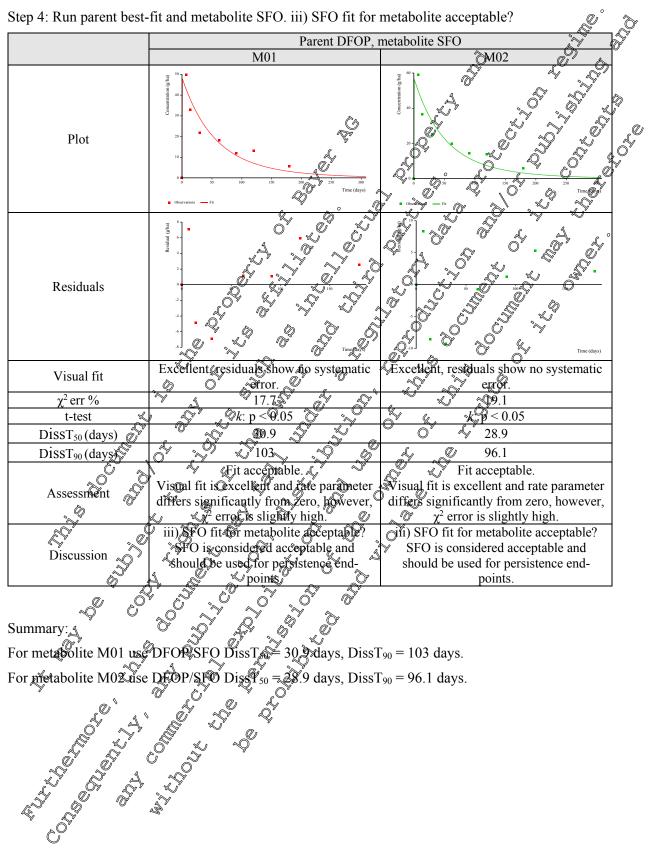






Step 2: Possible bi-phasic decline. Fit DFOP.

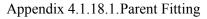




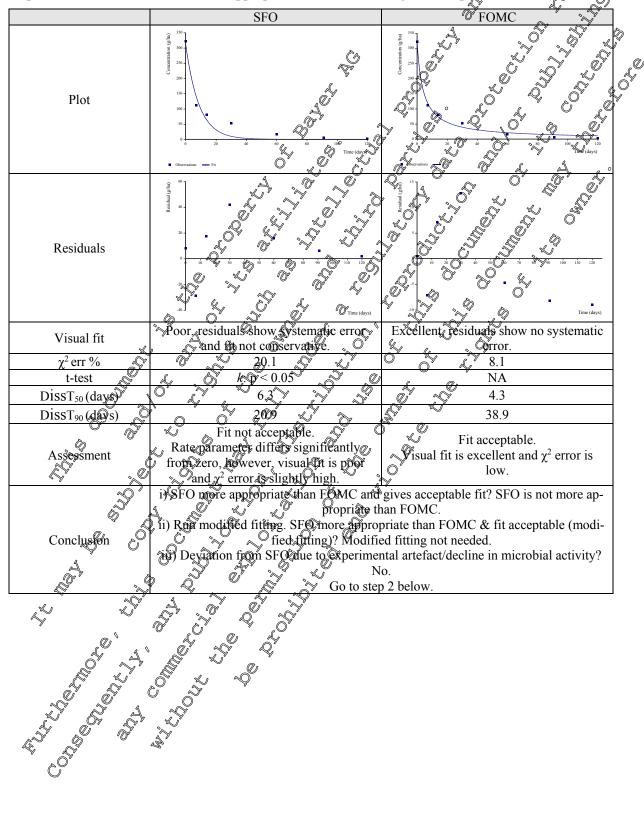
Appendix 4.1.17.2. Metabolite fitting (M01 and M02)



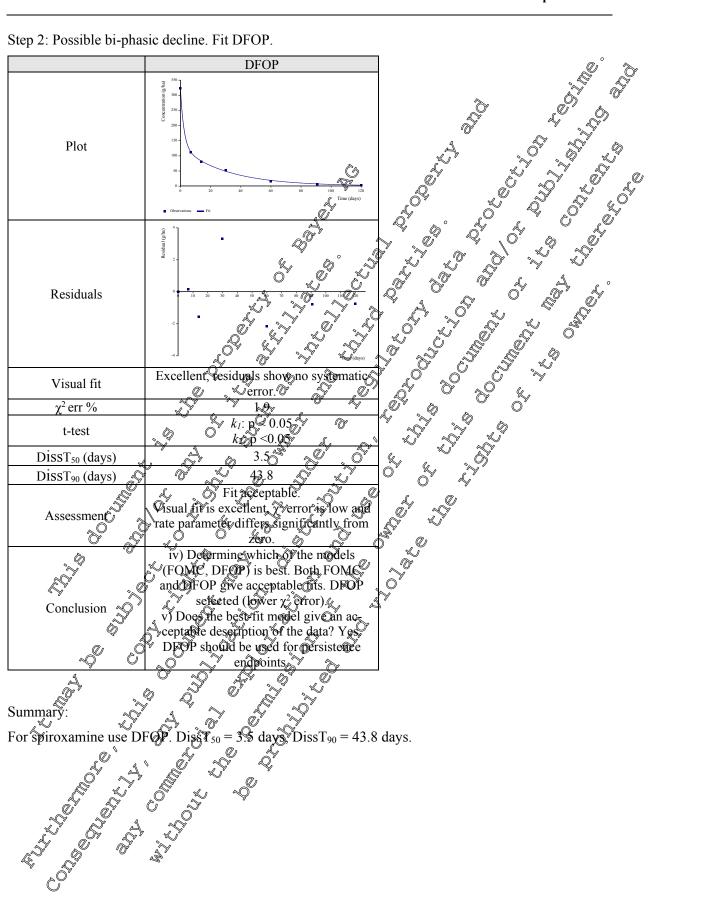
Appendix 4.1.18. Dissipation of spiroxamine in Nogarole Rocca soil trial no. 50136/0 (KCA 7.1.2.2.1/05 (M-006129-01-1))



Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)

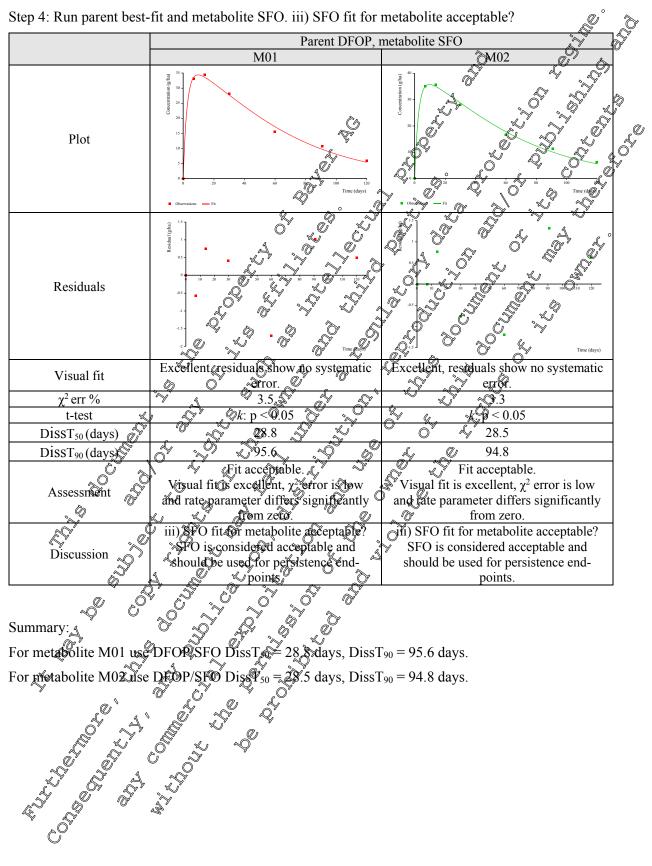






Step 2: Possible bi-phasic decline. Fit DFOP.





Appendix 4.1.18.2. Metabolite fitting (M01 and M02)

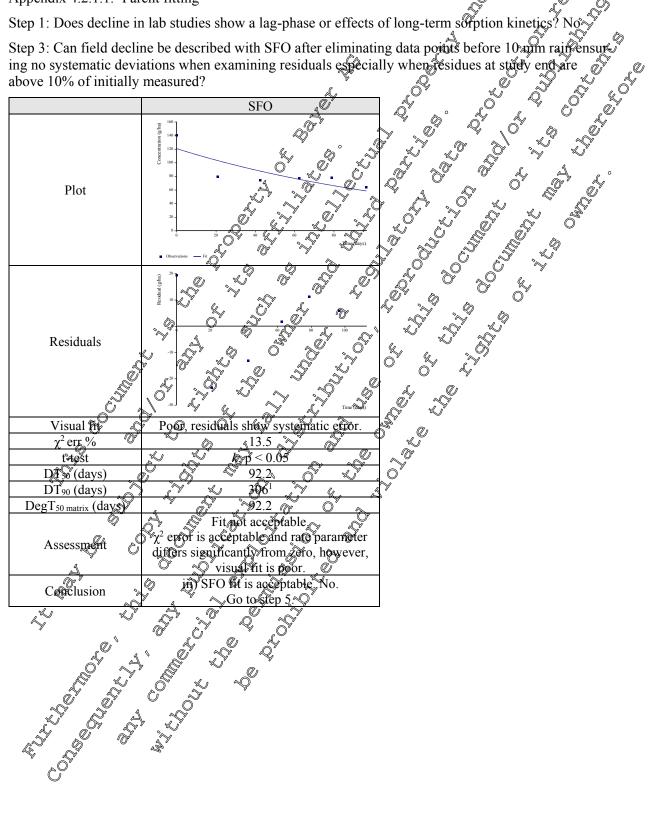


Appendix 4.2: Kinetic evaluation for modelling endpoints

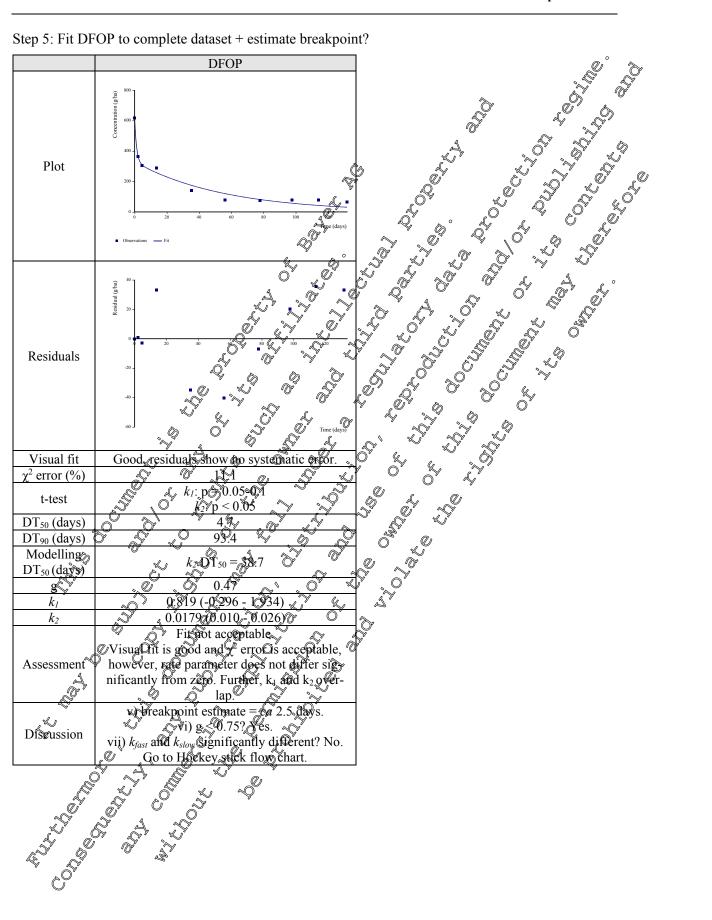
Degradation of spiroxamine in Höfchen soil trial no. 30122/1 (KCA 7.1.2.2.1/01 Appendix 4.2.1. 006116-01-1))

Appendix 4.2.1.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorption kinetics?



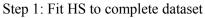


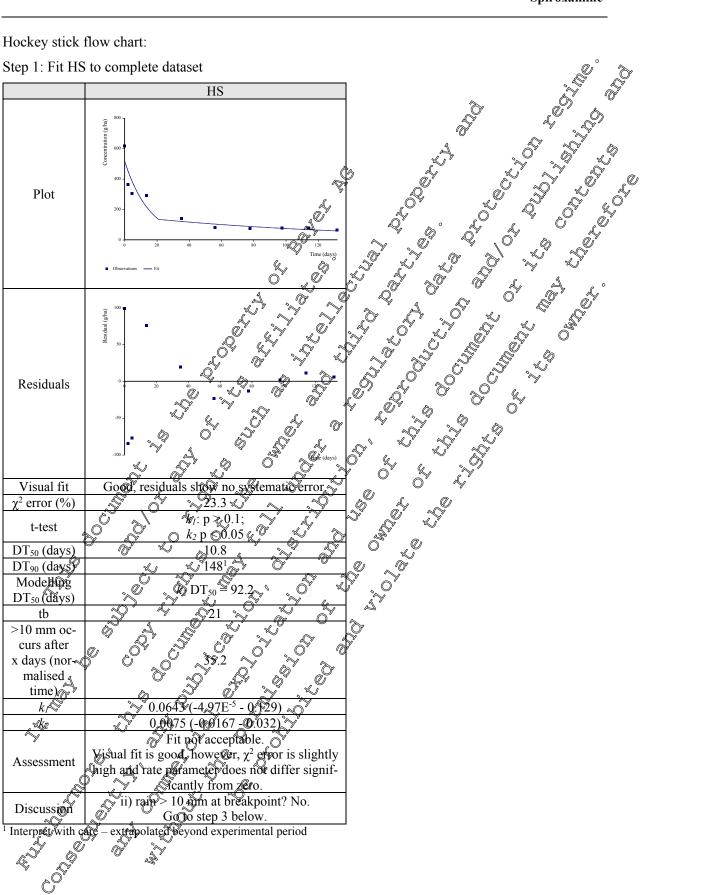


Step 5: Fit DFOP to complete dataset + estimate breakpoint?

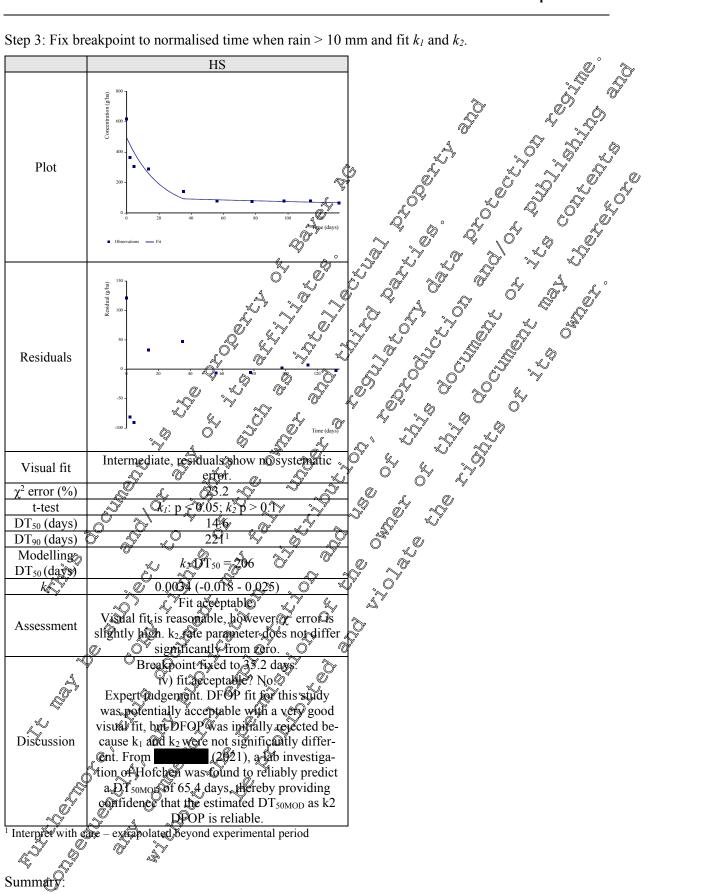


Hockey stick flow chart:









Step 3: Fix breakpoint to normalised time when rain > 10 mm and fit k_1 and k_2 .

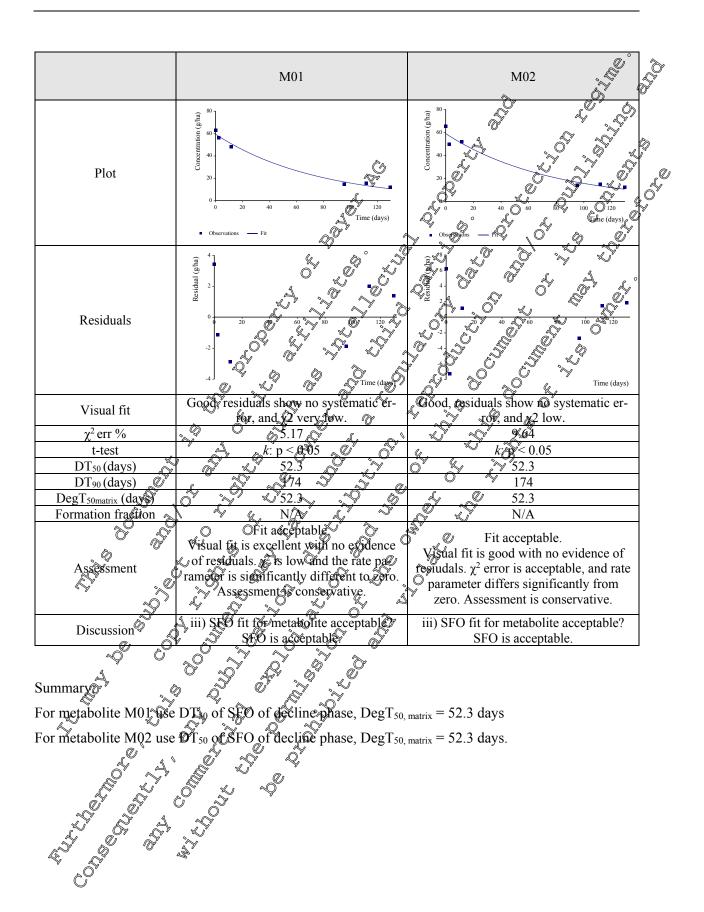
For spiroxamine modelling, use DFOP $DegT_{50,matrix}$ based on k_2 parameter = 38.7 days.



tep 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		
	M01	M02
Plot	Concentration (h)	M02 4 4 4 4 4 4 4 4 4 4 4 4 4
Residuals	• Otherwises - Fi	
Visual fit	Intermediate, residuals from potential Systematic error, and final three times Spoints are underestimated	Intermediate, residuals show potential systematic error and final three time points are underestimated
$\chi^2 \text{ err } \%$	10°	0 0 ⁹ 4 17.3
t-test	3077	k: p < 0.05
$\frac{\text{DT}_{50} (\text{days})}{\text{DT}_{90} (\text{days})} $		124
DegT _{50matrix} (days)	30.7 2 2	<i>Q</i> 37.3
Formation fraction	A.N/A	N/A
	Visual fit is intermediate, and final three time points underestimated. χ^2 error is Δ	Fit not acceptable. Visual fit is intermediate, and final three time points underestimated. χ^2 error is
Assessment	significantly for zero. However, the fi-	significantly from zero. However, the fi-
	nal 3 timepoints are raised versus the	nal 3 timepoints are raised versus the
~~~ U	wher data raising a data qualitorssue.	other data raising a data quality issue.
	Try a modified SFO with removal of in-	Try a modified SFO with removal of in-
<u> </u>	iii) SEO Stafor matrix ali Constant 1	termediate timepoints.
Discussion	SFO is not considered acceptable but potentially impacted by data quality	iii) SFO fit for metabolite acceptable? SFO is not considered acceptable.
	<ul> <li>acceptable, and rate parameter differs, significantly from zero. However, the find of individual to its are raised versus the other data raising a data qualitorissue. Try a and ified SFO, with removal of individual to its are raised versus to the other data raising a data qualitorismu.</li> <li>Try a and ified SFO, with removal of individual to its are raised versus to the other data raising a data qualitorismu.</li> <li>SFO fir for metabolite acceptable?</li> <li>SFO fir for metabolite acceptable but potentially impacted by data quality.</li> </ul>	

Appendix 4.2.1.2. Metabolite fitting (M01 and M02)







Appendix 4.2.2. Degradation of spiroxamine in Laacher Hof soil trial no. 30124/8 (KCA 7.1.2.2.1/01 (M-006116-01-1))

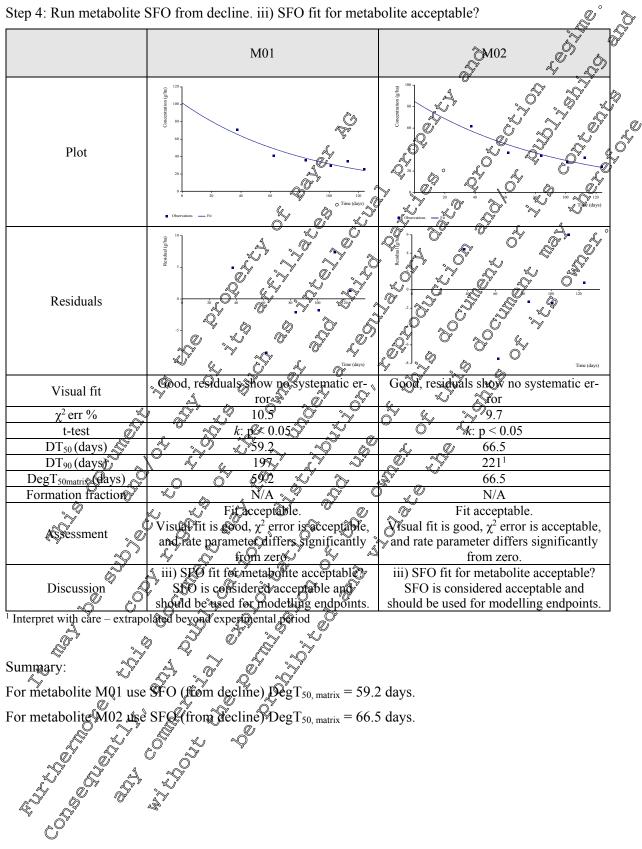
Appendix 4.2.2.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorror kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensuring no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?

above 10% of initially	measured?
	SFO SFO
Plot	por line of the second
Residuals Visual fit $\chi^2 \text{ err } \%$	
Visual fit	Good, residuals show no systems c errog
$\chi^2 \operatorname{err} \%$	$\sqrt{\frac{10.1}{2}}$
t-test	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
DT ₅₀ (days) O DT ₂₀ (days)	$\frac{44.1}{44.1}$
DegTsQ _{iatrix} (days)	$\frac{1}{2} \xrightarrow{4} 146^{1} \xrightarrow{6} 2$
	Fit acceptables a fr
Assessment	44.1 44.1 44.1 Fit acceptable Visual fit is good, $\chi^2$ error is acceptable and rate parameter differs significantly fit is acceptable. Yes.
Concluigon	nii) SPO fit is acceptable. Yes
Conclusion	Use the Deg 30 matrice
' Interpret with care – extra	splated beyond experimental periods
Summary:	
For spiroxamine use §	$\operatorname{KO}\operatorname{Deg}_{150\mathrm{max}} = 44.\mathrm{Q}$ days.
	44.1         Fit acceptable         visual fit is good, /2 errors acceptable         and rate parameter differs significant()         fii) SPO fit is acceptable. Yes.         iv) Use the Deg Tomatric         polated becomd experimental period





Appendix 4.2.2.2. Metabolite fitting (M01 and M02)

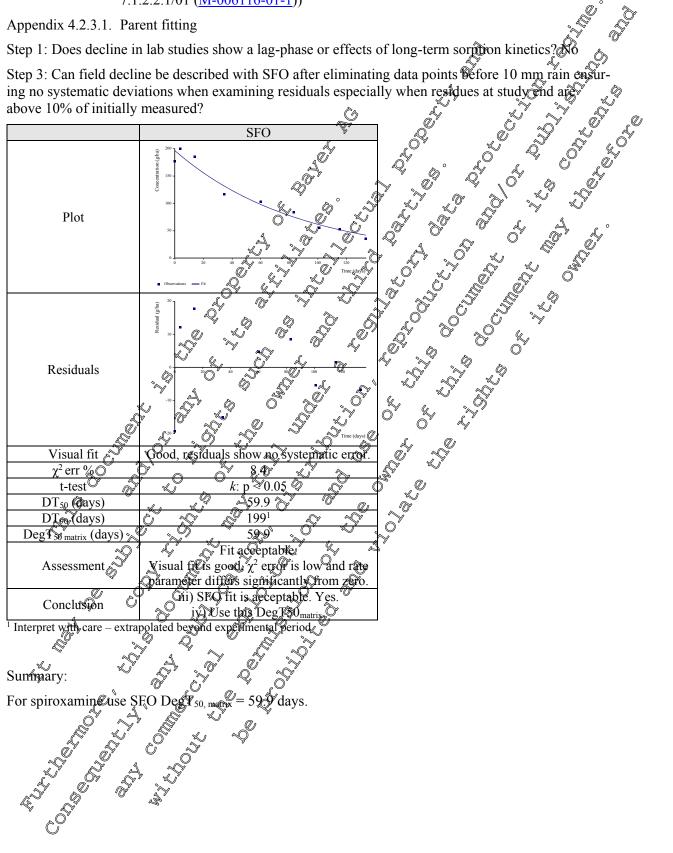


Degradation of spiroxamine in Elm Farm/Thurston soil trial no. 30262/7 (KCA Appendix 4.2.3. 7.1.2.2.1/01 (M-006116-01-1)) 

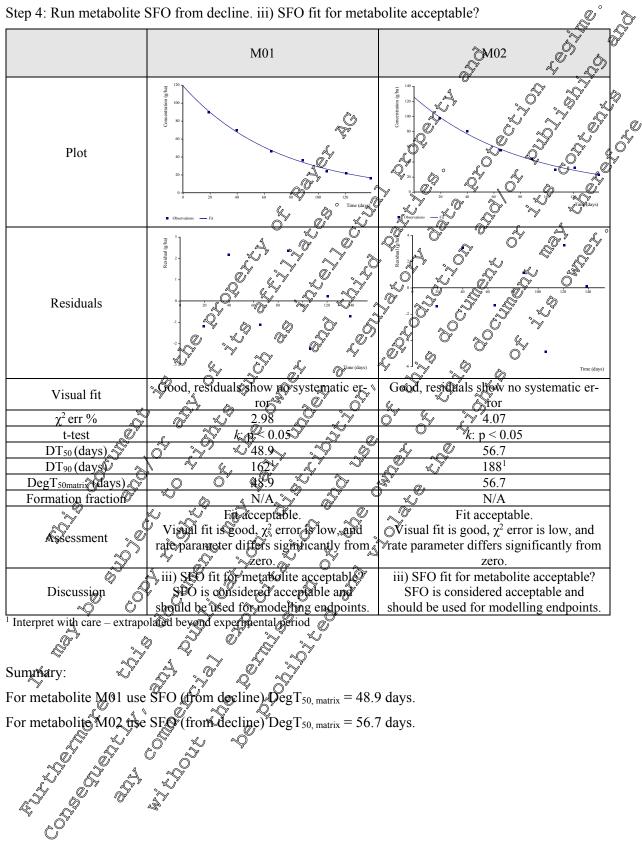
Appendix 4.2.3.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorror kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensur-ing no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?







Appendix 4.2.3.2. Metabolite fitting (M01 and M02)



Appendix 4.2.4. Degradation of spiroxamine in Pakenham soil trial no. 30263/5 (KCA 7.1.2.2.1/01 (M-006116-01-1))

Appendix 4.2.4.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorphion kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensuring no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?

above 10% of initially	measured?	
	SFO	
Plot	measured? SFO SFO (f) (f) (f) (f) (f) (f) (f) (f) (f) (f)	
Residuals	(u)	
Visual fit	Cood, residuals show no systematic error	
$\chi^2 \text{ err } \%$ t -test $DT_{50} \text{ (days)}$		
t-test	$\sim 0 k: p < 0.05 $	
DT ₅₀ (days) DT ₉₀ (days)	43.6 × 6	, Ö
Deg Tagmatrix (days)		
Assessment	104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 104 105 $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$ $145^{10}$	
Conclusion	0 iii) SFO fit is acceptable. Yes.	
¹ Interpret with care – extra	polated beyond experimental period	
Summary:		
For spiroxamine use	FO Deg $T_{50, \text{gravity}} = 43.6$ days.	
	FO DegT ₅₀ matrix = 43.6 days.	



Step 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		
	M01	
Plot		bonne acceptable?
Residuals		
Visual fit	Intermediate, residuals show no system-	Interprediate, residuals show no system-
$\chi^2  \mathrm{err}  \%$		<u>\$</u>
t-test	[∞] [∞] k: pg 0.05 [∞] √	○ (j. p < 0.05
DT ₅₀ (days)	<u>k</u> <u>6</u> ³ <u>6</u> ³ <u>6</u> ³ <u>6</u> ³ <u>6</u>	66.6
DT ₉₀ (days)		221 ¹
DegT _{50matrix} (days)		66.6 N/A
Formation faction		N/A
Assessment	<ul> <li>Fit acceptable.</li> <li>Visual fit is acceptable, χ² error is only sligbdy high, and rate parameter differs</li> <li>Significamly from zero </li> </ul>	Fit acceptable. Visual fit is accetpable, $\chi^2$ error is only Rightly high, and rate parameter differs significantly from zero.
J.	iii) SFO fit for metabolite acceptable?	iii) SFO fit for metabolite acceptable?
Discussion	SFO is considered acceptable and should be used for modelling endpoints.	SFO is considered acceptable and
	should be used for modelling endpoints.	should be used for modelling endpoints.
Summary:	stro (decline) DegT matrix = 59.5 days	5.
For metabolite	SEQuercline Decline $= 66.6  days$	2
For metaboliterivio 2 use	SFO (decline) $\text{DegT}_{50 \text{ matrix}} = 59.5 \text{ days}$ SFO (decline) $\text{DegP}_{50, \text{ matrix}} = 66.6 \text{ days}$	5.

## Appendix 4.2.4.2. Metabolite fitting (M01 and M02)

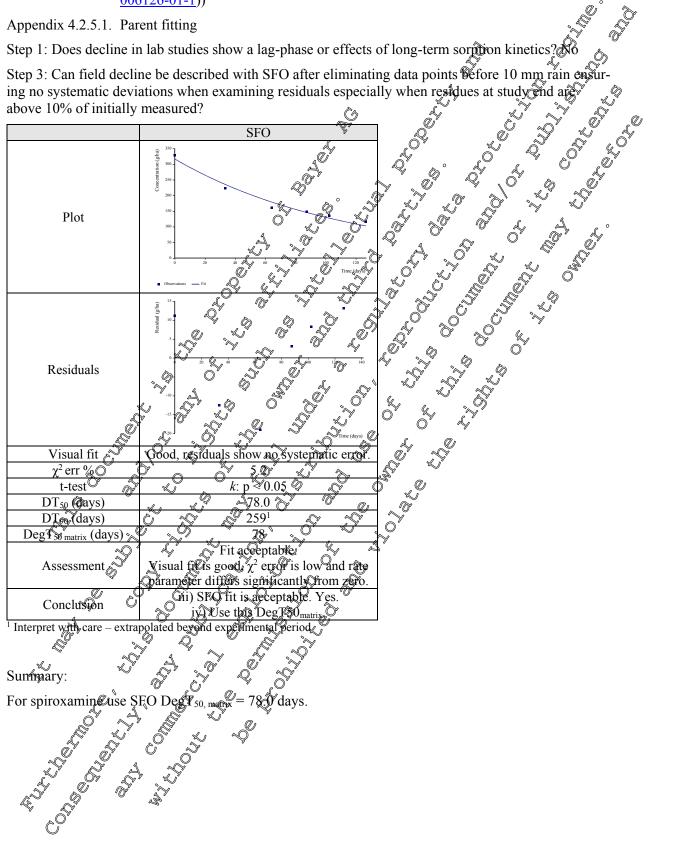


Degradation of spiroxamine in Höfchen soil trial no. 40006/8 (KCA 7.1.2.2.1/02 (M-Appendix 4.2.5. 006126-01-1)) 

Appendix 4.2.5.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensur-ing no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?





Step 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		
	M01	CM02
Plot		MO2
Residuals	Contraction of the second seco	
Visual fit	• Good, residuals show no systematic er-	Good, residuals show no systematic er- ror and fit is conservative
$\begin{array}{c c} \chi^2  \text{err } \% \\ \hline t \text{-test} \\ DT_{50}  (\text{days}) \\ \hline DT_{90}  (\text{days}) \\ \hline DegT_{50 \text{matrix}}  (\text{mays}) \\ \hline Formation fraction \\ \end{array}$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	6.32
Discussion	K K Fit acceptable.	Fit acceptable. Visual fit is good, $\chi^2$ error is low, and rate parameter differs significantly from zero.
	should be aged for modelling and points	iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for modelling endpoints.
¹ Interpret with care – extrapo Summary: For metabolite MQ1 use For metabolite M02 use	SFO (decline) Deg T ₆ , _{matrix} = 99.3 days SFO (decline) Deg T ₆ , _{matrix} = 112 days	

Appendix 4.2.5.2. Metabolite fitting (M01 and M02)

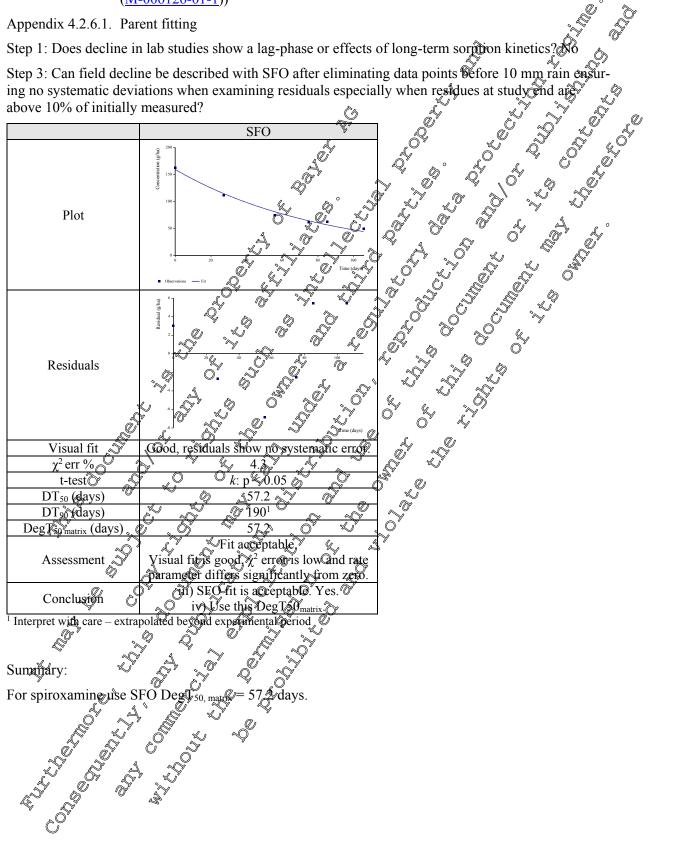


Degradation of spiroxamine in Laacher Hof soil trial no. 40007/6 (KCA 7.1.2.2.1/02 Appendix 4.2.6. (M-006126-01-1)) dig of

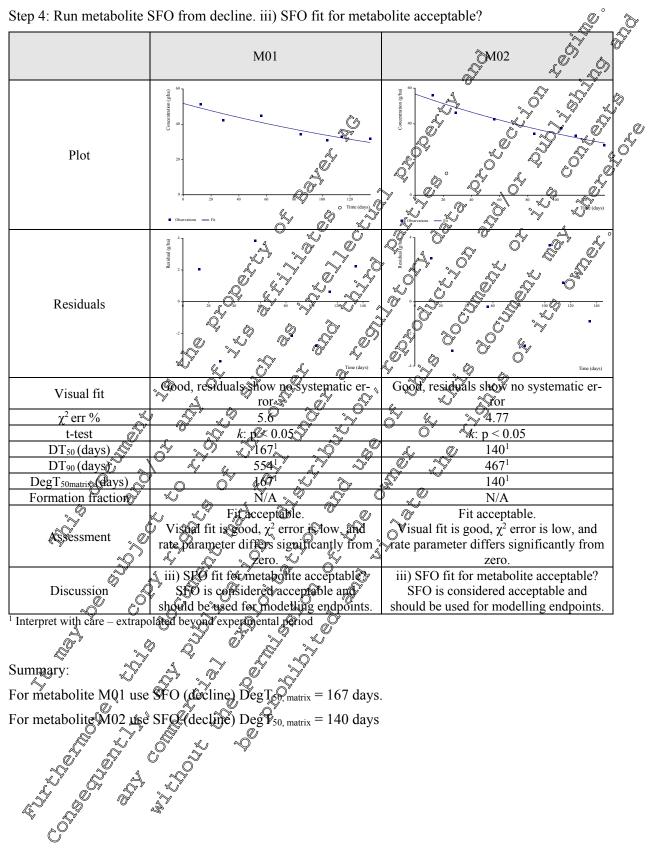
Appendix 4.2.6.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensur-ing no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?







Appendix 4.2.6.2. Metabolite fitting (M01 and M02)



Appendix 4.2.7. Degradation of spiroxamine in Maasen soil trial no. 40008/4 (KCA 7.1.2.2.1/02 (M-006126-01-1))

Appendix 4.2.7.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorption kinetics?

above 10% of initially	
	SFO SFO
Plot	$\frac{\operatorname{Measured}}{\operatorname{SFO}}$
Residuals Visual fit	
Visual fit	Good, residuals show no systematic error.
$\chi^2 \text{ err } \% \bigcirc$	
t-test	$\frac{\sqrt{5} + \frac{1}{2} + \frac{1}{$
DT ₅₀ (days) DT ₆₀ (days)	
Deg And matrix (days)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Assessment	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Conclusion	iii) SPO fit is acceptable. Yes.
Interpret with care – extra	Solated beyond experimental period
Summary:	
For spiroxamile use A	FO Deg T ₅₀ , matrix = 66.4 days.



Step 4: Run metabolite	SFO from decline. iii) SFO fit for metal	bolite acceptable?
	M01	Эмог Смог
Plot	Concentration (19)	
Residuals	Proton (g)	
	Cood, residuals Now no systematic er-	Goost, residuals show no systematic er-
$\chi^2  \text{err}  \%$	<u>5</u> <u>9.39</u> <u>5</u>	× & × 12.2
t-test	k: @> 0.1	k: p < 0.1, >0.05
DT ₅₀ (days)	× × × × × × × × × × × × × × × × × × ×	
DT ₉₀ (days)		
DegT _{50matrix} (Days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	196 ¹ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓
		Fit acceptable.
Assessment	Visual fit is good and $\chi^2$ error is as coprable, however rate parameter does	Sisual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly
<u>`</u> \$	Anot differ significantly from zero.	nom zero.
Discussion	iii) SEO fit for metabolite acceptable SPO is not considered acceptable.	<ul><li>iii) SFO fit for metabolite acceptable?</li><li>SFO is considered acceptable and</li><li>should be used for modelling endpoints.</li></ul>
interpret with care – extrapo	bland beyond experimental period	

### Appendix 4.2.7.2. Metabolite fitting (M01 and M02)

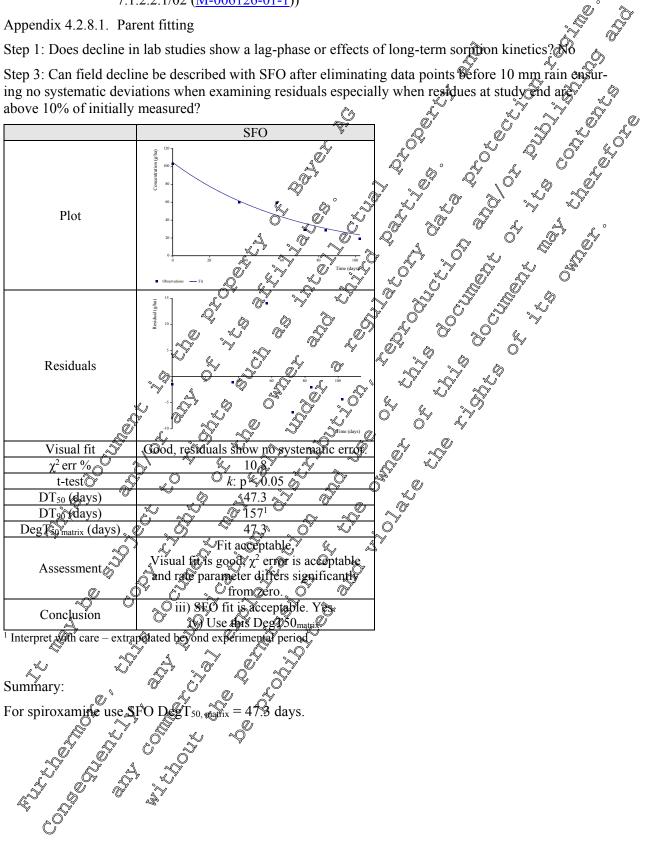
For metabolite M01 acceptable of decline cannot be obtained using SFO. For M01 use conservative default DegT₅₀ matrix = 1,000 days For metabolite M02 ase SFO (decline) DegT_{50, matrix} = 196 days



Degradation of spiroxamine in Swisttal-Hohn soil trial no. 40009/2 (KCA Appendix 4.2.8. 7.1.2.2.1/02 (M-006126-01-1)) dig of

Appendix 4.2.8.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?





Step 4: Run metabolite	Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?	
	Parent SFO, m	netabolite SFO
	M01	MI02
Plot		netabolite SFO MO2
Residuals		
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-
$\chi^2  \text{err}  \%$	11.28 0 5	× × × × × × × × ×
t-test	<i>k</i> : p < 0.05 ℃ ~	$k_{p} = 0.05$
DT ₅₀ (days)	· · · · · · · · · · · · · · · · · · ·	0 64.4
DT ₉₀ (days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	L Q 214 ¹
DegT _{50matrix} (days)	53:8 J J S	64.4
Formation fraction		N/A
Assessment	Fit not acceptable. Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.	Fit acceptable. Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.
Discussion	fu) SFQ fit for metabolite acceptable?	iii) SFO fit for metabolite acceptable?
Discussion	SFC4's considered acceptable and	SFO is considered acceptable and
1 Internet with and outro	shouts be used for modelling endpoints.	should be used for modelling endpoints.
¹ Interpret with care – extrap	olated beyond experimental period	
Summary.		
For metabolite M014 use	e SFO (decfine) $DegT_{50}$ matrix = 53.8 days	S.
For metabolite M02 use	$\dot{S}FO$ (decline) $Deg \mathcal{F}_{0, matrix} = 64.4 \text{ days}$	5
	Should be used for modelling endpoints. olated eyond experimental period SFO (decline) DegT ₅₀ matrix = 53.8 days SFO (decline) DegF _{80, matrix} = 64.4 days	

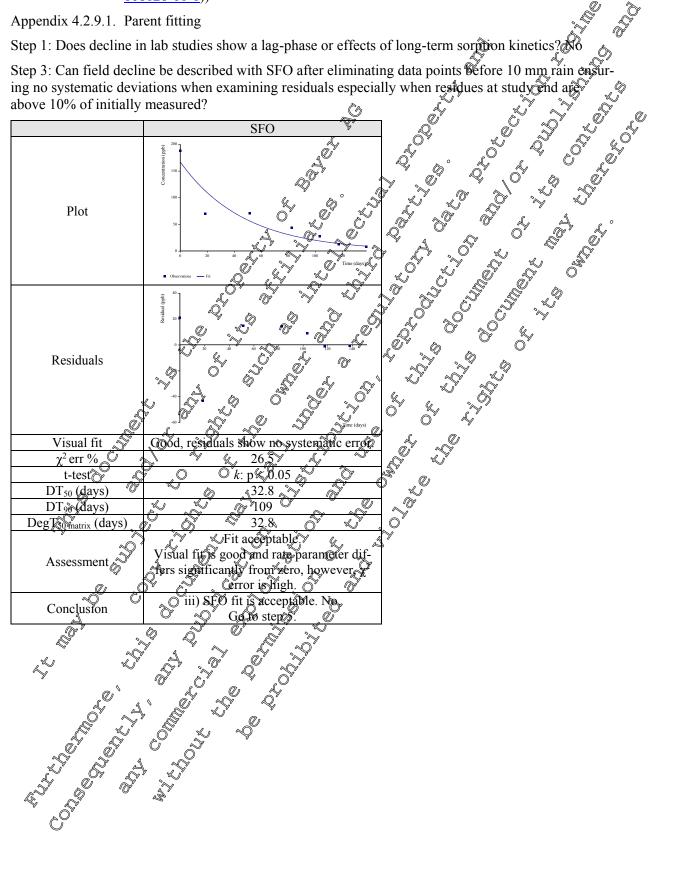
Appendix 4.2.8.2. Metabolite fitting (M01 and M02)



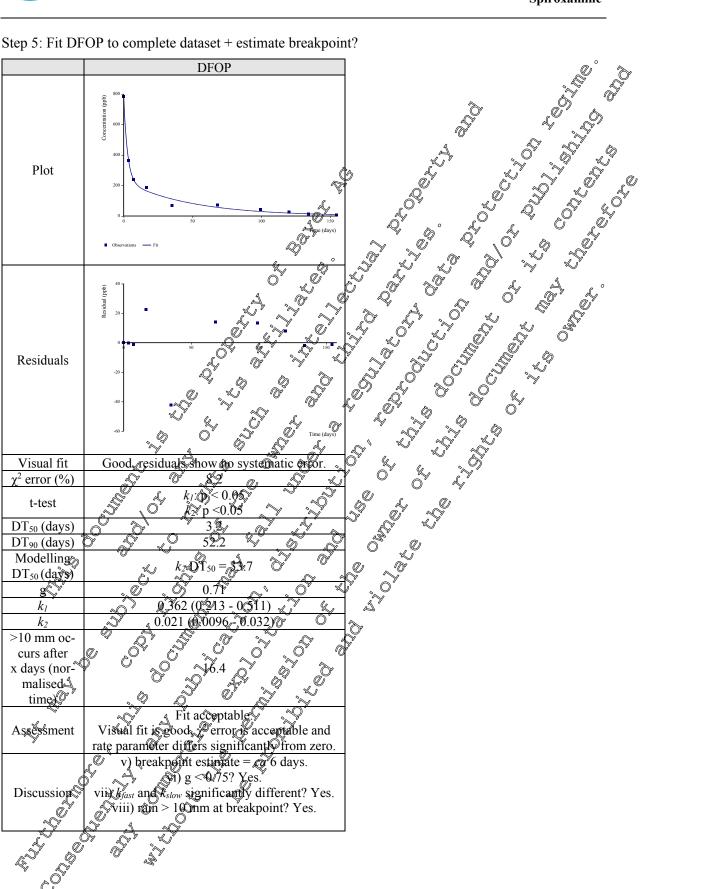
Appendix 4.2.9. Degradation of spiroxamine in Albig soil trial no. 40010/6 (KCA 7.1.2.2.1/02 (M-006126-01-1)) de la constante de la constant

Appendix 4.2.9.1. Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?







Step 5: Fit DFOP to complete dataset + estimate breakpoint?



#### Summary:

Following the decision flow in the guidance leads to the conclusion that for spiroxamine modelling endpoints are not derivable, however, this essentially results from the estimate of when > 10 mm of rainfall occurs compared to the estimated breakpoint. The recorded cumulative amount of rainfall on 9 mm and the next recorded measurement, yielding 45 mm cumulative rainfall, at the next sampling occasion (i.e. 30 d non normalised time or 16 4 d normalised time) are to the the next sampling. occasion (i.e. 30 d non normalised time or 16.4 d normalised time) results in the exceedance of 10 mm. It is considered very likely that cumulative rainfalt accessed 10 gm shortly algo 7.2 donormalised time). It is considered very likely that cumulative rainfalt accessed 10 gm shortly algo 7.2 donormalised time). It is considered very likely that cumulative rainfalt accessed to days, given messared rainfalt for tags site (see details in kinetic evaluation report Error! Reference source not found.) (Error! Reference source n 10 mm. It is considered very likely that cumulative rainfall exceeded 10 mm shortly after 7.2 donor-malised time, i.e. before the estimated breakpoint of 10 days, given measured rainfall for this site (see details in kinetic evaluation report Error! Reference source not formation to the site (see



Step 4: Run metabolite S	e SFO from decline. iii) SFO fit for metabolite acceptable?	
	Parent SFO, n	netabolite SFO
	M01	€M02
Plot	Correction Fit	netabolite SFO
Residuals		4 4 4 4 4 4 4 4 4 4 4 4 4 4
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-
$\chi^2  \mathrm{err}  \%$	22.28° 07 5°	× × × × × × × × × × × × × × × × × × ×
t-test	/%k: p < 0.05 ℃ ~~	[∞] & kyp < 0.05
DT ₅₀ (days)	\$5.9 \$7 \$7	0 70.4
DT ₉₀ (days)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	234 ¹
DegT _{50matrix} (days)	45:94 J N	<b>2 7 7 7 0</b> .4
Formation fraction		N/A
Assessment	<ul> <li>Fit acceptable.</li> <li>Visual fit is good, χ² orror is slightly</li> <li>high and rate parameter differs significantly from zero.</li> </ul>	Fit acceptable. Versual fit is good, $\chi^2$ error is slightly bigh, and rate parameter differs signifi- cantly from zero.
Discussion	hi) SFQ hit for metabolite acceptable?	iii) SFO fit for metabolite acceptable? SFO is considered acceptable and
Interpret with a diameter of	shouts be used for modelling endpoints.	should be used for modelling endpoints.
Summars.		
For metabolite M0Kuse	SFO (decline) $DegT_{50}$ Gatrix = 45.9 days	5.
For metabolite M02 use	Stor (decfine) Deg T _{50 matrix} = 45.9 days SFO (decfine) Deg T _{50 matrix} = 70.4 days	5.

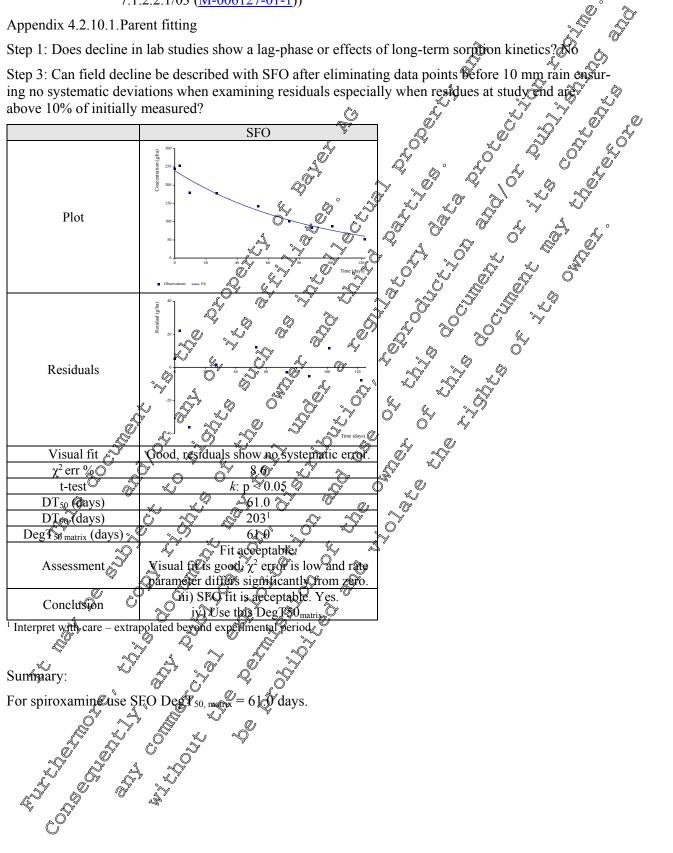
Appendix 4.2.9.2. Metabolite fitting (M01 and M02)



Appendix 4.2.10. Degradation of spiroxamine in Elm Farm/Thurston soil trial no. 40097/1 (KCA 7.1.2.2.1/03 (M-006127-01-1)) 

Appendix 4.2.10.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorror kinetics?





ep 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		
	Parent SFO, m	
	M01	M02
Plot	Operation - Fit	
Residuals		
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-
$\chi^2  \mathrm{err}  \%$	× <u>8.27</u>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
t-test 🔬	<i>k</i> : p < <b>0</b> .05	k 9 < 0.05
DT ₅₀ (days)		
DT ₉₀ (days)		2031
DegT _{50matrix} (days)	59.3 × × ×	<u>61</u>
Formation frotion	Fit acceptable	<i>©</i> Fit acceptable.
Assessment	Visual fit is good, $\chi^2$ error is low, and rate parameter differs significantly from zero.	Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.
Discussion	ii) SFO 51 for metabolite acceptable? A SFO 5 considered acceptable and should be used for modelling endpoints.	[*] iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for modelling endpoints.
Interpret with cath - extrap	lated beyond experimental period	
ummare or pretabolite M0497se	SFO (decome) $D_{eg}T_{50}$ matrix = 59.3 days	
or metabolite M@2 use	SFO (decline), Deg T ₆₀ matrix = 61 days	
	SFO (decline) Deg T ₅₀ matrix = 59.3 days SFO (decline) Deg T ₅₀ matrix = 61 days.	

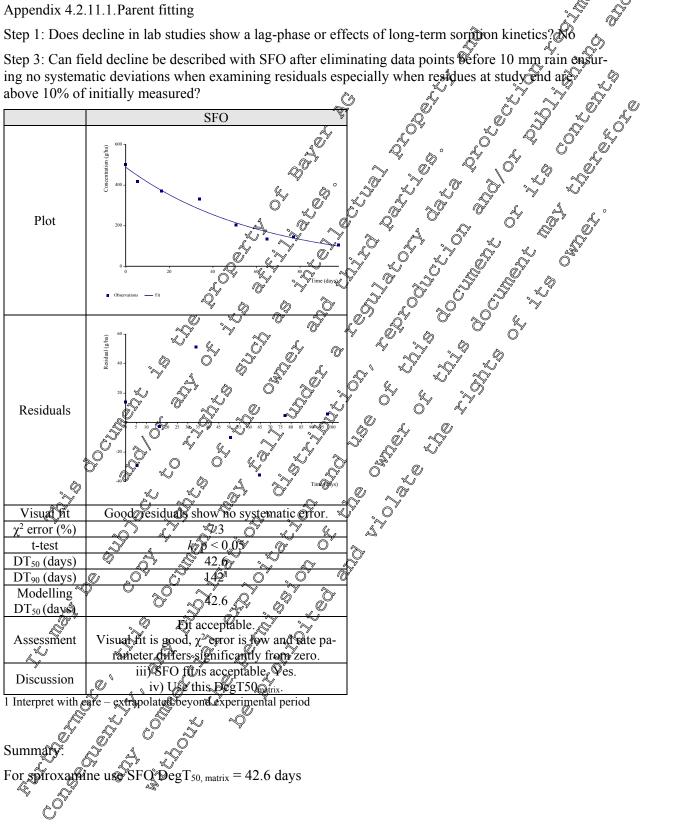
## Appendix 4.2.10.2. Metabolite fitting (M01 and M02)



Appendix 4.2.11. Degradation of spiroxamine in Pakenham soil trial no. 40099/8 (KCA 7.1.2.2.1/03 (M-006127-01-1)) de la constante de la constant

Appendix 4.2.11.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?





Step 4: Run metabolite	SFO from decline. iii) SFO fit for metal	polite acceptable?
		netabolite SFO
	M01	MO2
Plot		$\frac{1}{100} = \frac{1}{100} = \frac{1}$
Residuals	Otherwine         Fit           10         0           11         0           12         0           13         0           14         0           15         0           16         0           17         0           18         0           19         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0           10         0      <	
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-
$\chi^2  \text{err}  \%$	4.648 07 58	4 × 39.72
t-test	k: p < 0.05 ℃ ~	× × × p < 0.05
DT ₅₀ (days)		○ ○ ² 57.7
DT ₉₀ (days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
DegT _{50matrix} (days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	57.7 N/A
Formation fraction	Fit acceptable.	
ja na kana kana kana kana kana kana kana	Visual fit is good, $\chi^2$ or or is low, and	Fit acceptable. Voisual fit is good, $\chi^2$ error is low, and
Assessment	rate parameter differs significantly from	Falle parameter differs significantly from
		zero.
\$\$°	fir) SFQ fit for metabolite acceptable?	iii) SFO fit for metabolite acceptable?
Discussion	SFQU's considered acceptable and	SFO is considered acceptable and
	shouts be used for modelling endpoints.	should be used for modelling endpoints.
¹ Interpret with care – extrapo	olated beyond experimental period	
Summary.		
Summary.		
For metabolite M01 use	$e$ Sev (decrine) $\log g T_{50}$ matrix = 61.8 days	5.
For metabolite M02 use	$\dot{SFO}$ (decline) Deg $f_{0, matrix} = 57.7$ days	5.
	should be used for modelling endponts. olated beyond experimental period SFO (decline) DegTso patrix = 61.8 days SFO (decline) DegTso, matrix = 57.7 days	

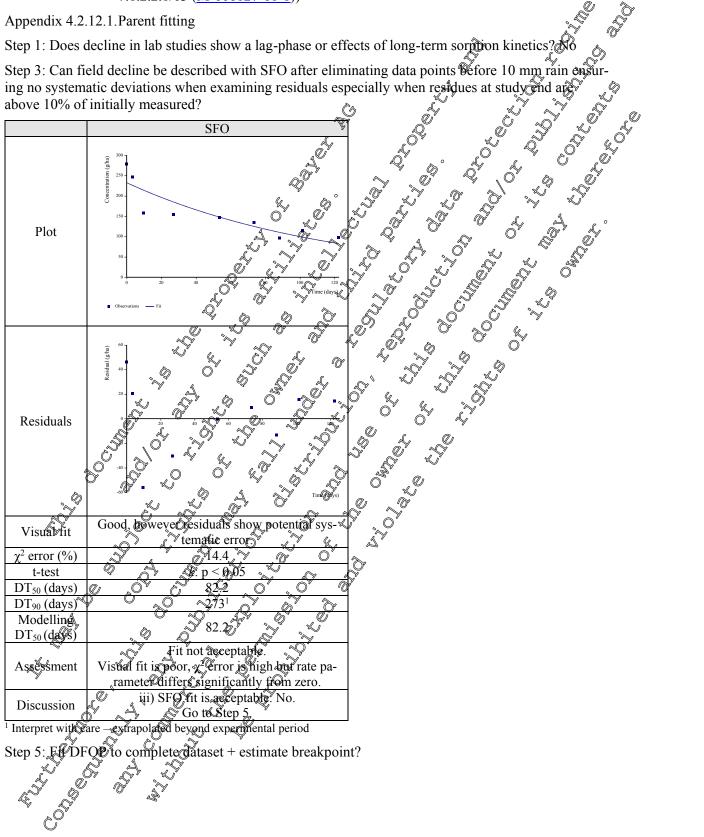
Appendix 4.2.11.2. Metabolite fitting (M01 and M02)



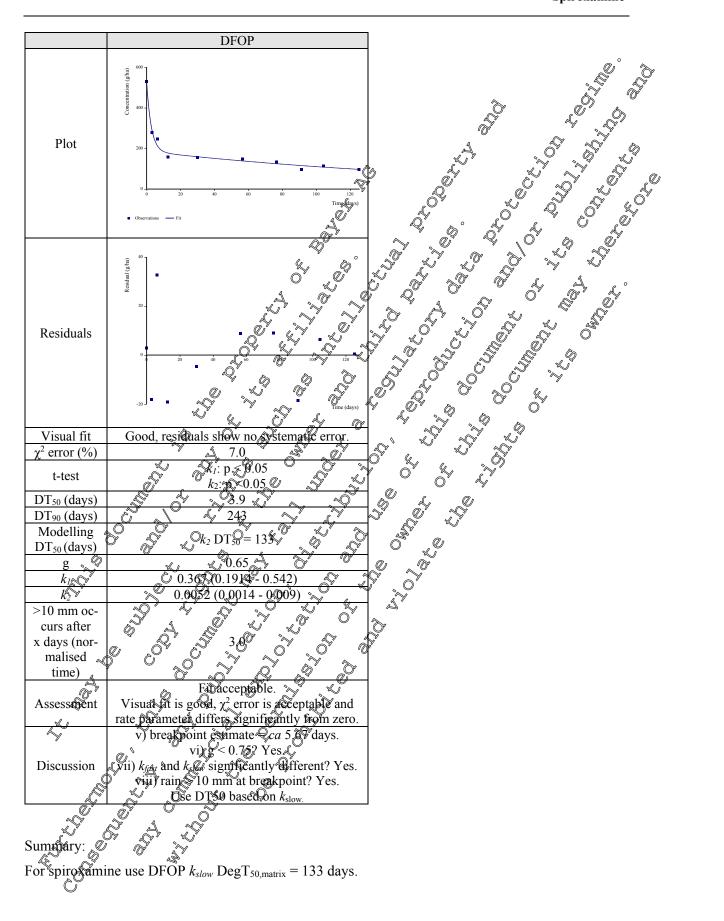
Appendix 4.2.12. Degradation of spiroxamine in Elm Farm/Thurston soil trial no. 40100/5 (KCA 7.1.2.2.1/03 (M-006127-01-1)) de la constante de la constant

Appendix 4.2.12.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?









SFO from decline. iii) SFO fit for metal	polite acceptable?
	netabolite SFO
M01	M02
	$\begin{array}{c} \mathbf{r} \\ \textbf{netabolite SFO} \\ \hline \\ $
Good, residuals thow small potential	Good residuals show no systematic er-
10.5 × × ×	<u>ب</u> کې کې 99.96
$k: p < \Psi.05 \bigcirc K$	k p < 0.05
	Ø″ <u>∑</u> §″ 98 ∑ [∞] N/A
Fit appartable	
Visual fit is good, $\chi^2$ error is acceptable, and the parameter differs significantly from zero.	Fit acceptable. Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.
ili) SFQ fit for metabolite acceptable?	iii) SFO fit for metabolite acceptable?
	SFO is considered acceptable and
should be used for modelling endpounts.	should be used for modelling endpoints.
SFO (decifine) DegT _{50(patrix} = 96.2 days	3.
SFO (decline) $\operatorname{Deg}_{50, \text{ matrix}}^{\circ} = 98 \text{ days.}$	
	Parent SFO, n M01 M01 $(u_0) u_0 u_0$ $(u_0) $

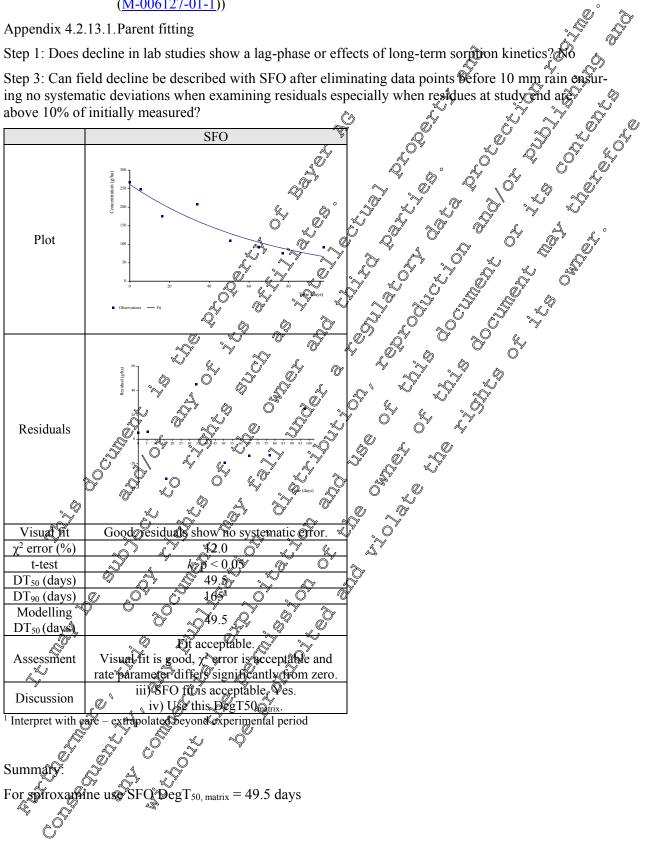
Appendix 4.2.12.2. Metabolite fitting (M01 and M02)



Appendix 4.2.13. Degradation of spiroxamine in Pakenham soil trial no. 40101/3 (KCA 7.1.2.2.1/03 (M-006127-01-1)) de la constante de la constant

Appendix 4.2.13.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?





Step 4: Run metabolite S	SFO from decline. iii) SFO fit for metab	polite acceptable?
		netabolite SFO
	M01	M02
Plot	Concontration (give)	
Residuals		
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-
$\chi^2  \mathrm{err}  \%$	9.57 y y	<u> </u>
t-test 🔬	<i>Qk</i> : p < <b>0</b> .05	k
DT ₅₀ (days)	1 $1$ $1$ $1$ $1$ $1$ $1$ $1$ $1$ $1$	<u> </u>
DT ₉₀ (days)		<i>Q</i> 323 [°] <i>Q</i> 97.3
DegT _{50matrix} (days)	NOA XY &	N/A
Assessment	Fit acceptable Visual fifths good, $\chi^2$ error is acceptable and rate parameter differs significantly from zero.	Fit acceptable. Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.
Discussion	iti) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for modelling endpoints.	iii) SFO fit for metabolite acceptable? SFO is considered acceptable and should be used for modelling endpoints.
Interpret with call - extrapo	lated beyond experimental period	should be used for moderning enupoints.
Summar	SFO (decline) Deg $T_{50}$ where $T_{50}$ and $T_{50}$ where $T_{50}$ and $T_{50}$	ys.
For metabolite M02 use	SFO (decline) DegT ₅₀ matrix = 101.0 day SFO (decline) DegT ₅₀ matrix = 97.3 days	3.

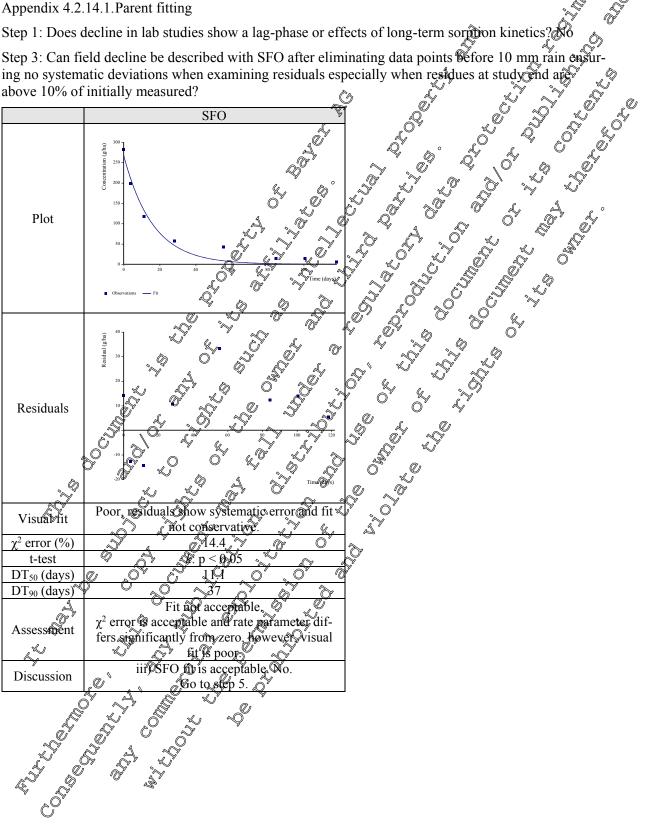
Appendix 4.2.13.2. Metabolite fitting (M01 and M02)



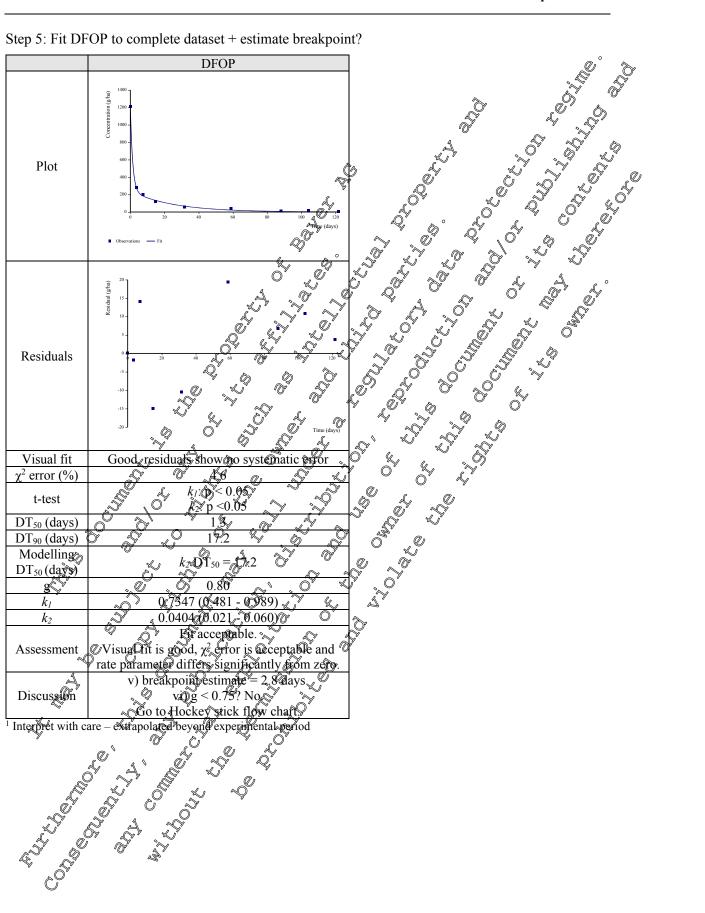
Appendix 4.2.14. Degradation of spiroxamine in Touffreville soil trial no. 40193/5 (KCA 7.1.2.2.1/03 (M-006127-01-1)) and and a second

Appendix 4.2.14.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?



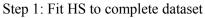


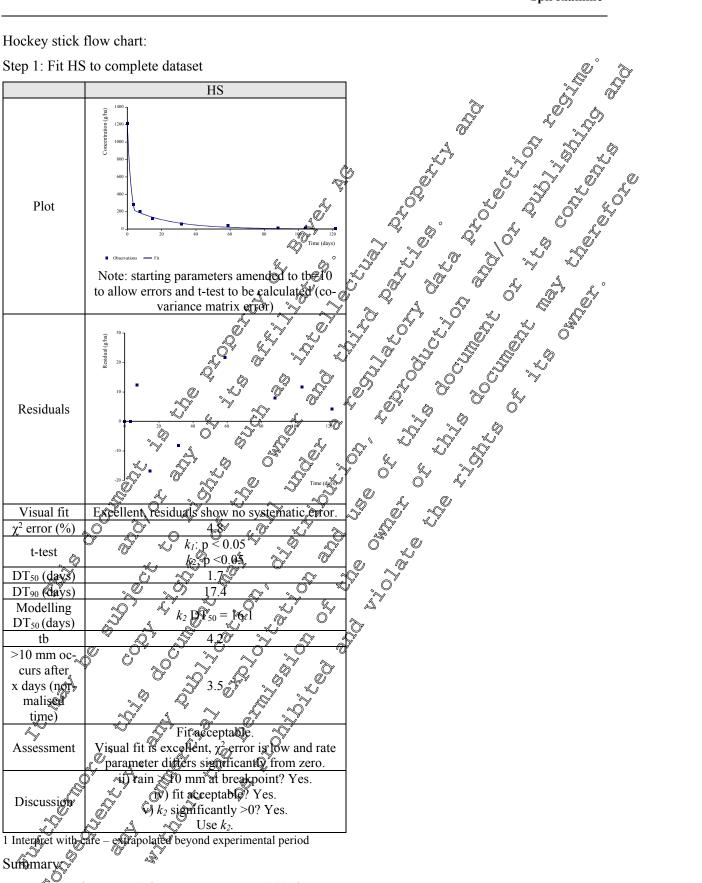


Step 5: Fit DFOP to complete dataset + estimate breakpoint?



Hockey stick flow chart:





For sphexamine use HS  $k_{slow}$  DegT_{50, matrix} = 16.1 days.



Step 4: Run metabolite S	SFO from decline. iii) SFO fit for metal	polite acceptable?
		netabolite SFO
	M01	M02
Plot	Concentration (Upp)	
Residuals	tendand (gran tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendand tendan	
Visual fit	Good, residuals show no systematic er-	Good residuates show no systematic er-
$\chi^2  \mathrm{err}  \%$	× <u>11.6</u> <i>y y</i>	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
t-test 🔨	<i>v Qk</i> : p < <b>9</b> .05 <i>Q y</i>	× × × p < 0.05
DT ₅₀ (days)		
DT ₉₀ (days)	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	93.21
DegT _{50matrix} (days)	28.9 × 5 [°]	<u>∅</u> ″ <u>×</u> 28.1 <u>×</u> ″ N/A
Formation frontion	Fit acceptable.	Eit accentable
Assessment	Visual fit is good, $\chi^2$ error is acceptable, and the parameter differs significantly from zero.	Visual fit is good, $\chi^2$ error is acceptable, and rate parameter differs significantly from zero.
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	iii) SFO it for netabolite acceptable?	iii) SFO fit for metabolite acceptable?
Discussion	SFQU's considered acceptable and	SFO is considered acceptable and
	should be used for modelling endpounts.	should be used for modelling endpoints.
Summars For metabolite M0Krise	SFO (dectine) Deg T_{56} (matrix = 28.9 days	3.
or metabolite M02 use	Should be used for modelling endpoints. Slated beyond experimental period SFO (decline) DegT _{50 (matrix} = 28.9 days SFO (decline) DegT _{50 (matrix} = 28.1 days	S.

Appendix 4.2.14.2. Metabolite fitting (M01 and M02)

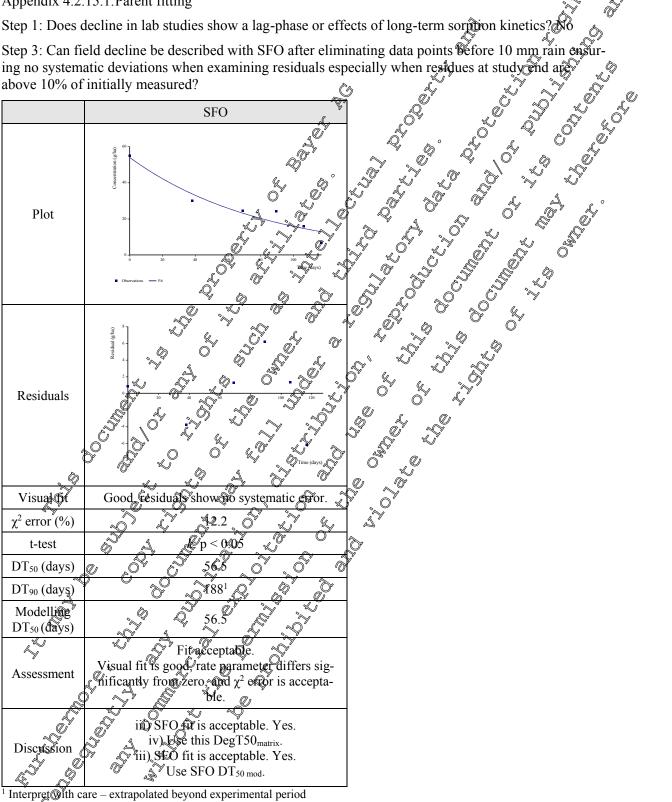


Appendix 4.2.15. Degradation of spiroxamine in Laudun soil trial no. 40198/6 (KCA 7.1.2.2.1/04 (M-006128-01-1))

Appendix 4.2.15.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorriton kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensur-ing no systematic deviations when examining residuals especially when residues at study and arguing above 10% of initially measured?



Summary:

For spiroxamine use SFO $DT_{50 \text{ mod}} = 56.5$ days.



and the second of the second o to the transformed and the transformed to the trans

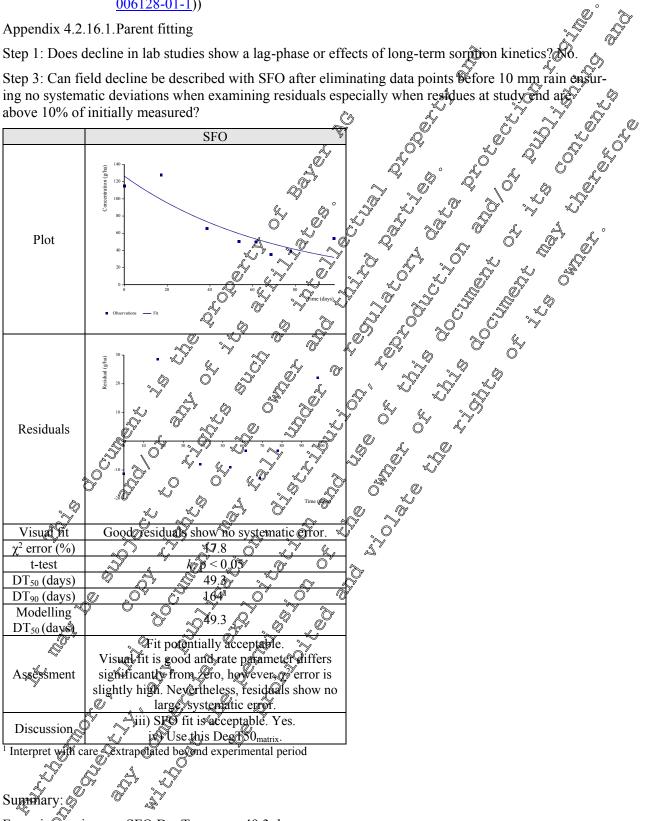


Appendix 4.2.16. Degradation of spiroxamine in Filetto soil trial no. 40424/1 (KCA 7.1.2.2.1/04 (M-006128-01-1)) al a

Appendix 4.2.16.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?

Step 3: Can field decline be described with SFO after eliminating data points before 10 mm rain ensur-ing no systematic deviations when examining residuals especially when residues at study and are above 10% of initially measured?



For spir amine use SFO DegT_{50, matrix} = 49.3 days.



tep 4: Run metabolite	metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		ð
		netabolite SFO	
	M01	M02))
Plot	Otherwines - Fi	netabolite SFO	
Residuals		Time (days)	, o
Visual fit	Good, residuals show no systematic er-	Good residuals show no systematic er-	
$\chi^2 \text{ err } \%$	412	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	_
t-test	k: p < 0.05 ℃ ~	k: p=0.1, >0.05	
DT ₅₀ (days)		0	
DT ₉₀ (days)		a a 91.91	
DegT _{50matrix} (days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	27.7	
Formation fraction	AND A A	N/A	
A séperment	 Fit acceptable. Visual fit is good, χ² or or is low, and rate parameter differs significantly from zero. iii) SFQ fit for metabolite acceptable? SFQ fit considered acceptable and severable 	Fit acceptable. Visual fit is good, χ^2 error is low, and rate parameter differs significantly from zero. iii) SFO fit for metabolite acceptable? SFO is considered acceptable and	
A	shouts be used for modelling endpoints.	should be used for modelling endpoints.	
Interpret with core – exterpo ummars? or metabolite M0K use or metabolite M02 use	SFO (decfine) DegT _{50 (matrix} = 28 days. SFO (decfine) DegT _{50 (matrix} = 27.7 days	S.	

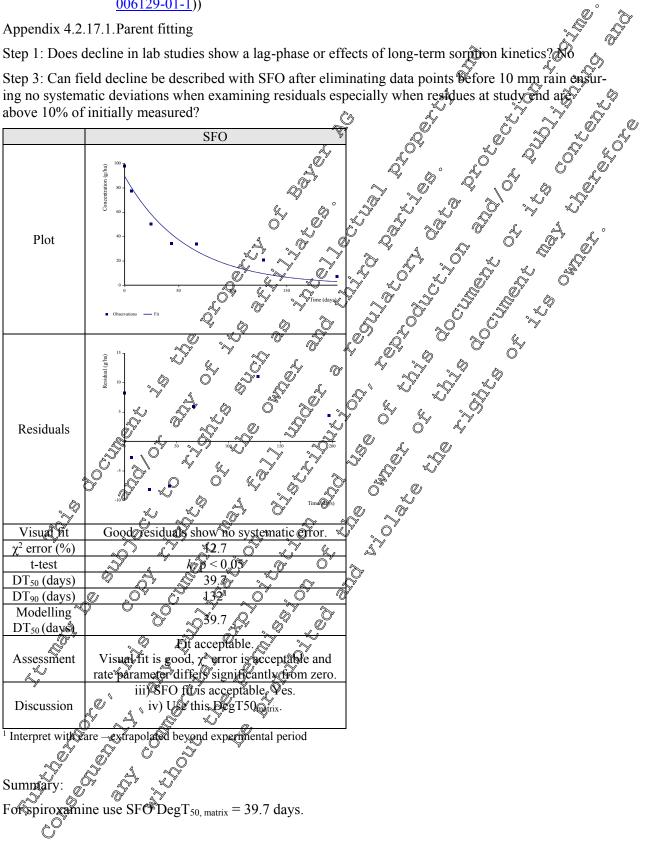
Appendix 4.2.16.2. Metabolite fitting (M01 and M02)



Appendix 4.2.17. Degradation of spiroxamine in Laudun soil trial no. 50135/2 (KCA 7.1.2.2.1/05 (M-006129-01-1))

Appendix 4.2.17.1.Parent fitting

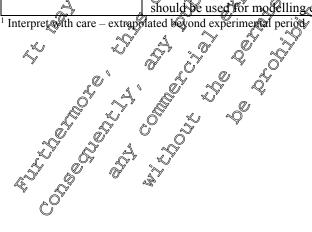
Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?





tep 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?		
	M01	MO2
Plot	Concurrence Fit	
Residuals	Intering (fth)	
Visual fit	CatermeDate, residuals flow potential systematic error and final two times points underestimated	Intermediate, residuals show potential systematic error and final three time points underestimated
$\chi^2 \mathrm{err} \%$	~~~ Q2.7 ~~ ~~	0 × 24.2
t-test	β β β < 0.05 β	/ k: p < 0.05
DT ₅₀ (days)		
DT ₉₀ (days)		81.7 ¹
DegT _{50matrix} (days)		
Formation fraction	N/AO^{2}	N/A
Ê, ^y . Ø,	Vis of fit is intermediate. of final time	Fit not acceptable.
Assessment 🔊	apoints underestimated with server	Visual fit is intermediate, and final time points underestimated, with χ^2 error
	slight@high_Howeve@rate parameter	slightly high. However, rate parameter
	Affers significantly from zero	differs significantly from zero.
Ő, Øs	iii0SFO fit for metabolite acceptable?	iii) SFO fit for metabolite acceptable?
Discussion	SFO is considered acceptable and	SFO is considered acceptable and
A	should be used for modelling endpoints.	should be used for modelling endpoints.
Interpret with care – extrapt	Rated beyond experimental period	· · · · · · · · · · · · · · · · · · ·

Appendix 4.2.17.2. Metabolite fitting (M01 and M02)

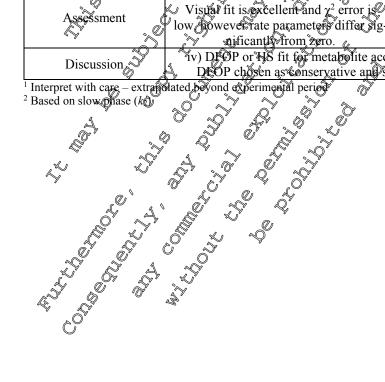




°

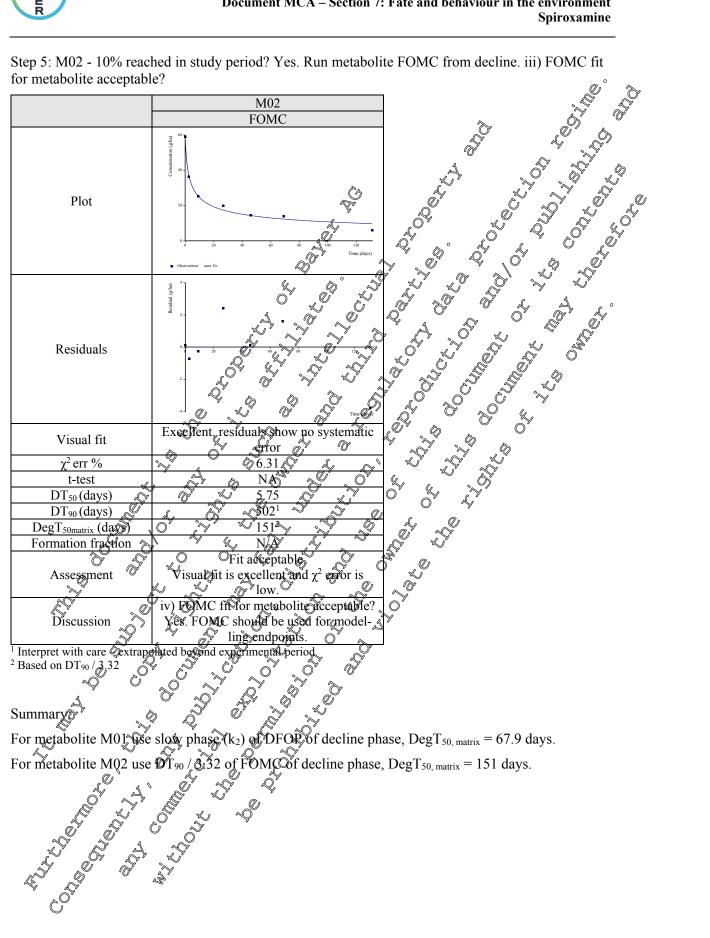
Step 5: M01 - 10% reached in study period? No. Run metabolite DFOP and HS from decline. iii) DFOP or HS fit for metabolite acceptable?

	*	
	M0) <u>1</u>
	DFOP	HS O
Plot	Currenting Fit	HS HS HS HS HS HS HS HS HS HS HS HS HS H
Residuals	• Overview = Fit	Excellent, residuals show no systematic
Visual fit		Excellent, residuals show no systematic
$\chi^2 \text{err} \%$	\$4.98 \$ 1 A	²
t-test	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \end{array} \\ $	k 0 ≤ 0.05
DT ₅₀ (days)	5 39 3 5 m	4.35
DT ₉₀ (days)	0 ⁹ i 149 i 0 i 0 i 0 i 0 i 0 i 0 i 0 i 0 i 0 i 0	143 ¹
DegT _{50matrix} (days)	67.29 L · · ·	63.8 ²
Formation fraction		N/A N/A
Assessment	Fit acceptable. Visual fit is excellent and χ^2 error is low however ate parameters differ sig- sificantly from zero.	Fit acceptable. Sult fit is excellent, χ^2 error is low, and rate parameters differ significantly from zero.
Discussion	Yv) DFOP or HS fit for metabolite accep DFOP chosen as conservative approved stated beyond experimental period	table? Both are considered acceptable. uld be used for modelling endpoints.





Step 5: M02 - 10% reached in study period? Yes. Run metabolite FOMC from decline. iii) FOMC fit for metabolite acceptable?

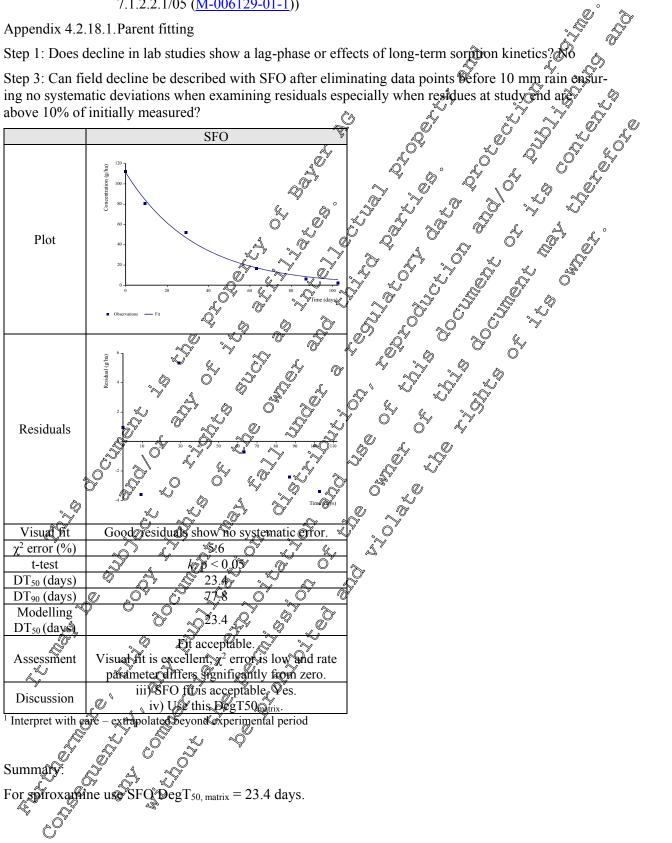




Appendix 4.2.18. Degradation of spiroxamine in Nogarole Rocca soil trial no. 50136/0 (KCA 7.1.2.2.1/05 (M-006129-01-1)) di di

Appendix 4.2.18.1.Parent fitting

Step 1: Does decline in lab studies show a lag-phase or effects of long-term sorribon kinetics?

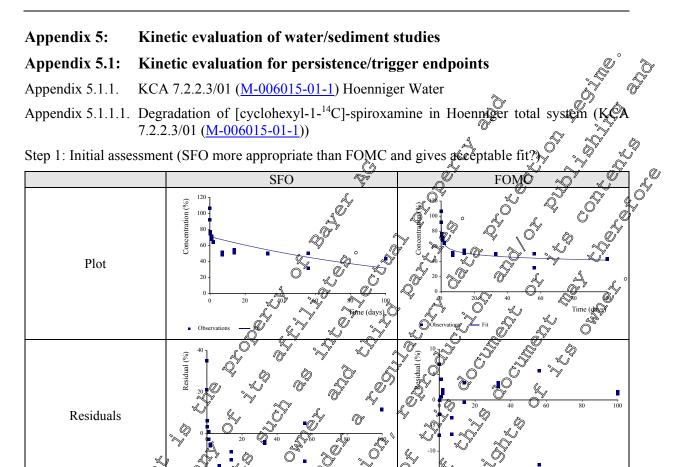




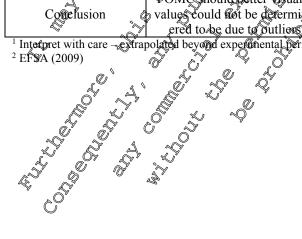
Step 4: Run metabolite SFO from decline. iii) SFO fit for metabolite acceptable?						
	M01	MO2				
Plot						
Residuals	0 Observations - Fit					
Visual fit	Cood, residuals how no systematic er-	Good, residuals show no systematic er-				
$\chi^2 \text{err } \%$	5.69 Dr in	5.34				
t-test	k: p& 0.05 %	© %: p < 0.05				
DT ₅₀ (days)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	44.3				
DT ₉₀ (days)	<u> </u>	<u>V</u> <u>147</u>				
DegT _{50matrix} (Pays)	2304 × 7 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	44.3				
Formation fraction		N/A				
Discussion	Visual fit is good, χ^2 error is low, and rate parameter differs significantly from	Fit acceptable. Visual fit is good, χ^2 error is low, and rate parameter differs significantly from zero.				
Discussion	iii) SLO fit for metabolite acceptable SDO is considered acceptable and shuld be used for a considered acceptable and	iii) SFO fit for metabolite acceptable?SFO is considered acceptable andshould be used for modelling endpoints.				
¹ Interpret with care – extrapo	blated beyond experimental period	should be used for moderning endpoints.				
Summary:						
For metabolite M01 use FO (decline) $DegT_{co, matrix} = 23.4$ days.						
For metabolite M02 use SFC (decline) Deg $V_{50, matrix} = 44.3$ days.						
	store in the second sec					

Appendix 4.2.18.2. Metabolite fitting (M01 and M02)

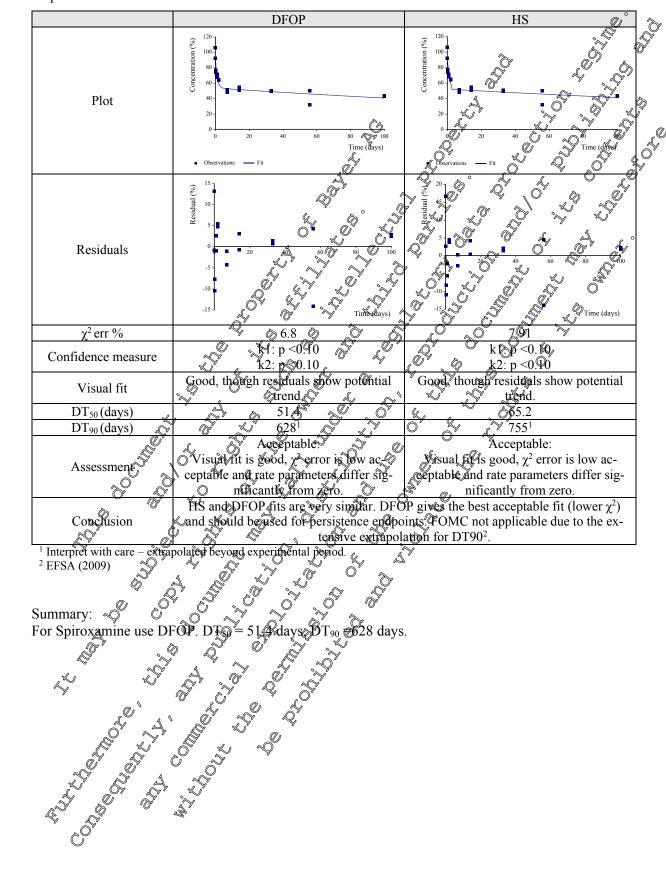




		Time (days)	-1:0° 4	Time (days)	
$\chi^2 \text{ err } \%$	× × × 16.6			3.67	
Confidence measure	[™] ‰k: p ≤0.1	0 % . ~		ot applicable	
	Poor, residuals show		K te	ough residuals show po- ential trend.	
DT ₅₀ (days)	<u>,</u>			19.6	
Define (days)	2851	Ô ^Y 4 ^Y .	0″	>10,0001	
	Visual tit is poor, χ^2_{2} cf the parameter differs signature of χ^2_{2} cf the parameter differs signature of χ^2_{2} cf χ^2_{2} cf $\chi^2_$	r % is high bts gnificantly from	Visual fit is ac good; however, from the study DT90 is co	t acceptable: cceptable and $\chi^2 \text{ err } \%$ is significant extrapolation γ period to the estimated onsidered unreliable ²	
POMcChould patter visually and statistically fit compared to SFO, however, DT ₉₀					
Conclusion va	Conclusion values could not be determined using FOMC fit. Deviation from SFO is not consid-				
ered to be due to butliens or experimental artefacts. Investigate DFOP and HS.					
Interpret with care - extrapolated beyond experimental period					

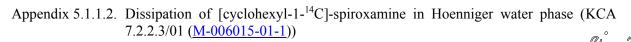


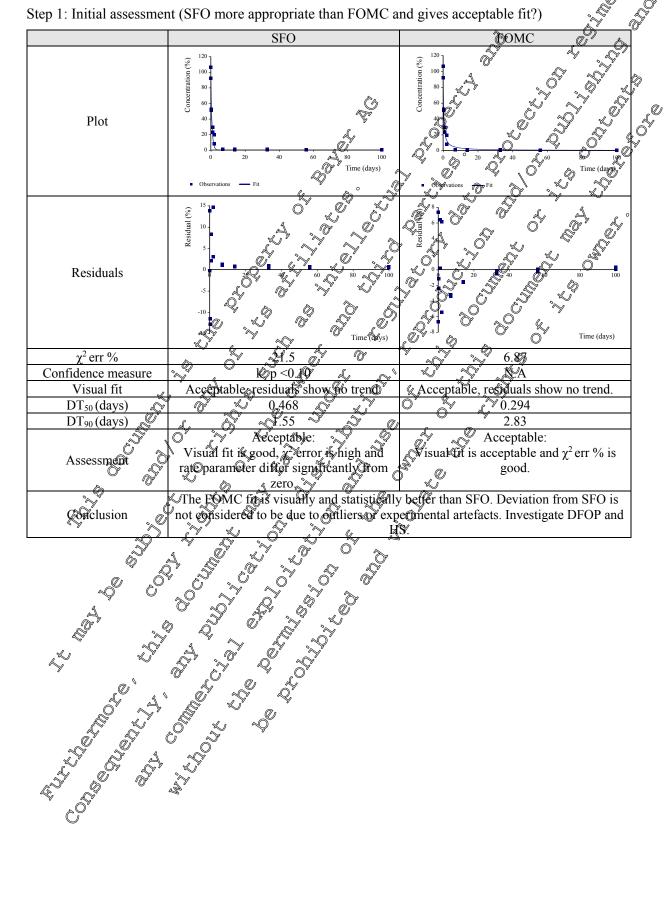




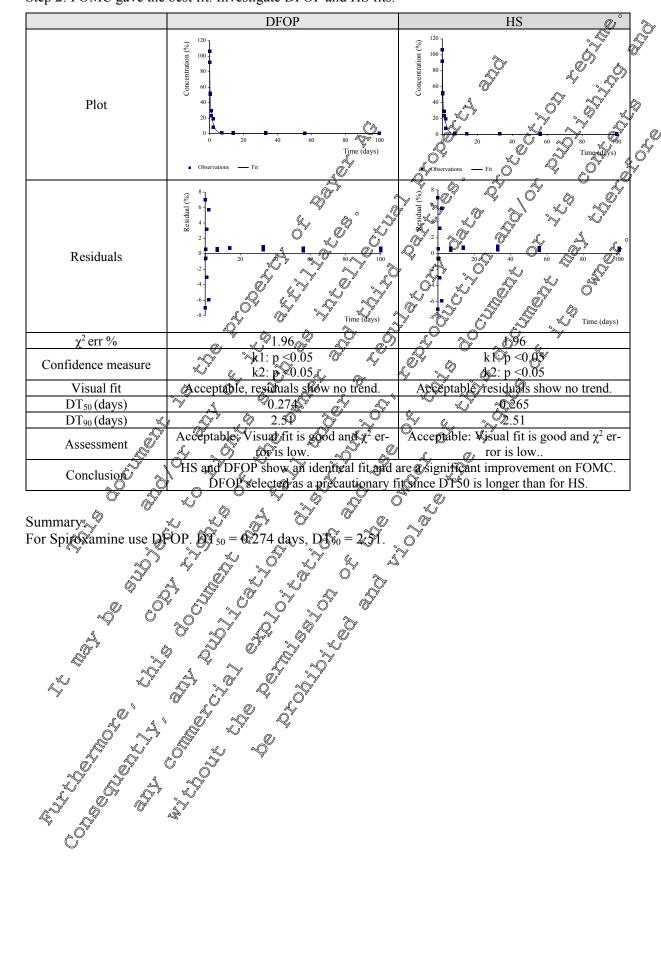
Step 2: FOMC better than SFO fit. Fit DFOP and HS







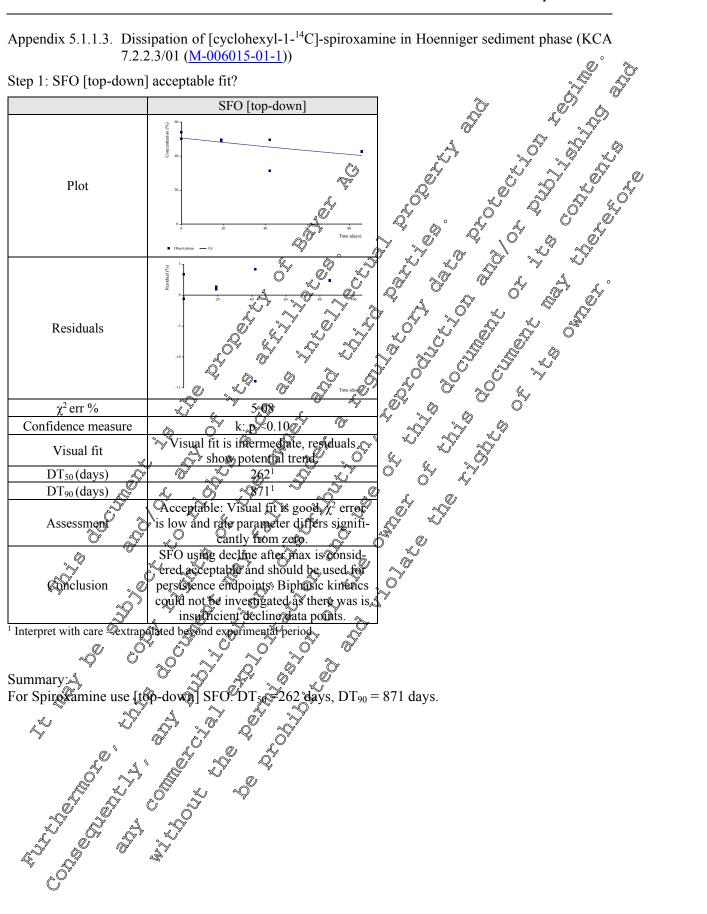




Step 2: FOMC gave the best fit. Investigate DFOP and HS fits.



Appendix 5.1.1.3. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Hoenniger sediment phase (KCA 7.2.2.3/01 (M-006015-01-1))

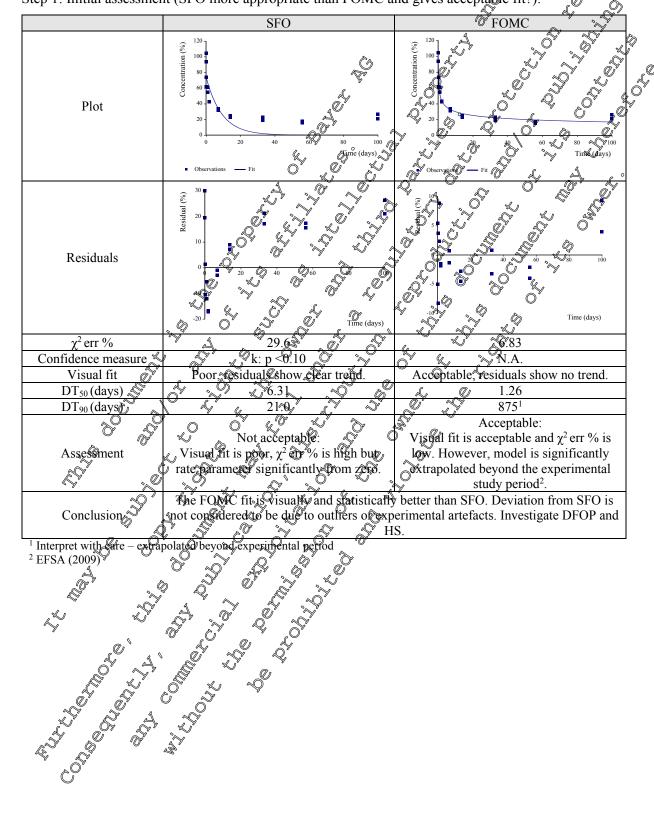




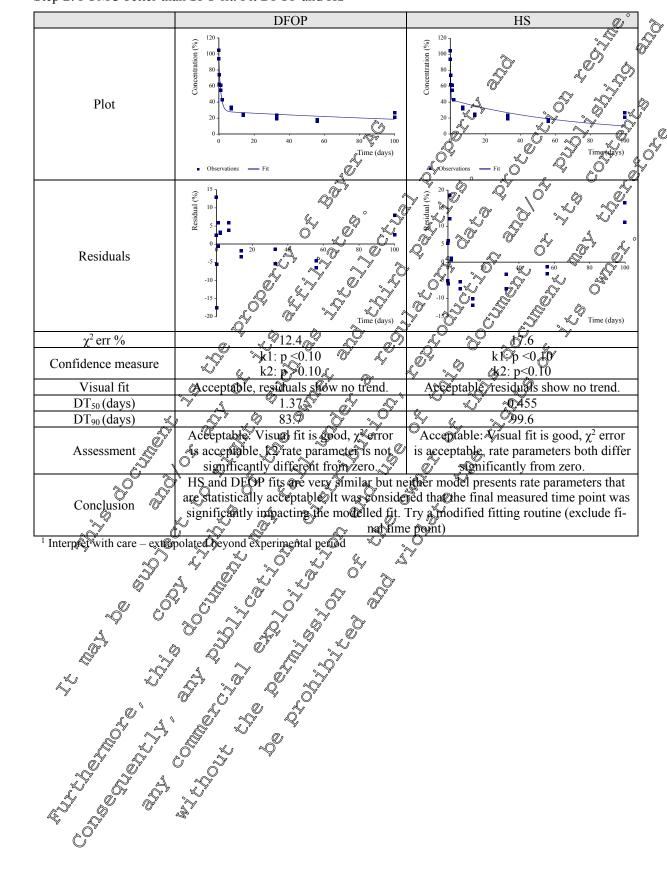
Appendix 5.1.2. KCA 7.2.2.3/01 (<u>M-006015-01-1</u>) Stilwell

Appendix 5.1.2.1. Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in Stilwell total system (KCA 7.2.2.3/01 (M-006015-01-1))

Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?).

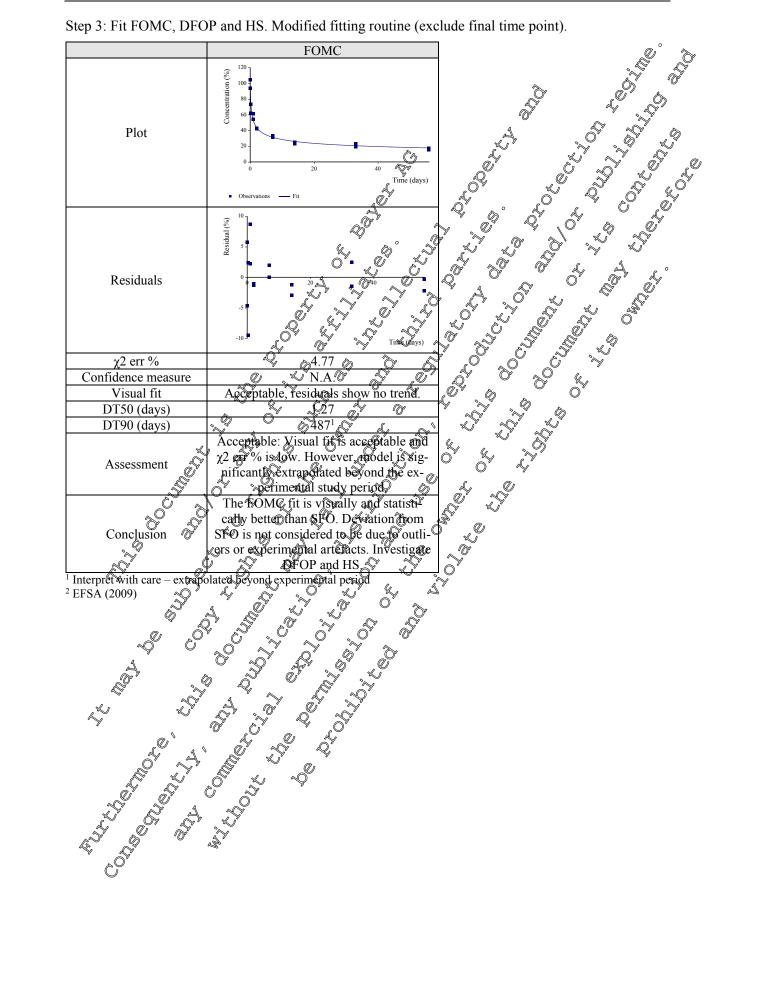






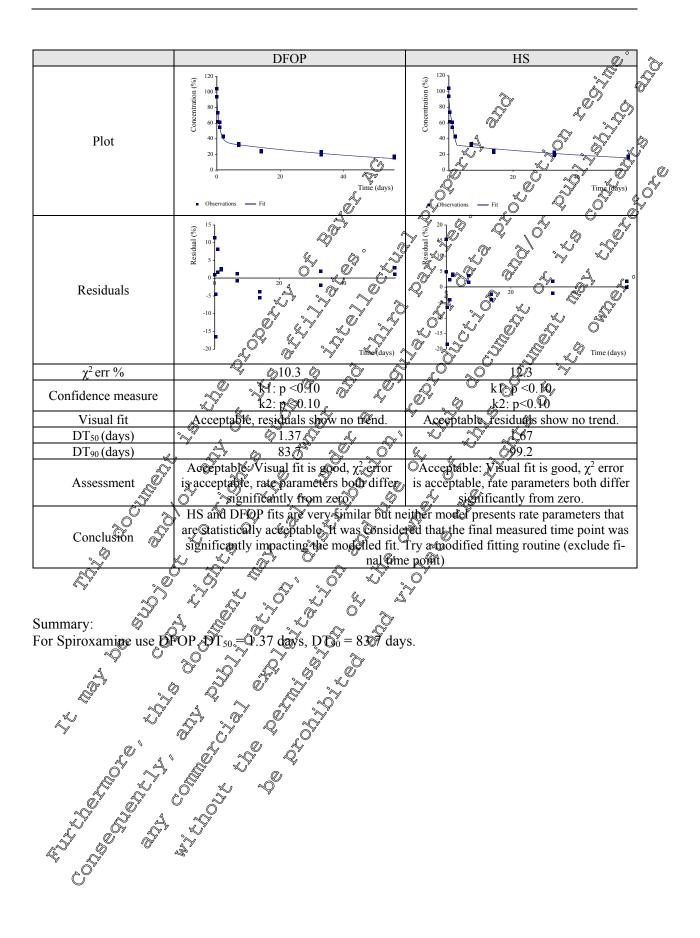
Step 2: FOMC better than SFO fit. Fit DFOP and HS





Step 3: Fit FOMC, DFOP and HS. Modified fitting routine (exclude final time point).







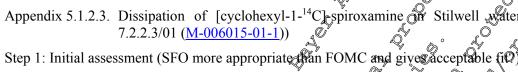
pliase KCA

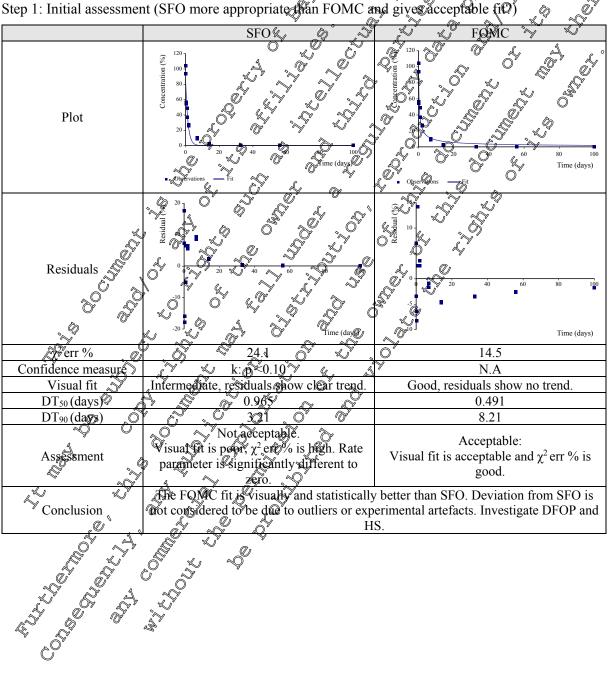
Appendix 5.1.2.2. Degradation of M06 in Stilwell total system (KCA 7.2.2.3/01 (M-006015-01-1))

As no decline phase was observed for M06 it is not possible to estimate degradation rates from the prtal system.

Summary:

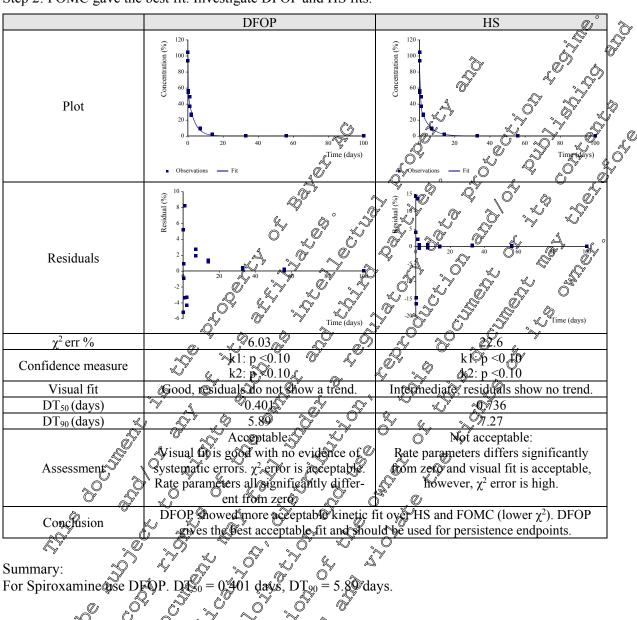
M06 dissipation conservative default $DT_{50} = 1,000$ days







K,



Step 2: FOMC gave the best fit. Investigate DFOP and HS fits.

Appendix 5 1.2.4. Dissipation 50M06 for Stilvell water phase (KCA 7.2.2.3/01 (<u>M-006015-01-1</u>)) No observations of M06 > 5% in any time point for the water phase.

Appendix 5.1.25. Dissipation of [c@lohesvl-1-¹⁴C]-spiroxamine in Stilwell sediment phase (KCA 7.2, 2.3/0 (M-000015-0))

As no decline phase was observed for spiroxamine it is not possible to estimate degradation rates for the sediment 2

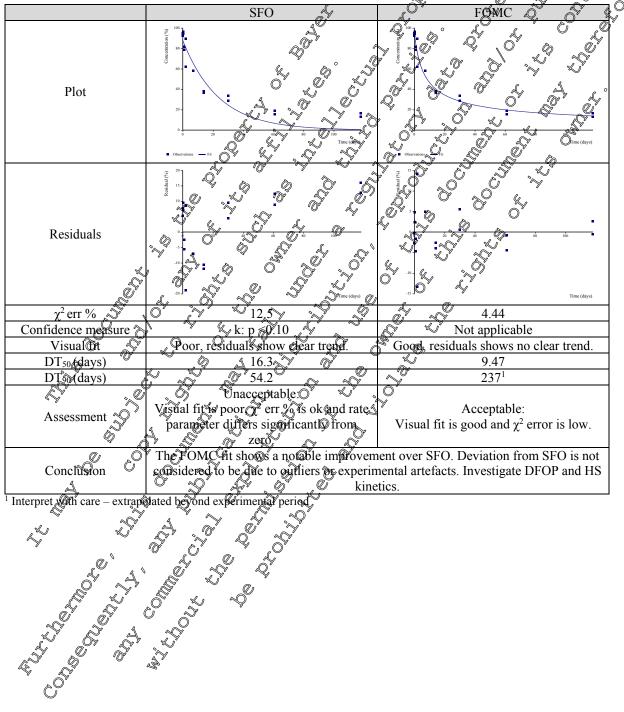
For Spirocamine use conservative default $DT_{50} = 1,000$ days



Appendix 5.1.2.6. Dissipation of M06 in Stilwell sediment phase (KCA 7.2.2.3/01 ($\underline{M-006015-01-1}$)) No observations of M06 > 5% in any time point for the sediment phase.

Appendix 5.1.3. KCA 7.2.2.3/04 (<u>M-303324-01-1</u>) Anglerweiher System

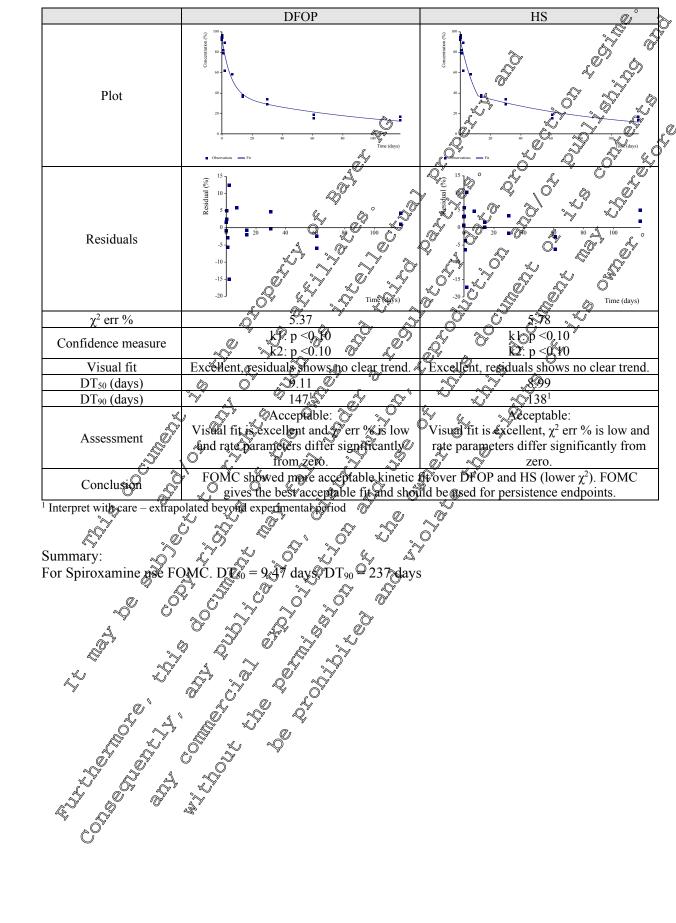
Step 1: Initial assessment (SFO more appropriate than FOMC and give acceptable fiv)



Appendix 5.1.3.1. Degradation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Anglerweiher otal system (KCA 7.2.2.3/04 (<u>M-303324-01-1</u>))

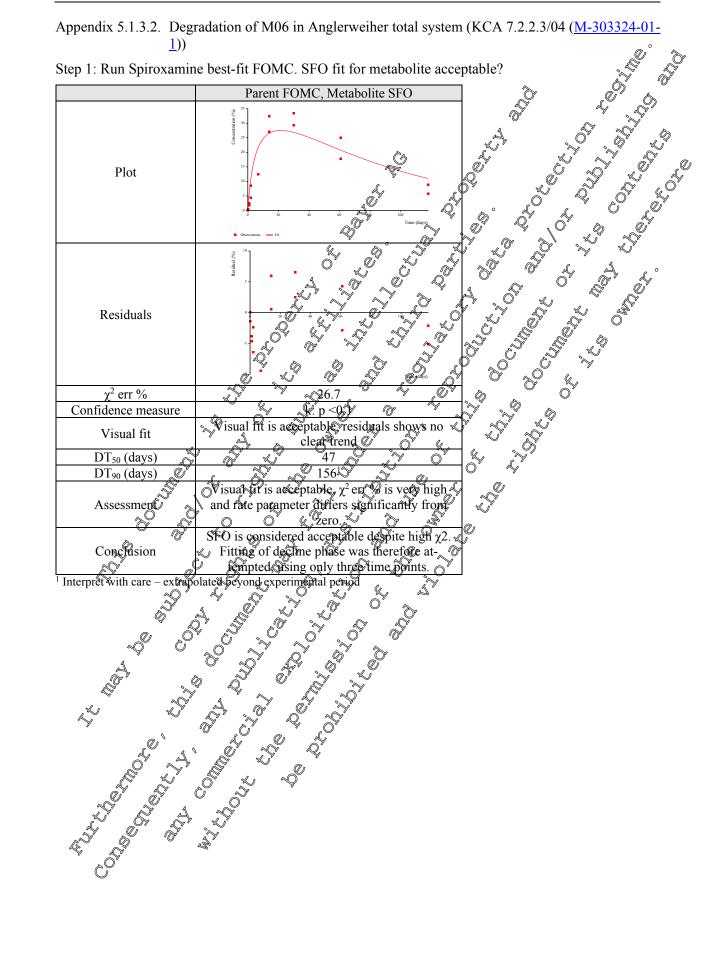


Step 2: DFOP and HS fit investigated.

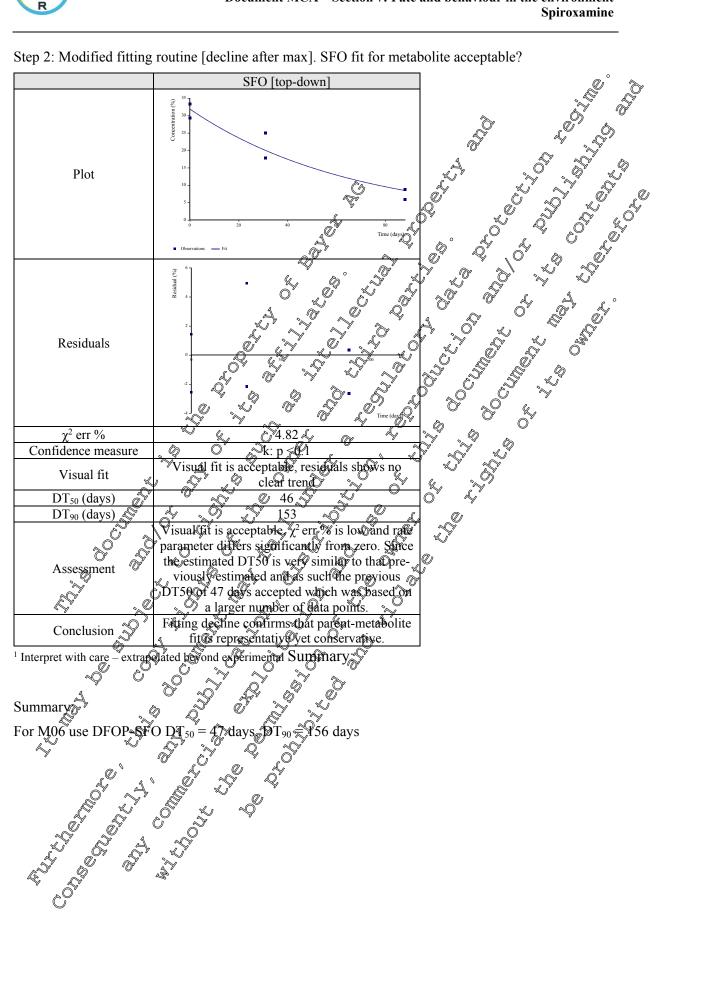




Appendix 5.1.3.2. Degradation of M06 in Anglerweiher total system (KCA 7.2.2.3/04 (M-303324-01-1))

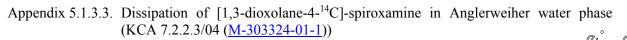


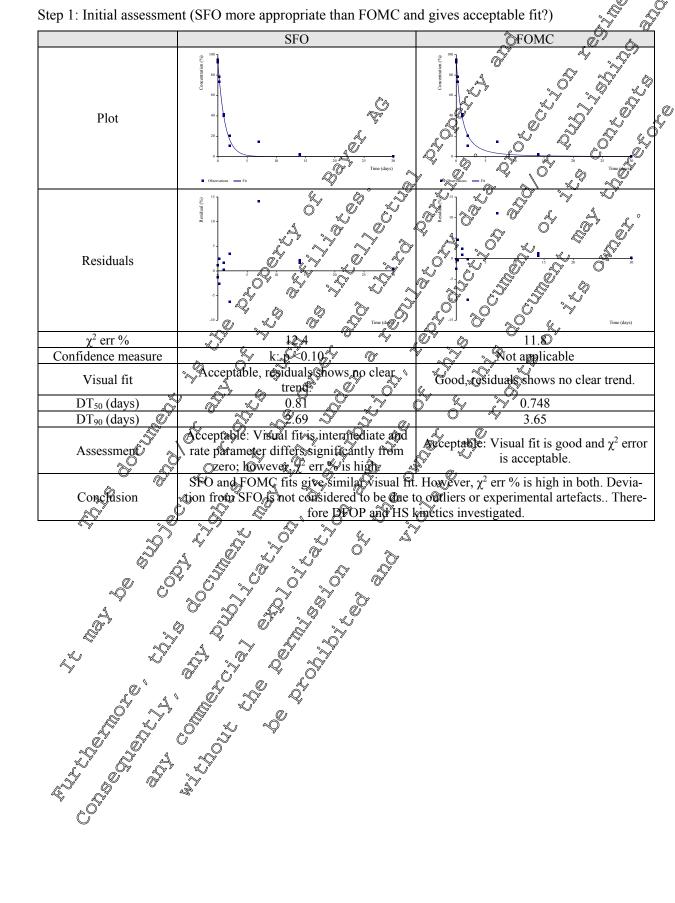




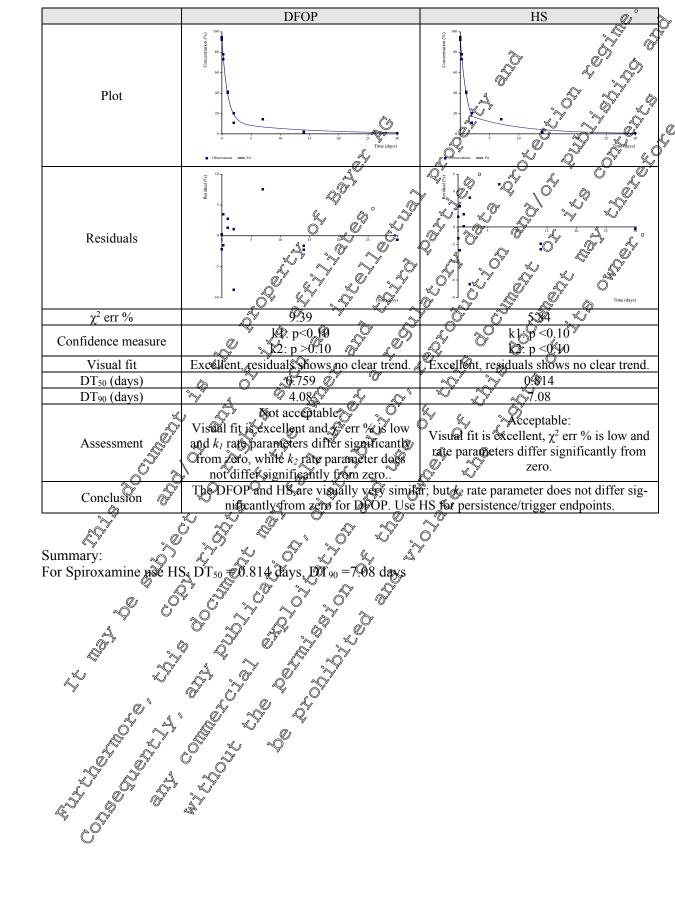
Step 2: Modified fitting routine [decline after max]. SFO fit for metabolite acceptable?







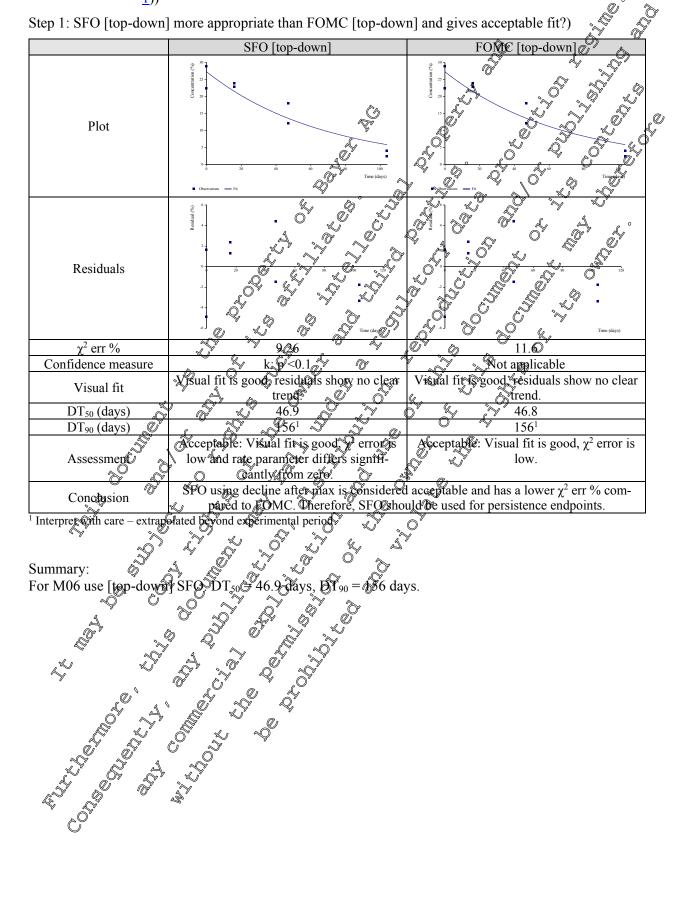




Step 2: DFOP and HS fit investigated.



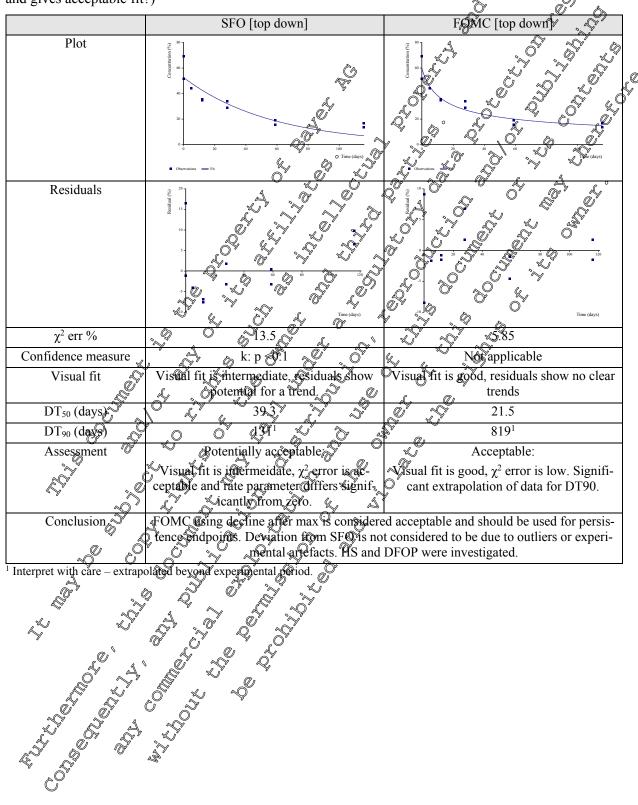
Appendix 5.1.3.4. Dissipation of M06 in Anglerweiher water phase (KCA 7.2.2.3/04 ($\underline{M-303324-01-1}$))



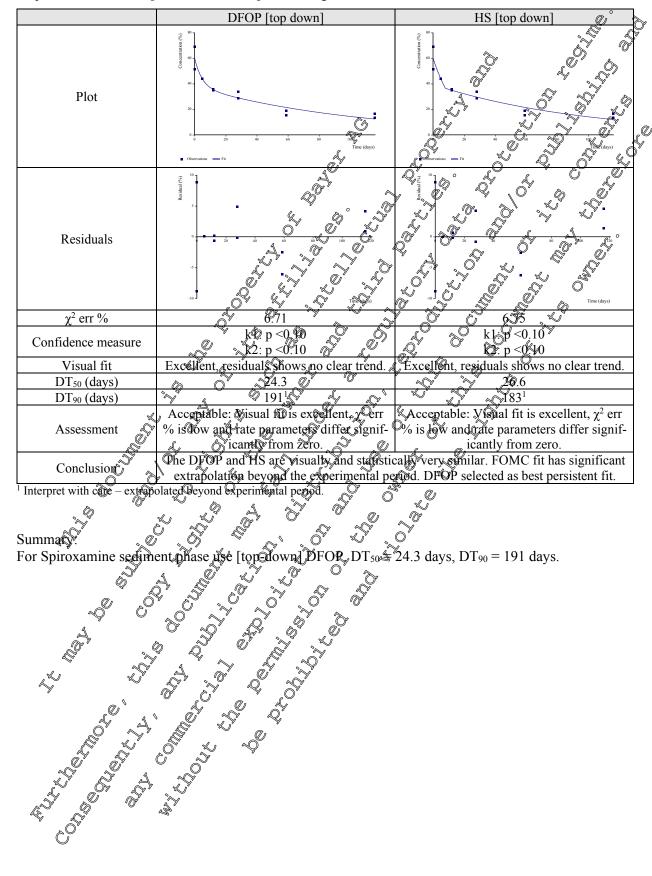


Appendix 5.1.3.5. Dissipation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Anglerweiher sediment phase (KCA 7.2.2.3/04 (<u>M-303324-01-1</u>))

Step 1: Initial assessment (SFO [decline after max] more appropriate than FOMC [decline after max] and gives acceptable fit?)



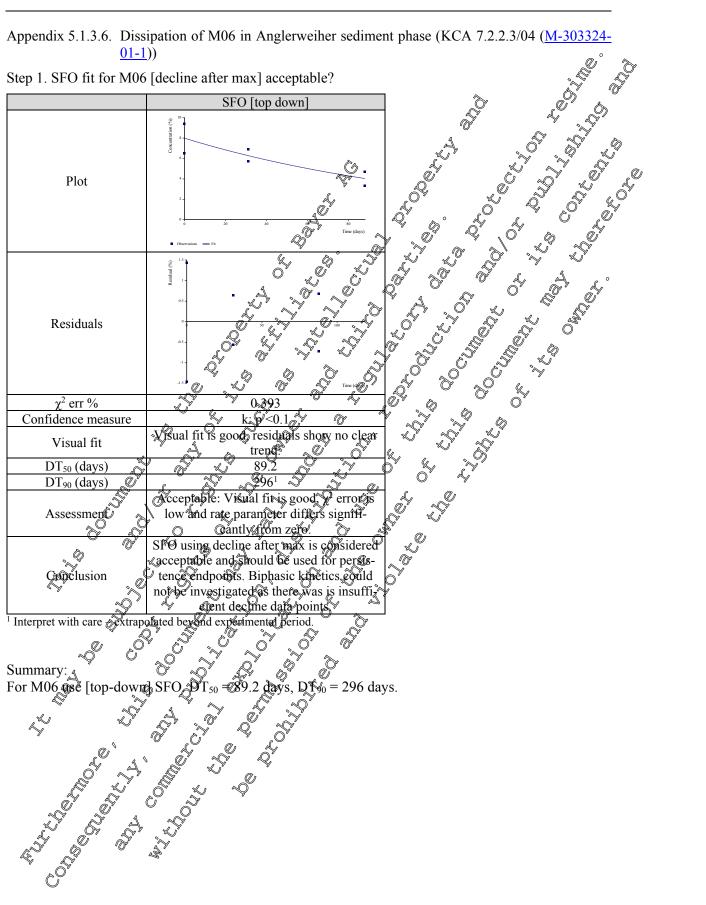




Step 2: DFOP and HS [decline after max] fit investigated.



Appendix 5.1.3.6. Dissipation of M06 in Anglerweiher sediment phase (KCA 7.2.2.3/04 (M-303324-(01-1))

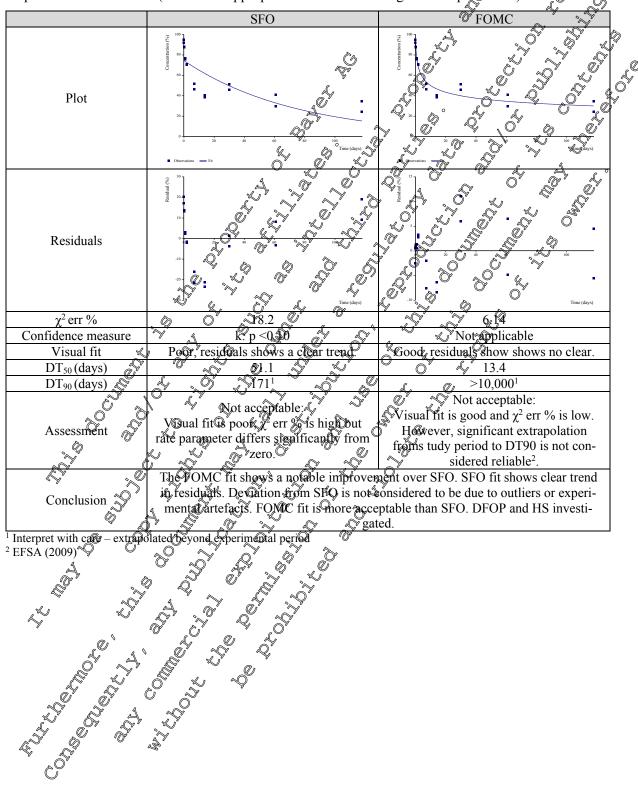




Appendix 5.1.4. KCA 7.2.2.3/04 (M-303324-01-1) Hoenniger Water system

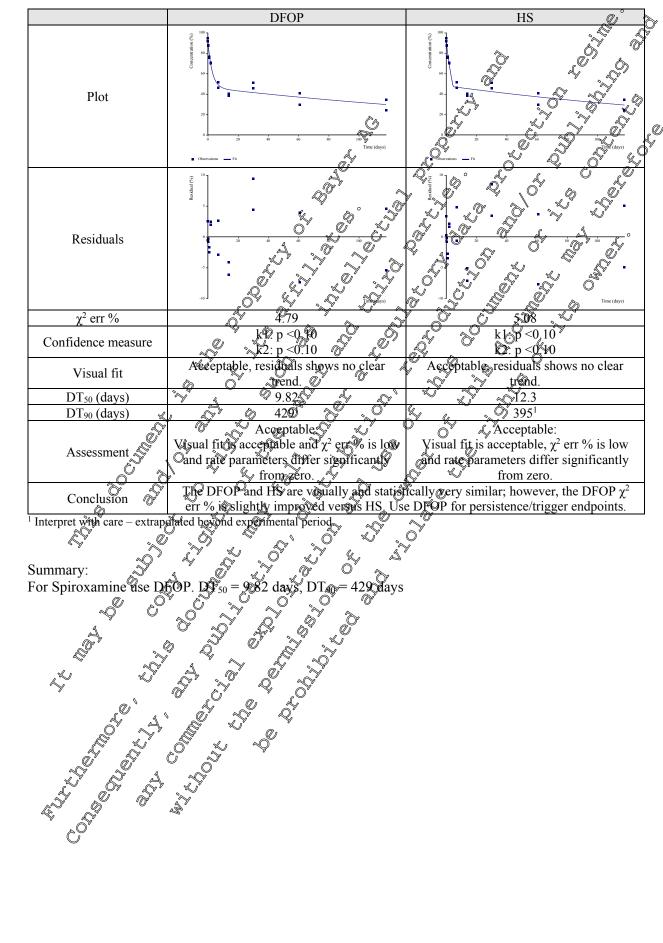
Appendix 5.1.4.1. Degradation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Hoenniger total system (KCA 7.2.2.3/04 (<u>M-303324-01-1</u>))

Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)

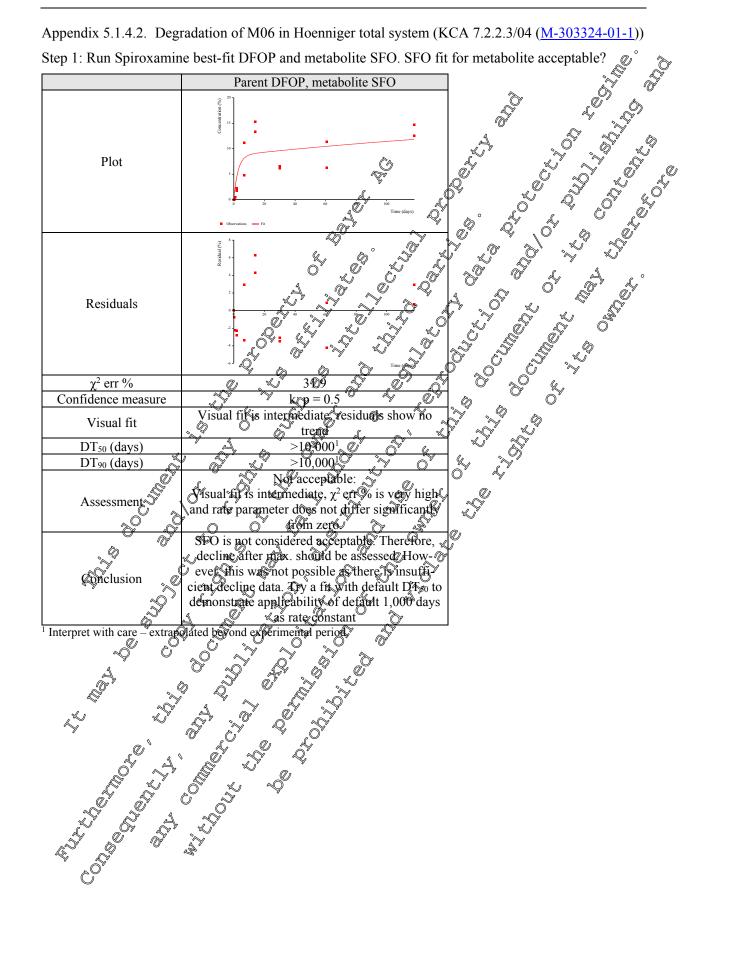




Step 2: DFOP and HS fit investigated.

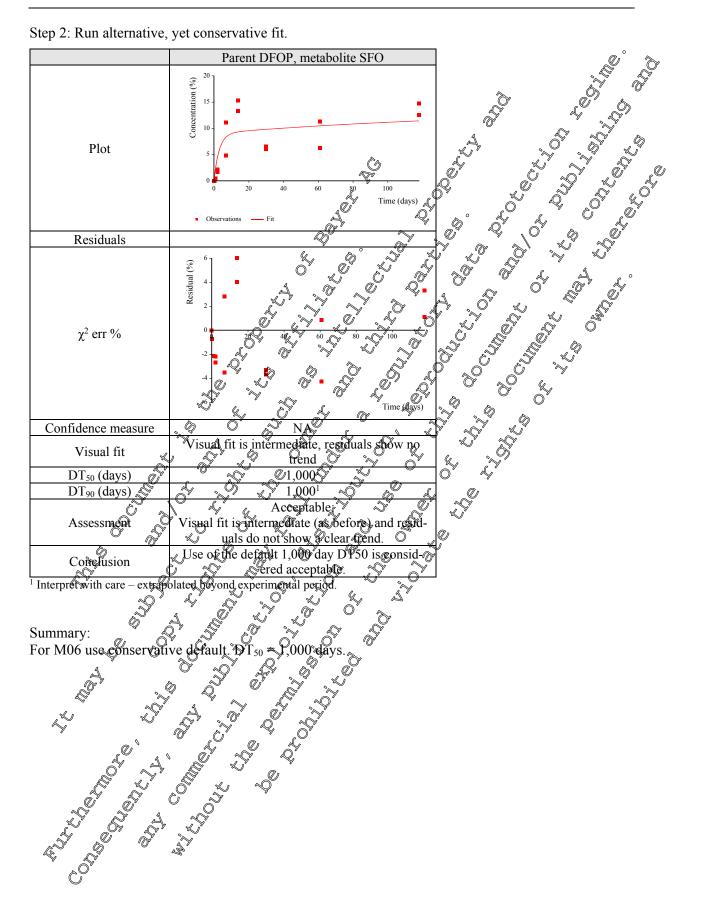






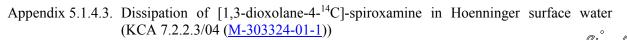
Appendix 5.1.4.2. Degradation of M06 in Hoenniger total system (KCA 7.2.2.3/04 (M-303324-01-1))

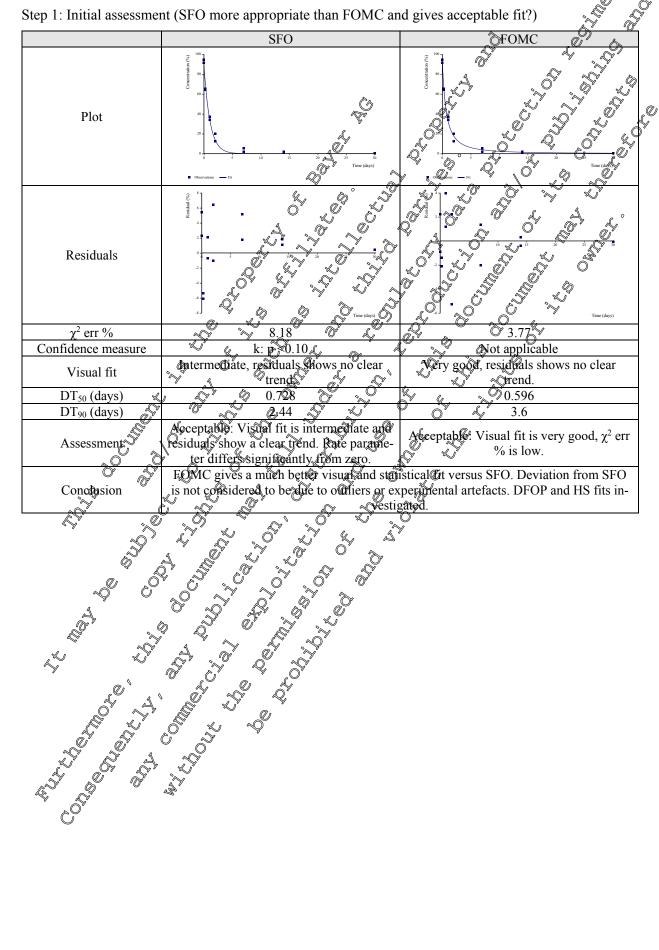




Step 2: Run alternative, yet conservative fit.

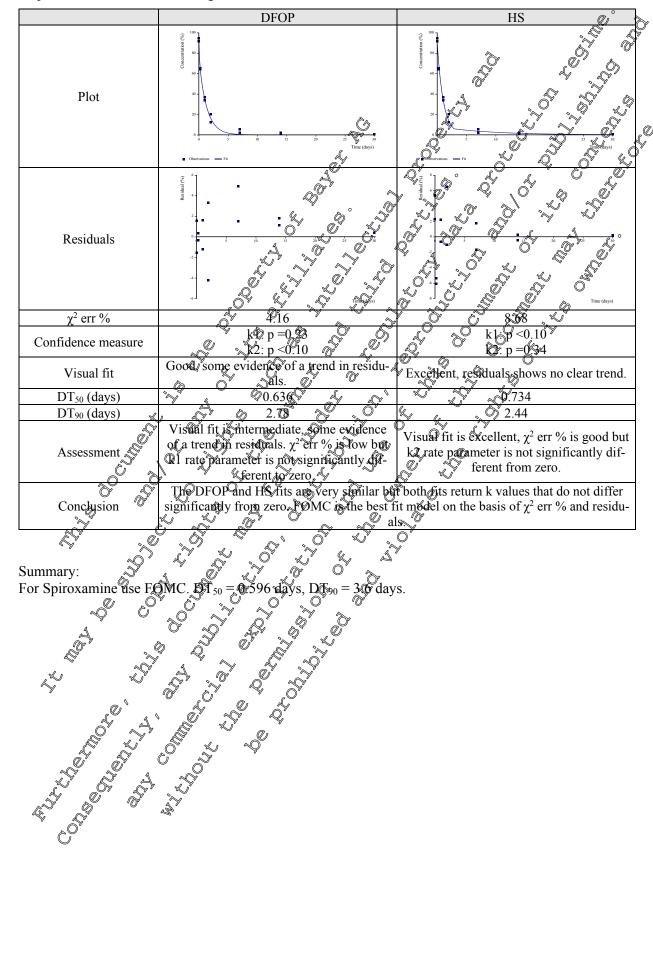








Step 2: DFOP and HS fit investigated.



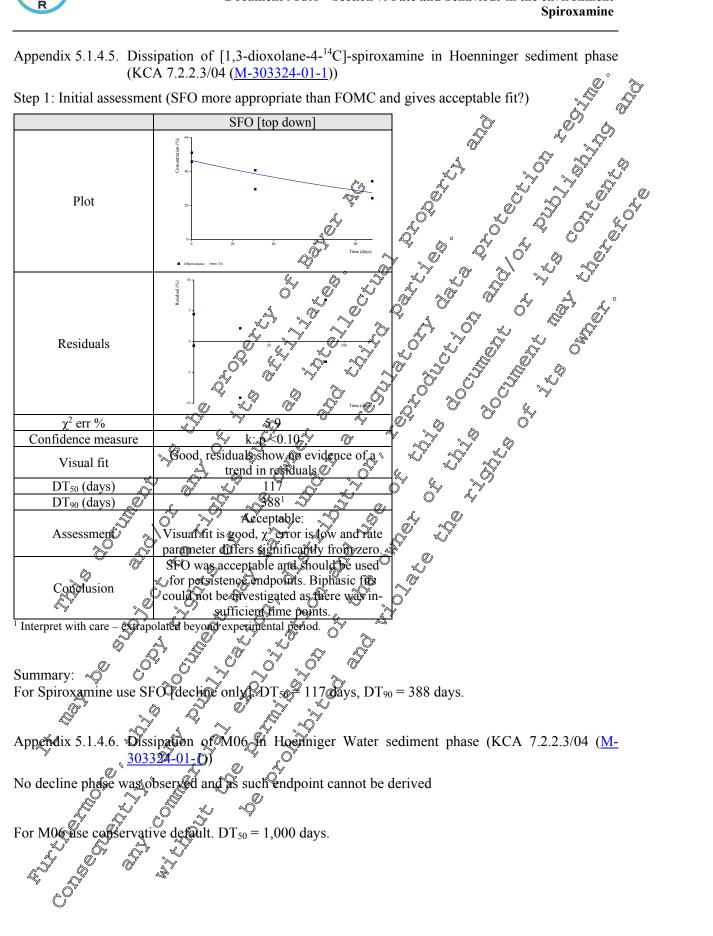


Step 1: SFO [top-down] more appropriate than FOMC [top-down] and gives acceptable fit?) Metabolite SFO [top down] Metabolite FOMC [top down Plot cesidua. Residuals $\chi^2 \, \text{err} \, \%$ Not applic Die Confidence measure Ìk: p ≲@,√ Ô'n Visual fit is poor, some exidence of a ery good, residuals shows no clear Visual fit trend in residuals trend. DT₅₀ (days) 32.8 着 \$.31 DT₉₀ (days) $10,000^{1}$ Formation fraction Not applicable Not applicable Sual fit is poor x² err% is ver high & Accoptable Wisual fit is very good, χ^2 err and rate parameter does not differ signifie Assessment % is low. contly from zero Summary: For M06 use FOMC [decline only]. DT = 8.26 days DT₉₀ = >10,000 days. SFO [decline only] is not considered acceptable. Deviation from SFO is not consid-Ò ered to be due to outliers or experiment wartefaces. FOMC [decline only] showed ac-Geptable fit, therefore DFOP [Secline only] and HS [decline only] kinetics should be investigated, however, there are insufficient time points.

Appendix 5.1.4.4. Dissipation of M06 in Hoenniger water phase (KCA 7.2.2.3/04 (<u>M-303324-01-1</u>)) Step 1: SEQ [top down] more appropriate than EQMC [top down] and gives acceptable fit²)



Appendix 5.1.4.5. Dissipation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Hoenninger sediment phase (KCA 7.2.2.3/04 (M-303324-01-1))

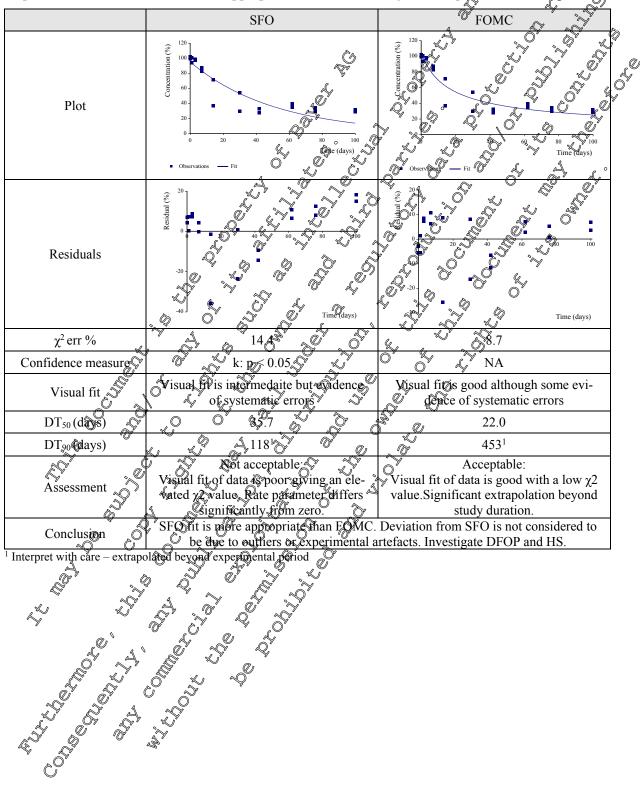




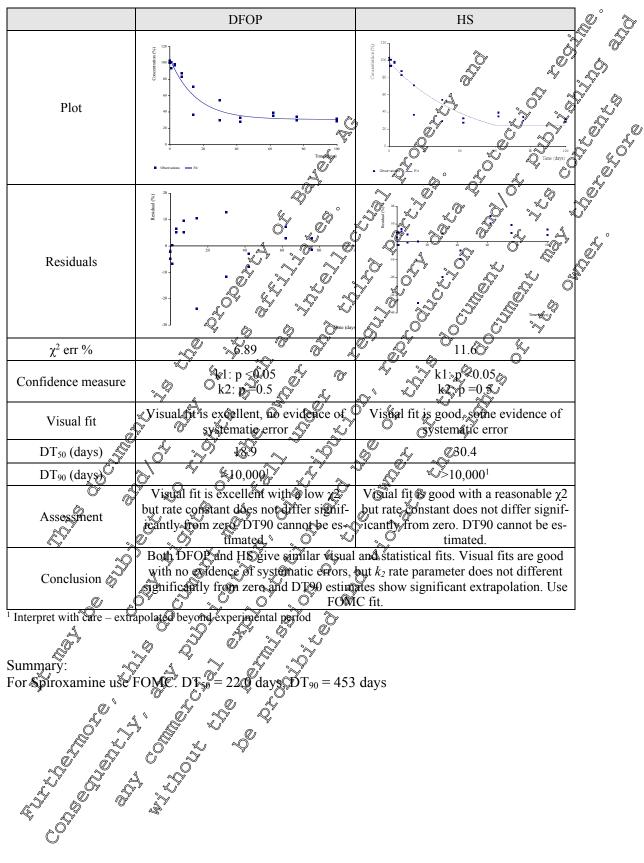
Appendix 5.1.5. KCA 7.2.2.3/07 (M-763128-01-1) Calwich Abbey

Appendix 5.1.5.1. Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in Calwich Abbey total system (KCA 7.2.2.3/07 (<u>M-763128-01-1</u>))

Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)



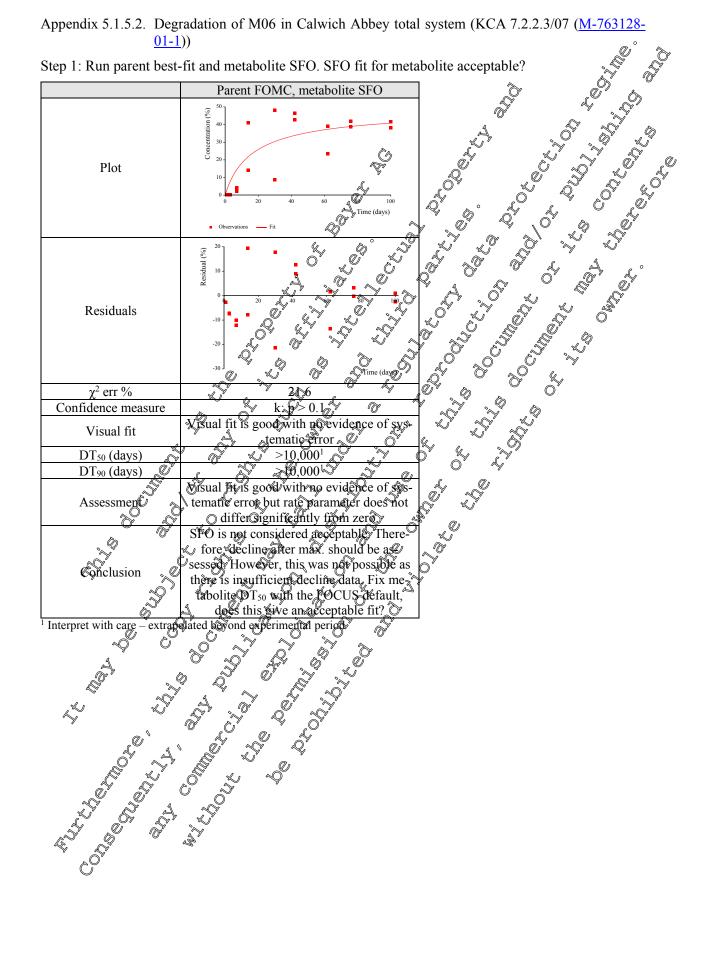




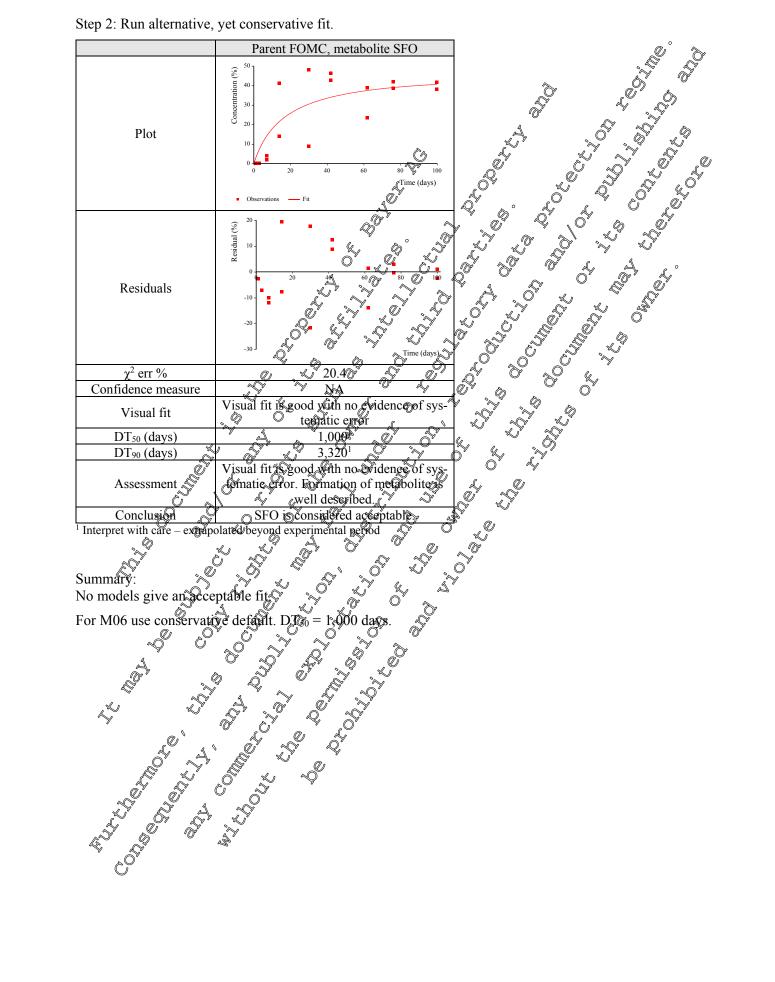
Step 3: FOMC better than SFO fit. Fit DFOP and HS.



Appendix 5.1.5.2. Degradation of M06 in Calwich Abbey total system (KCA 7.2.2.3/07 (M-763128-(01-1))



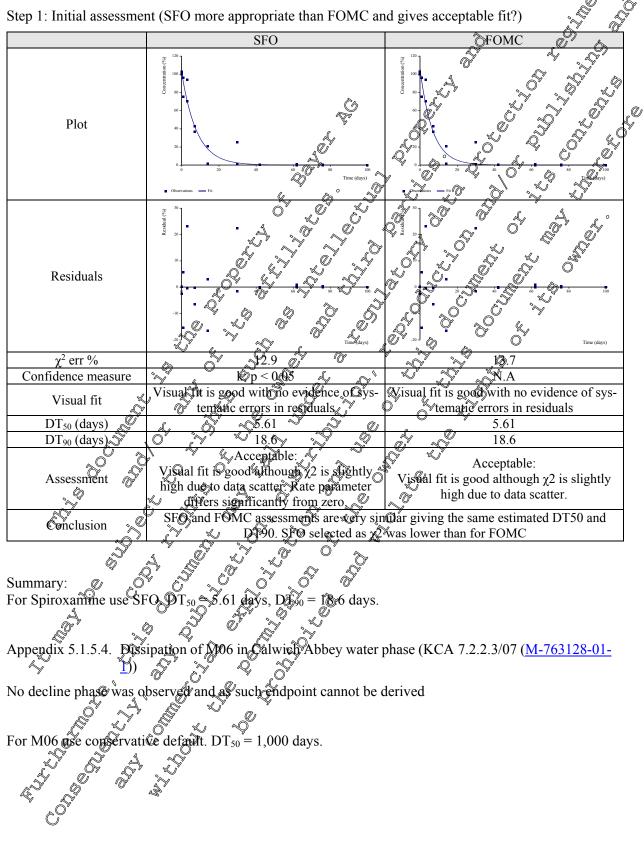




Step 2: Run alternative, yet conservative fit.



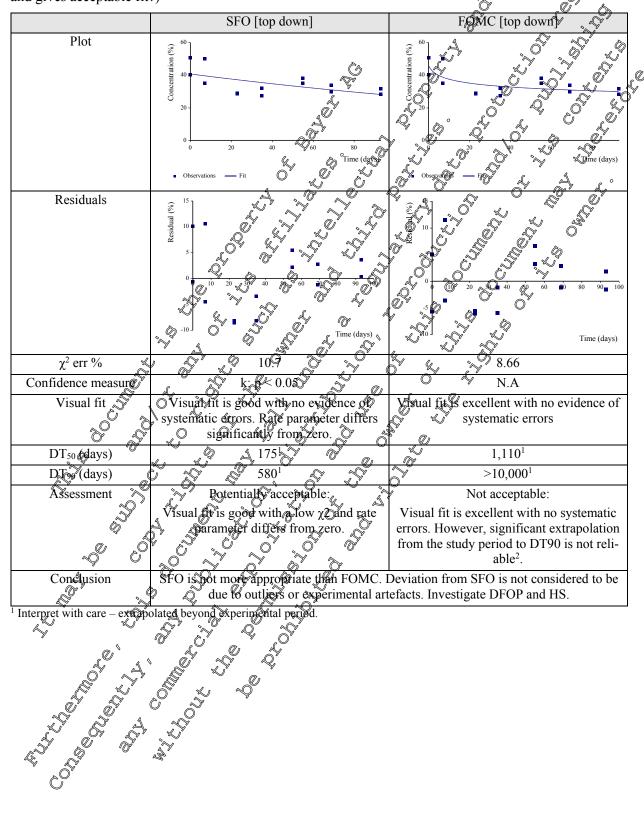
Appendix 5.1.5.3. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Calwich Abbey water phase (KCA 7.2.2.3/07 (<u>M-763128-01-1</u>))



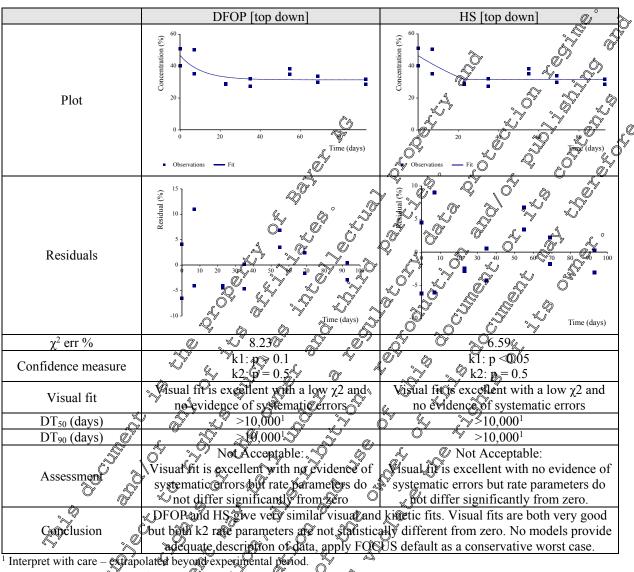


Appendix 5.1.5.5. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Calwich Abbey sediment phase (KCA 7.2.2.3/07 (<u>M-763128-01-1</u>))

Step 1: Initial assessment (SFO [decline after max] more appropriate than FOMC [decline after max] and gives acceptable fit?)







Step 2: DFOP and HS [decline after max] fit investigated.

Summary: ativo defante D For Spiroxamine use conser days.

Appendix 5.1.5.6. Dissipation of 106 in Calwick Abbey sediment phase (KCA 7.2.2.3/07 (M-763128--1 YR

No decline phase was observed and s such endpoint cannot be derived.

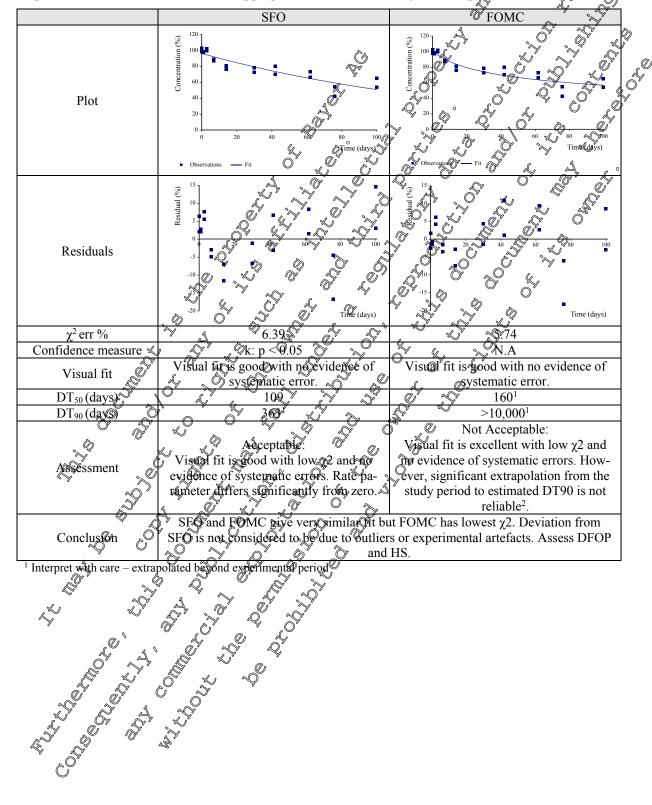
For M06 use conservative default, DT₅₆ 1,000 days.



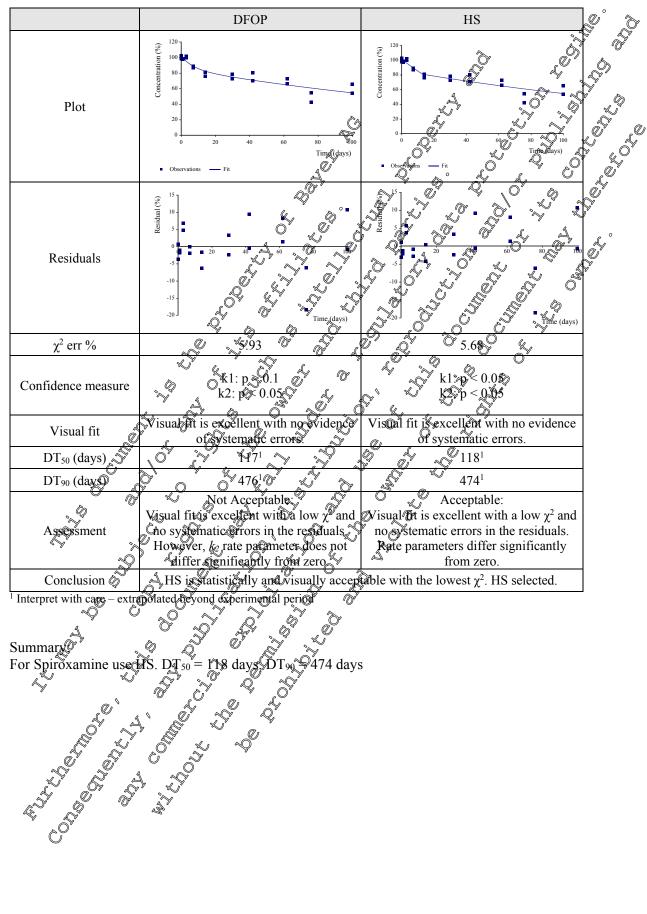
Appendix 5.1.6. KCA 7.2.2.3/07 (M-763128-01-1) Emperor Lake

Appendix 5.1.6.1. Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in Emperor Lake total system (KCA 7.2.2.3/07 (<u>M-763128-01-1</u>))

Step 1: Initial assessment (SFO more appropriate than FOMC and gives acceptable fit?)



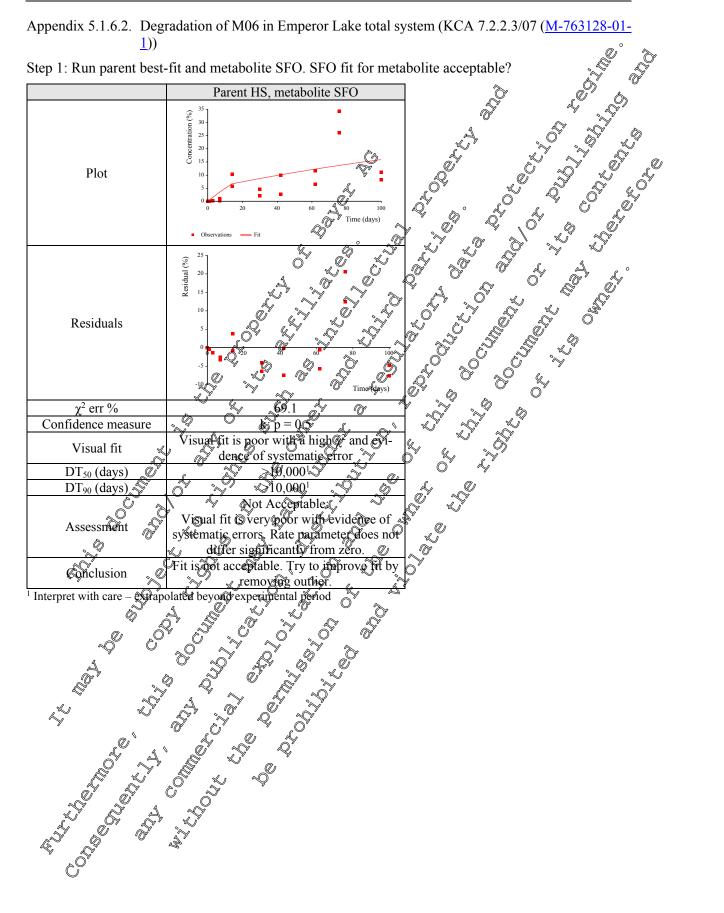




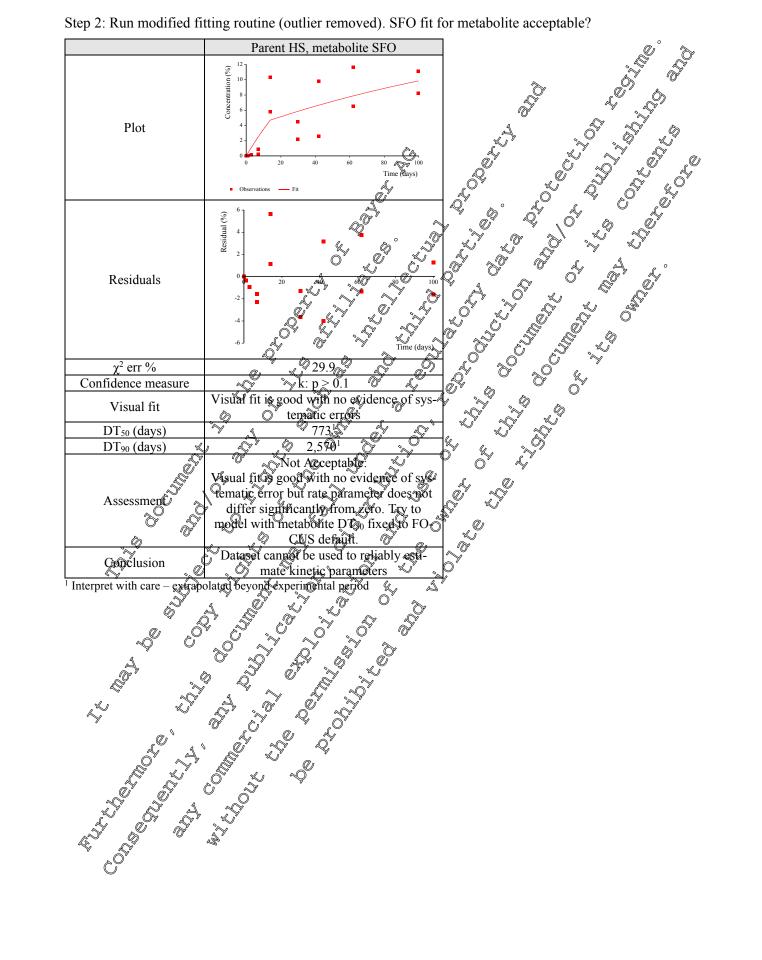
Step 3: FOMC better than SFO fit. Fit DFOP and HS.



Appendix 5.1.6.2. Degradation of M06 in Emperor Lake total system (KCA 7.2.2.3/07 (M-763128-01-1))







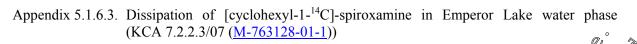
Step 2: Run modified fitting routine (outlier removed). SFO fit for metabolite acceptable?

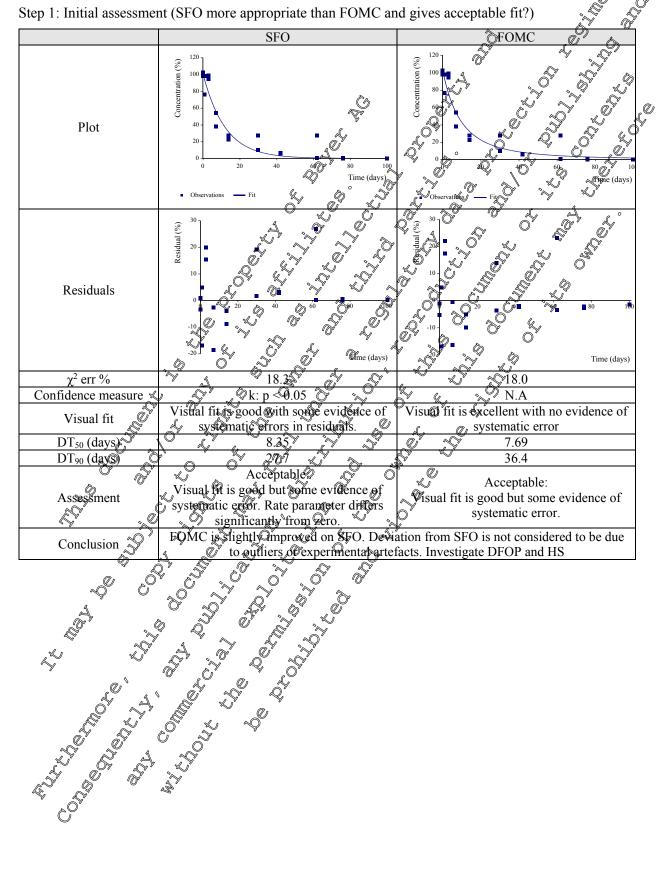


A Charles a construction of the construction o toth. Spiroxamine HS, metabolite SFO where the second Concentration (%) 10 8

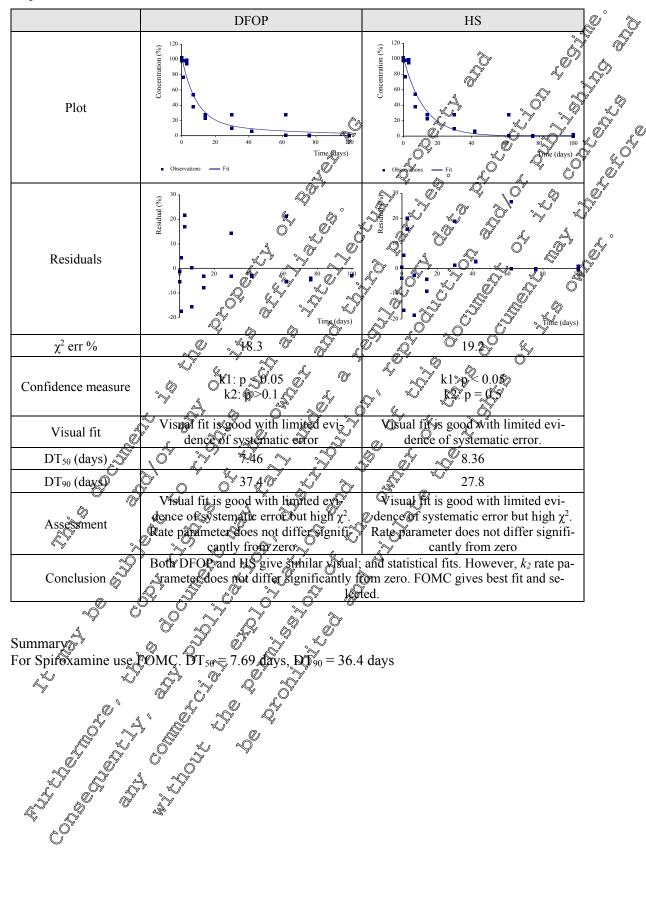
Step 2: Run alternative conservative fits











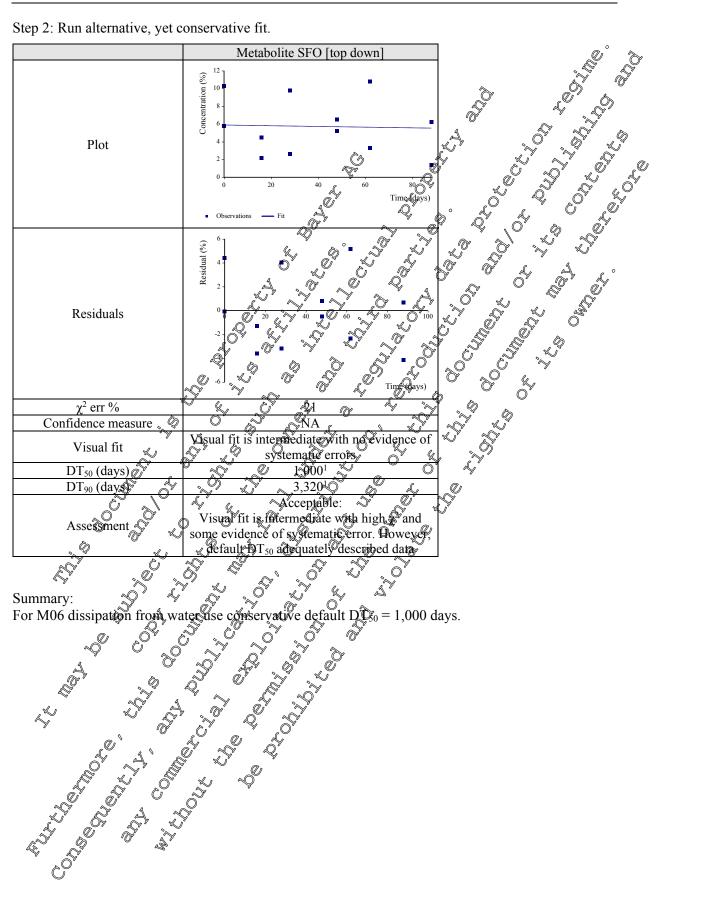
Step 3: FOMC better than SFO fit. Fit DFOP and HS.



Step 1: SFO [top-down] more appropriate than FOMC [top-down] and gives acceptable fit?) \Im°		
	Metabolite SFO [top down]	Metabolite FOMC [top down]
Plot	0 0 0 0 0 0 0 0 0 0 0 0 0 0	Observation — File Contraction (days)
Residuals	(0) (0) (0) (0) (0) (0) (0) (0)	Image: Second
$\chi^2 \text{ err } \%$		20.2 0
Confidence measure	k: p >0.05 0 0	N. A
Visual fit	Visual fit is internitediate with some evi-	& dence of systematic errors
DT ₅₀ (days) DT ₉₀ (days)		∑ ¹ 2/ ∑ ¹ 0,000 ¹ >10,000 ¹
Assessment Conclusion	HS would not improve the fit. Insufficient diction of endpoints. Try to fit default DT	Not Acceptable: Votual fit is intermediate with high χ^2 and me evidence of systematic error. Signif- icant extrapolation from study period to DT90 is not considered reliable ² . s. IOvas considered that running DFOP and decline phase to allow for an accurate pre- tion – does the fit give an acceptable descrip- he data?
¹ Interpret with care – extr ² EFSA (2009)	action of and points. Thy of the dedicating of the dedication of t	

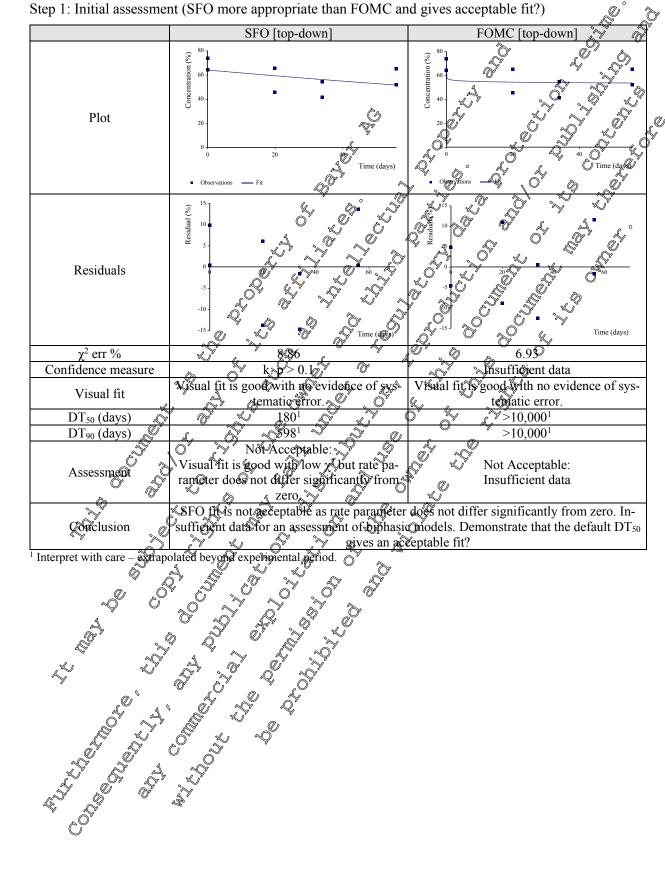
Appendix 5.1.6.4. Dissipation of M06 in water





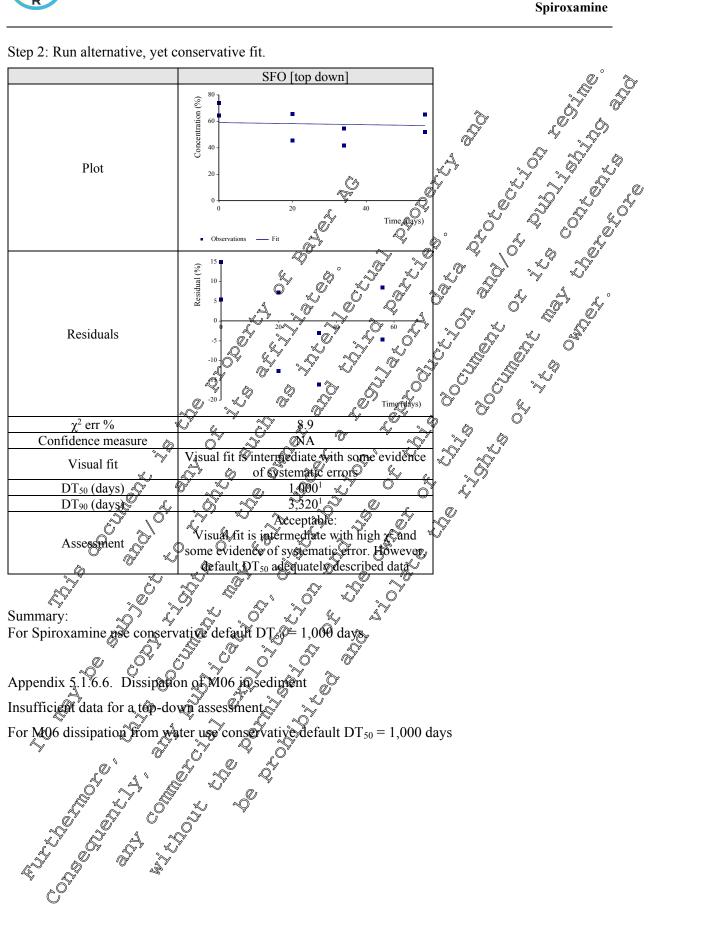
Step 2: Run alternative, yet conservative fit.





Appendix 5.1.6.5. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in sediment Step 1: Initial assessment (SEO more appropriate than EOMC and gives acceptable

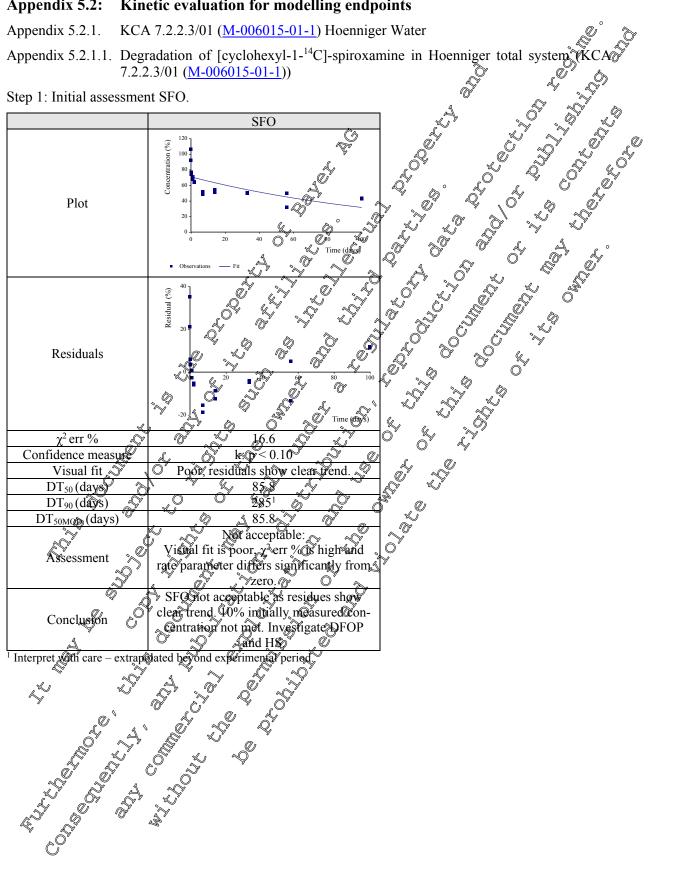




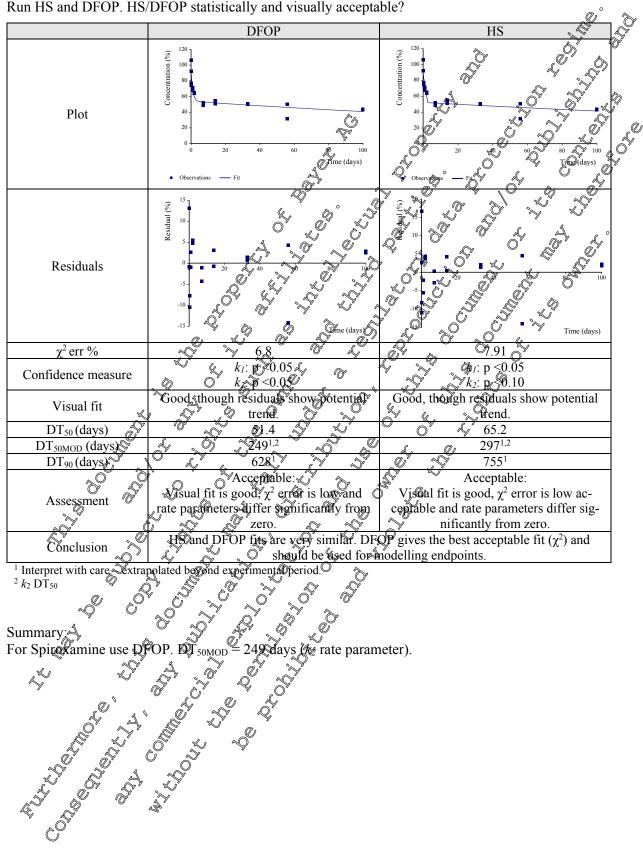
Step 2: Run alternative, yet conservative fit.



Appendix 5.2: Kinetic evaluation for modelling endpoints



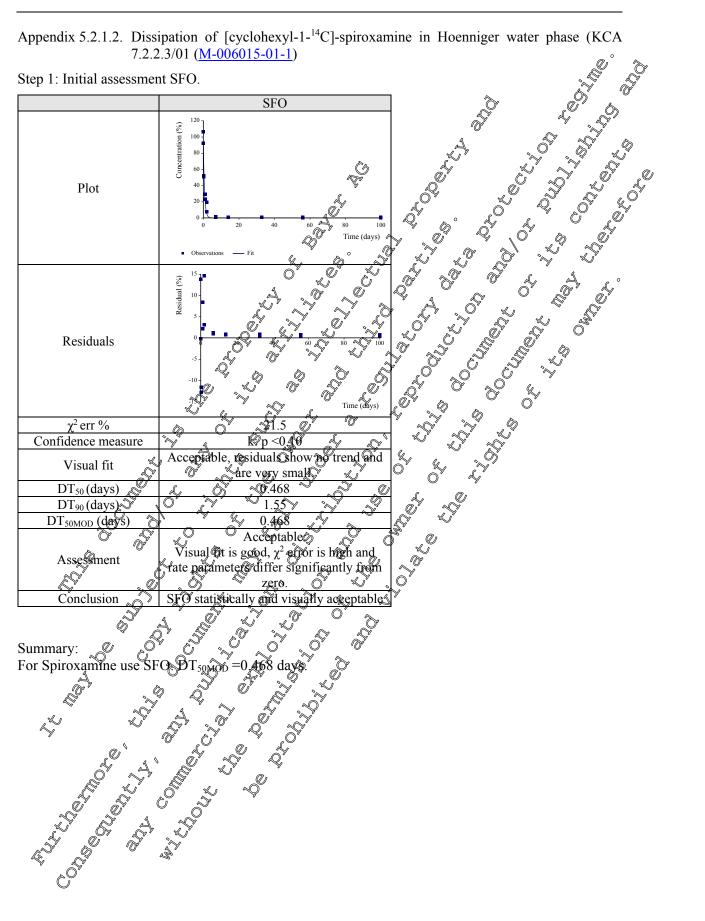




Step 2: 10% initially measured concentration not reached within experimental period. Run HS and DFOP. HS/DFOP statistically and visually acceptable?

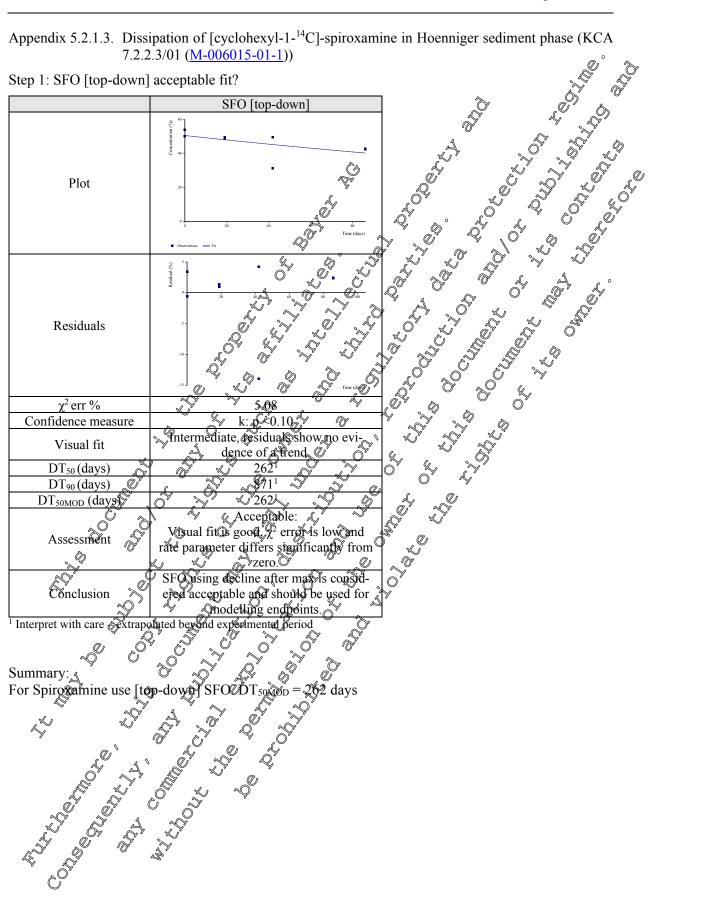


Appendix 5.2.1.2. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Hoenniger water phase (KCA 7.2.2.3/01 (M-006015-01-1)





Appendix 5.2.1.3. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Hoenniger sediment phase (KCA 7.2.2.3/01 (M-006015-01-1))

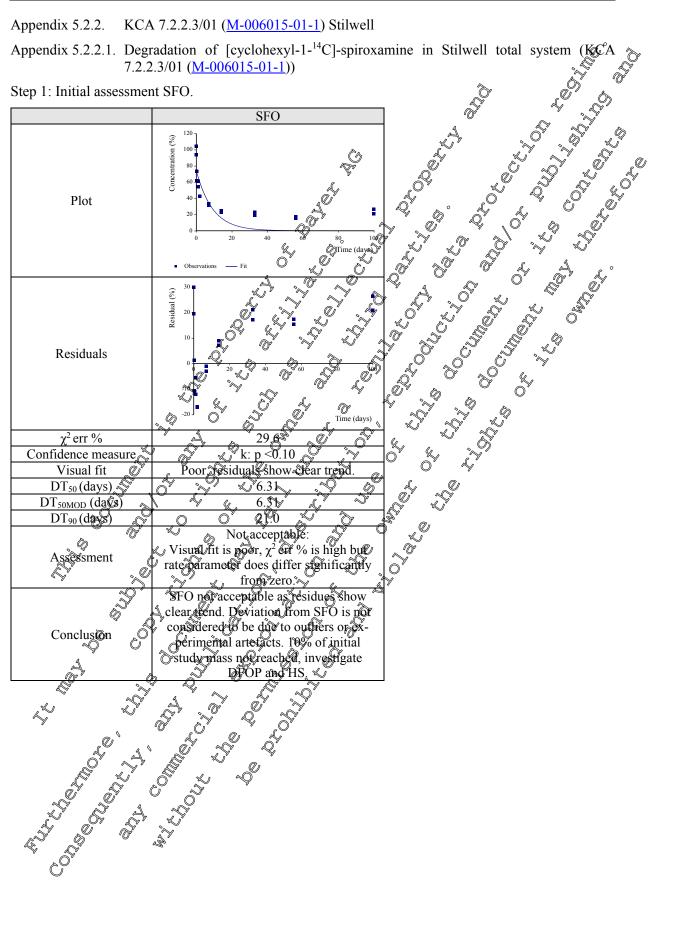




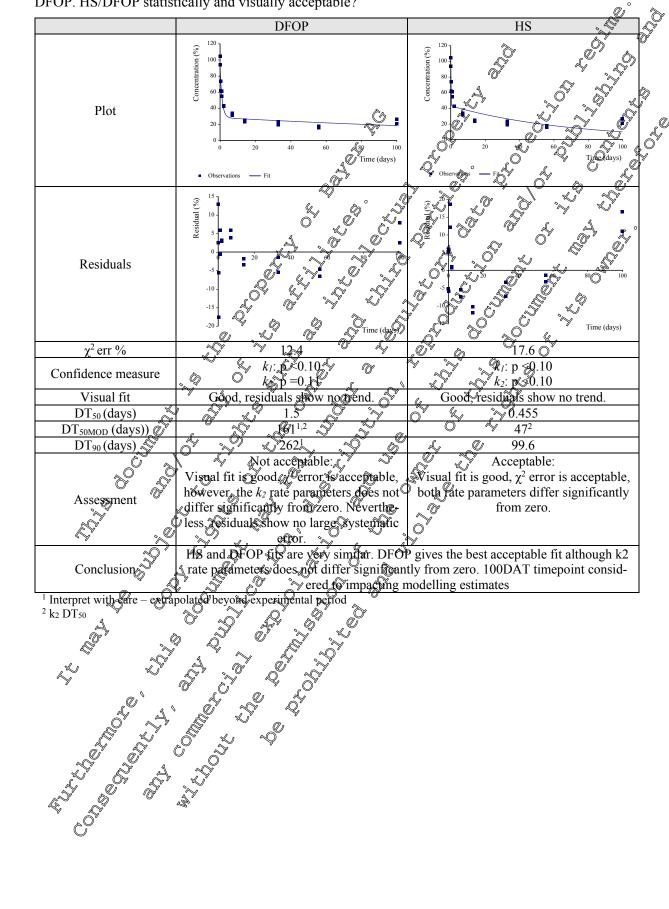
Appendix 5.2.2. KCA 7.2.2.3/01 (M-006015-01-1) Stilwell

Appendix 5.2.2.1. Degradation of [cyclohexyl-1- 14 C]-spiroxamine in Stilwell total system (KcA 7.2.2.3/01 (M-006015-01-1))

Step 1: Initial assessment SFO.

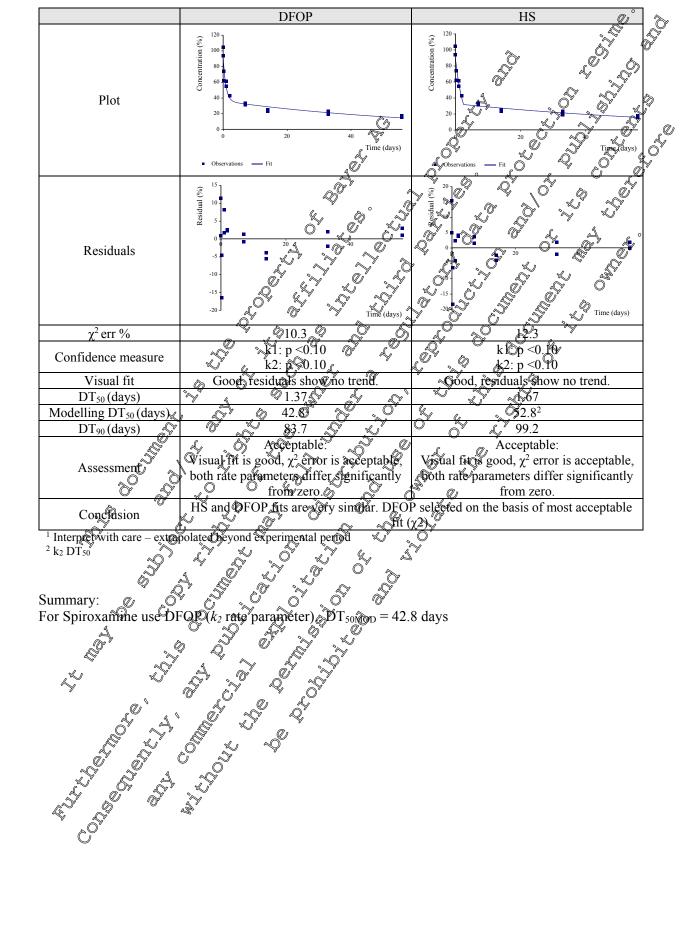






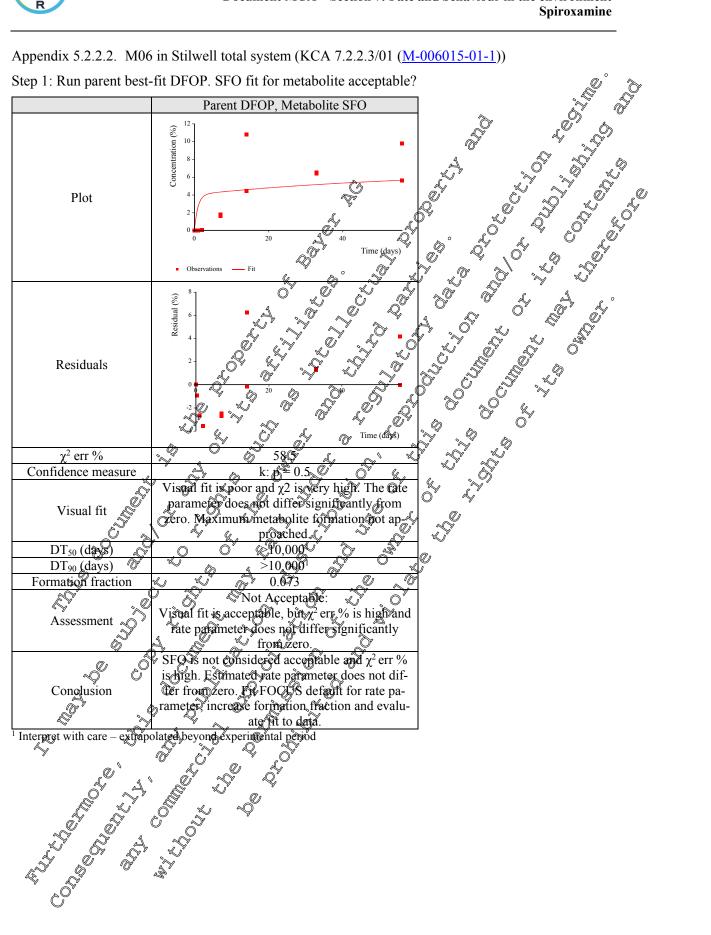
Step 2: 10% initially measured concentration not reached within experimental period. Run HS and DFOP. HS/DFOP statistically and visually acceptable?





Step 2: Modified fit: exclusion of 100DAT

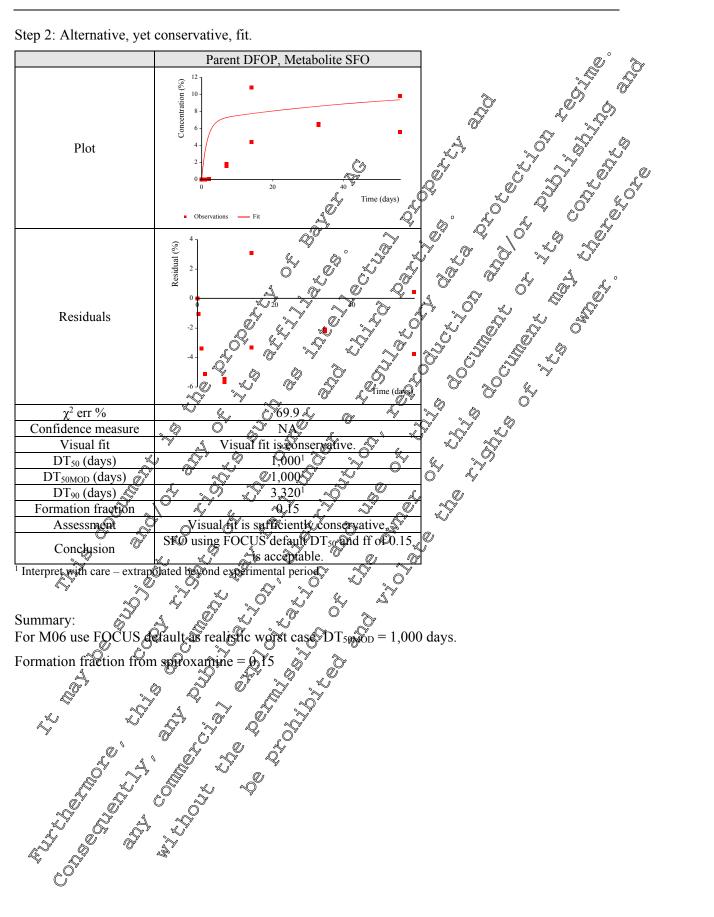




Appendix 5.2.2.2. M06 in Stilwell total system (KCA 7.2.2.3/01 (M-006015-01-1))

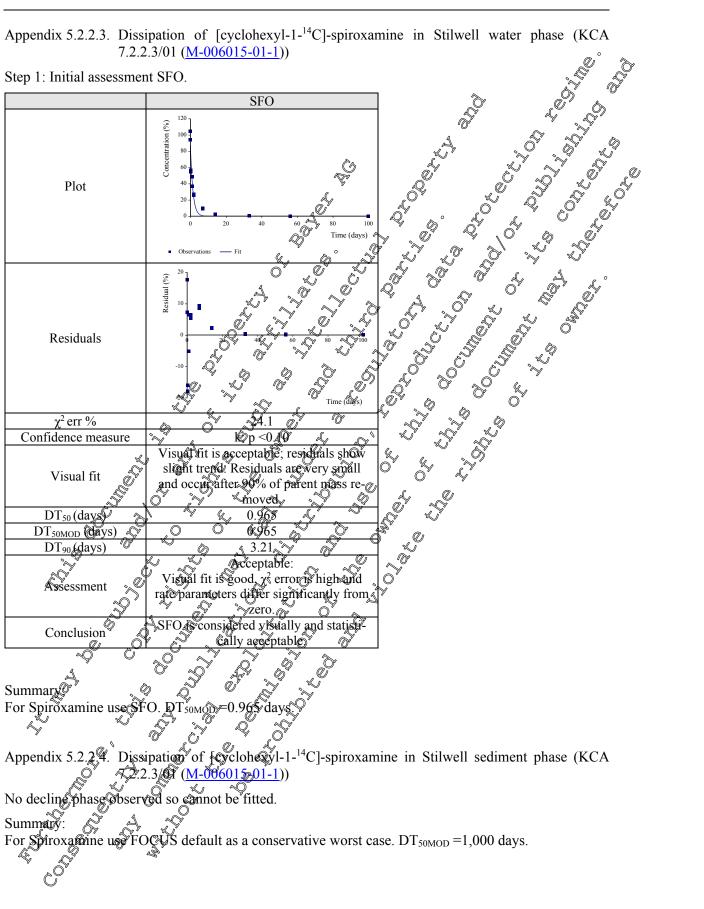


Step 2: Alternative, yet conservative, fit.





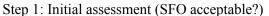
Appendix 5.2.2.3. Dissipation of [cyclohexyl-1-14C]-spiroxamine in Stilwell water phase (KCA 7.2.2.3/01 (M-006015-01-1))

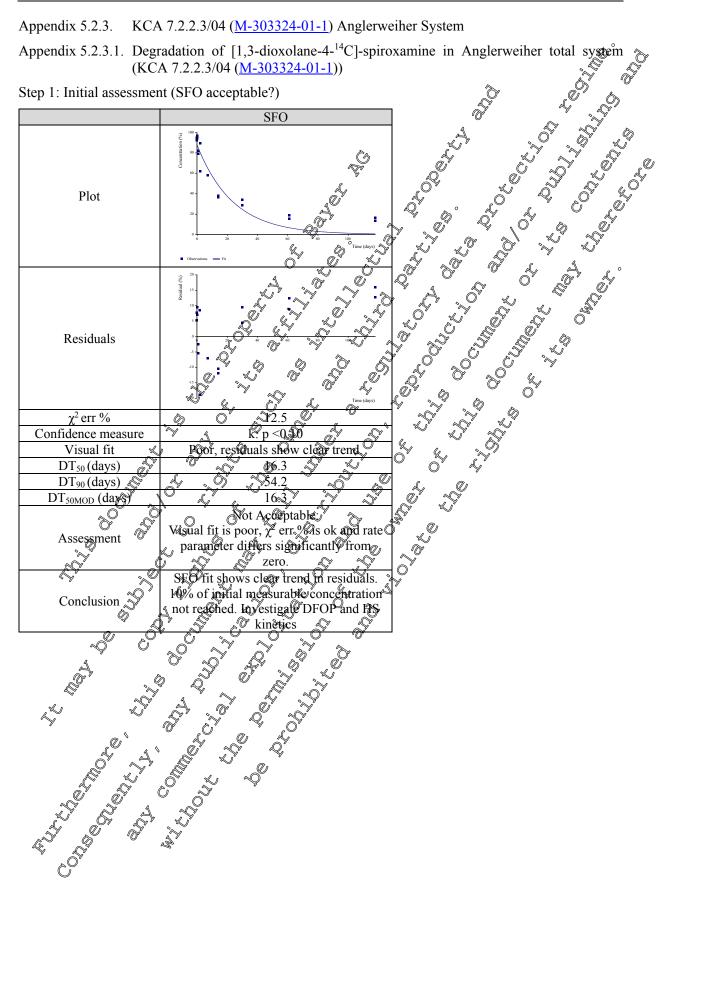




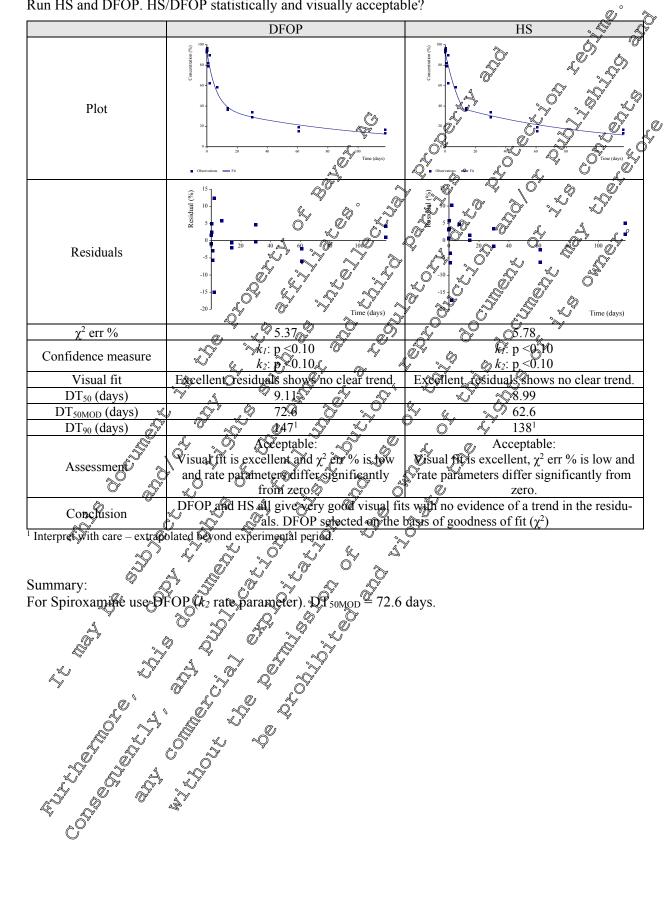
Appendix 5.2.3. KCA 7.2.2.3/04 (M-303324-01-1) Anglerweiher System

Appendix 5.2.3.1. Degradation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Anglerweiher total system (KCA 7.2.2.3/04 (M-303324-01-1))





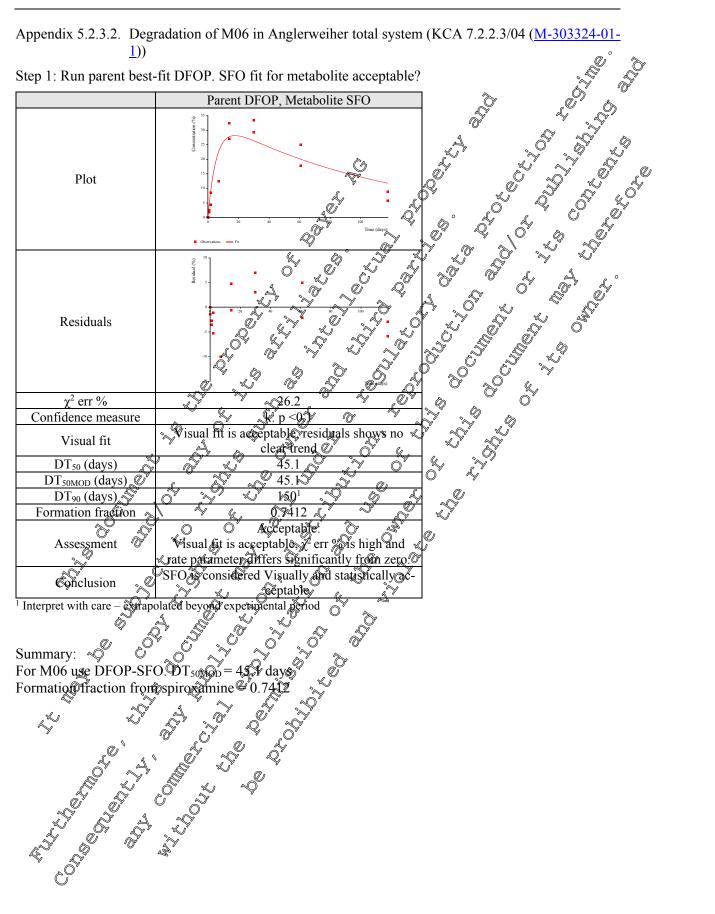




Step 2: 10% initially measured concentration not reached within experimental period. Run HS and DFOP. HS/DFOP statistically and visually acceptable?

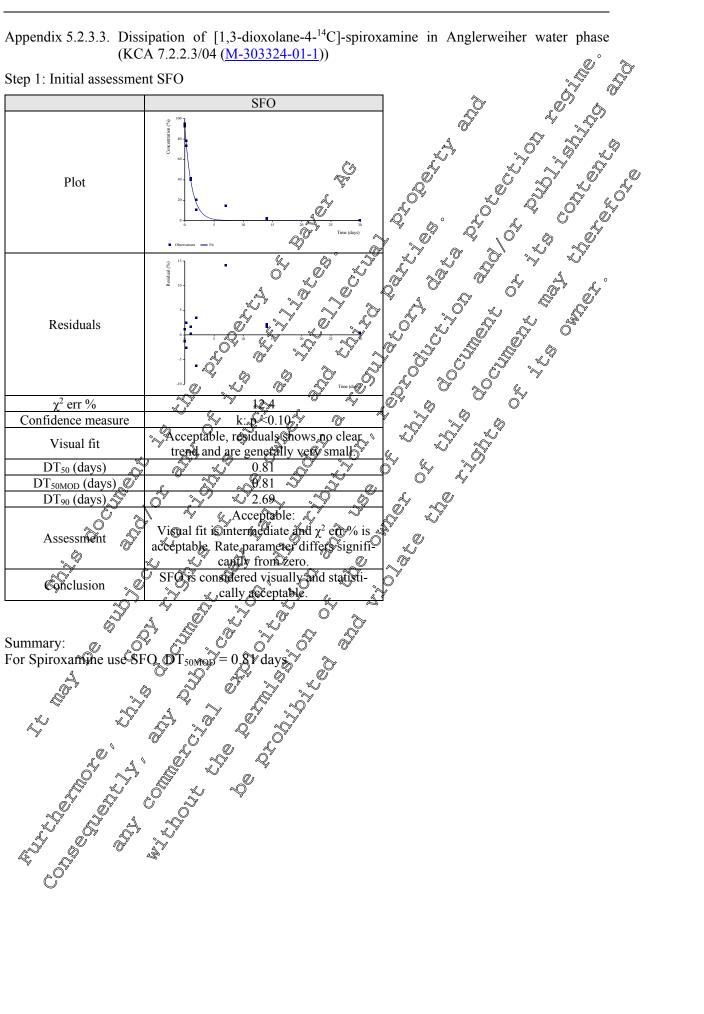


Appendix 5.2.3.2. Degradation of M06 in Anglerweiher total system (KCA 7.2.2.3/04 (M-303324-01-1))

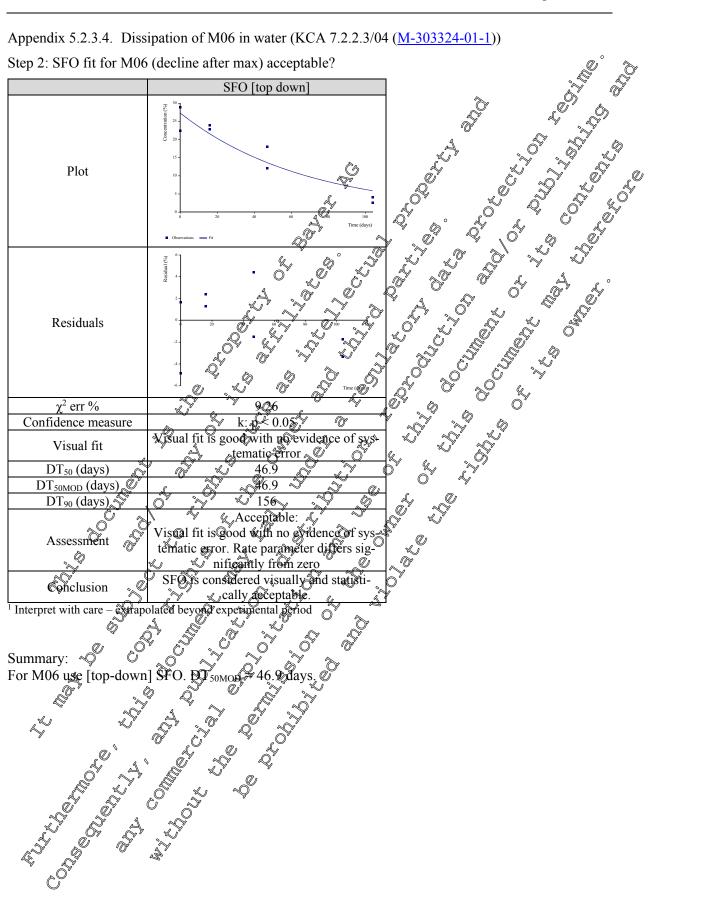




Appendix 5.2.3.3. Dissipation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Anglerweiher water phase (KCA 7.2.2.3/04 (M-303324-01-1))



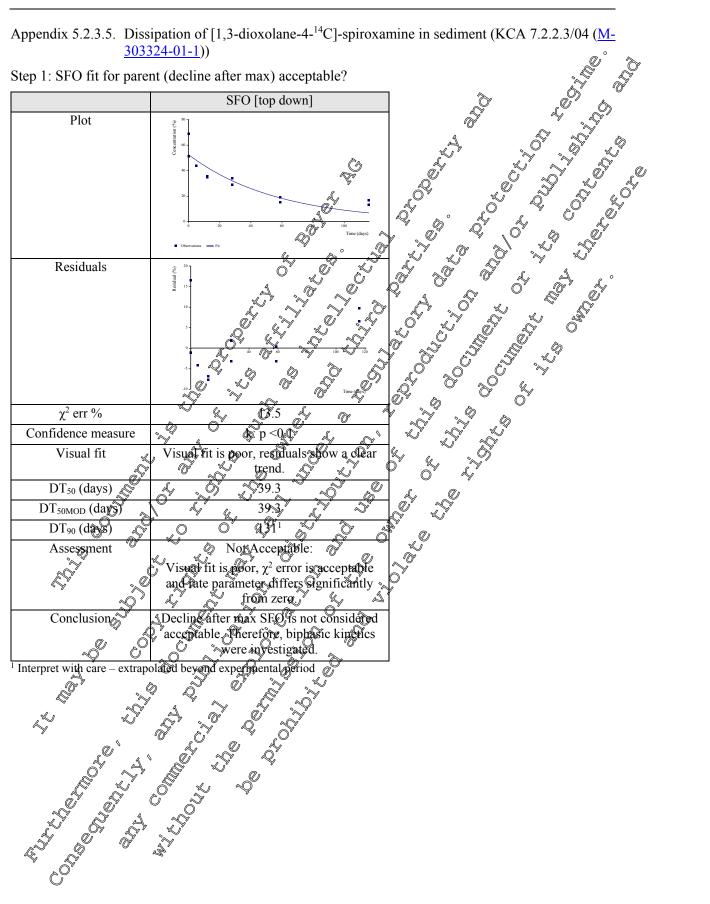




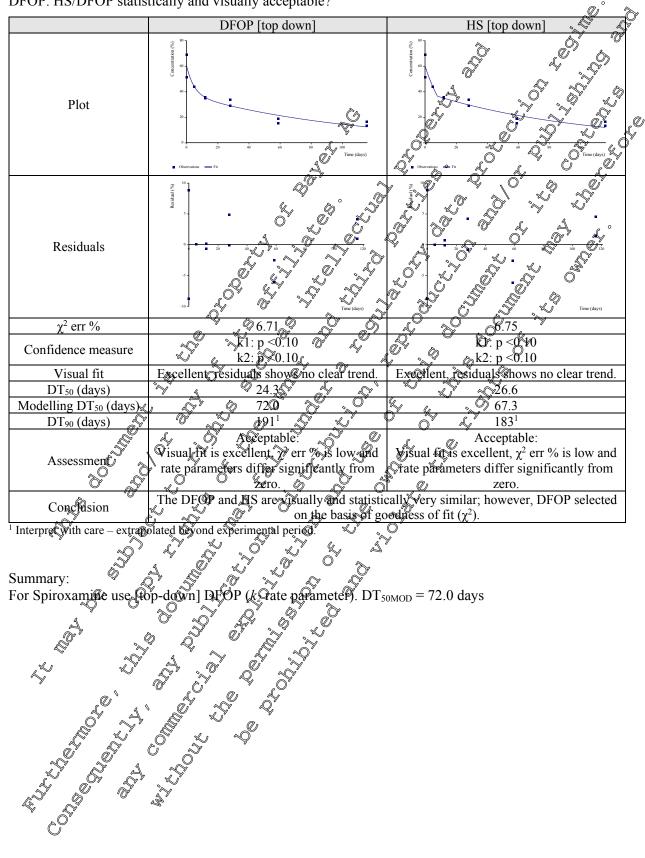
Appendix 5.2.3.4. Dissipation of M06 in water (KCA 7.2.2.3/04 (M-303324-01-1))



Appendix 5.2.3.5. Dissipation of [1,3-dioxolane-4-14C]-spiroxamine in sediment (KCA 7.2.2.3/04 (M-303324-01-1))

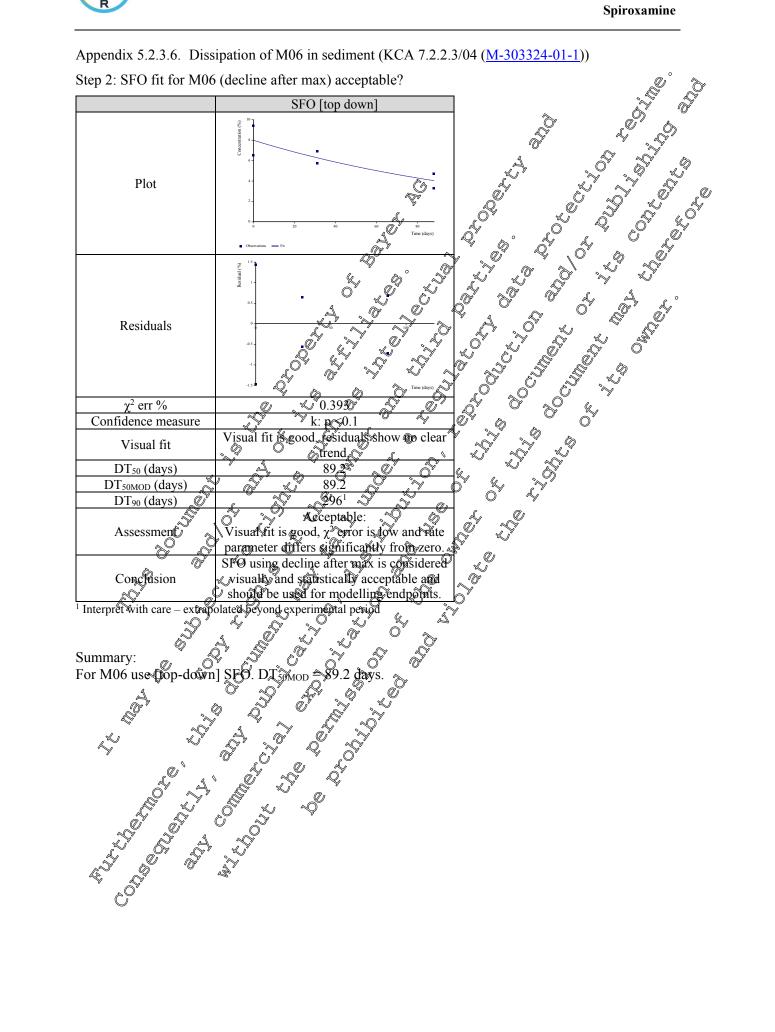






Step 2: 10% initially measured concentration not reached within experimental period. Run HS and DFOP. HS/DFOP statistically and visually acceptable?

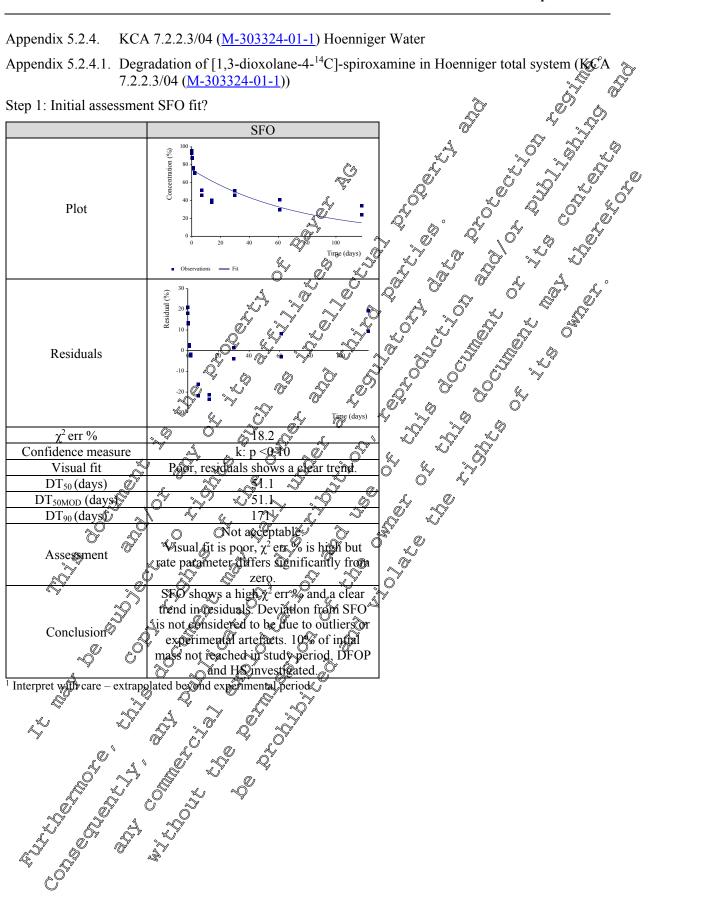




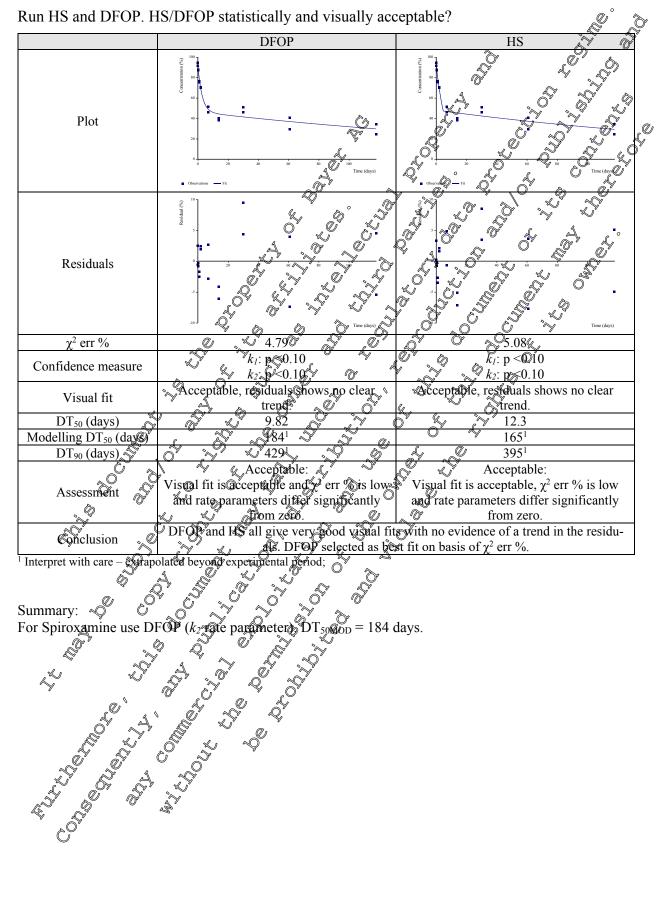


Appendix 5.2.4. KCA 7.2.2.3/04 (M-303324-01-1) Hoenniger Water

Appendix 5.2.4.1. Degradation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Hoenniger total system (KCA 7.2.2.3/04 (M-303324-01-1))



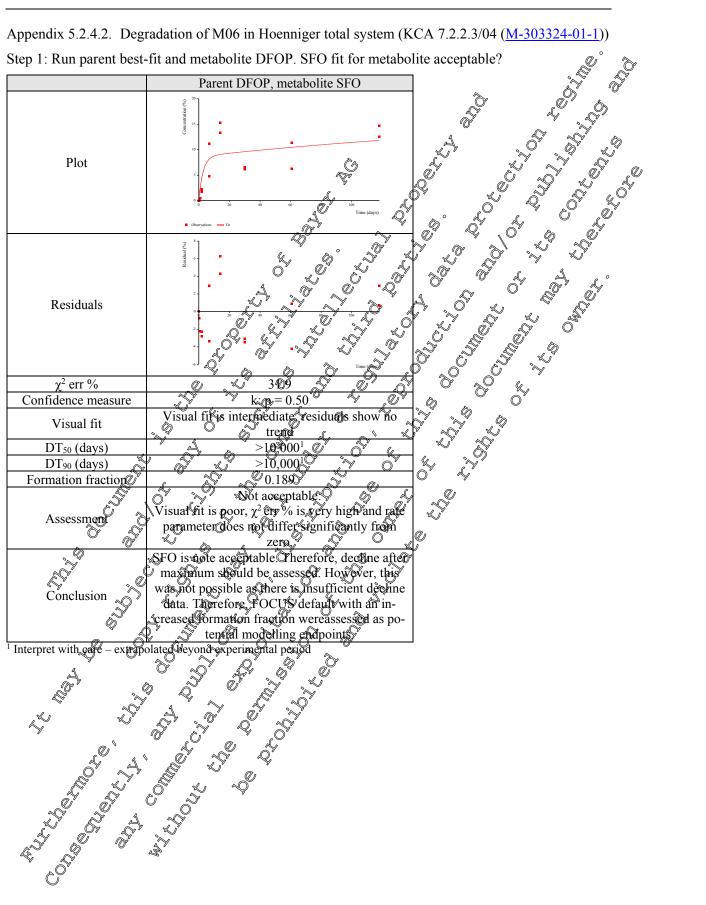




Step 2: 10% initially measured concentration not reached within experimental period.

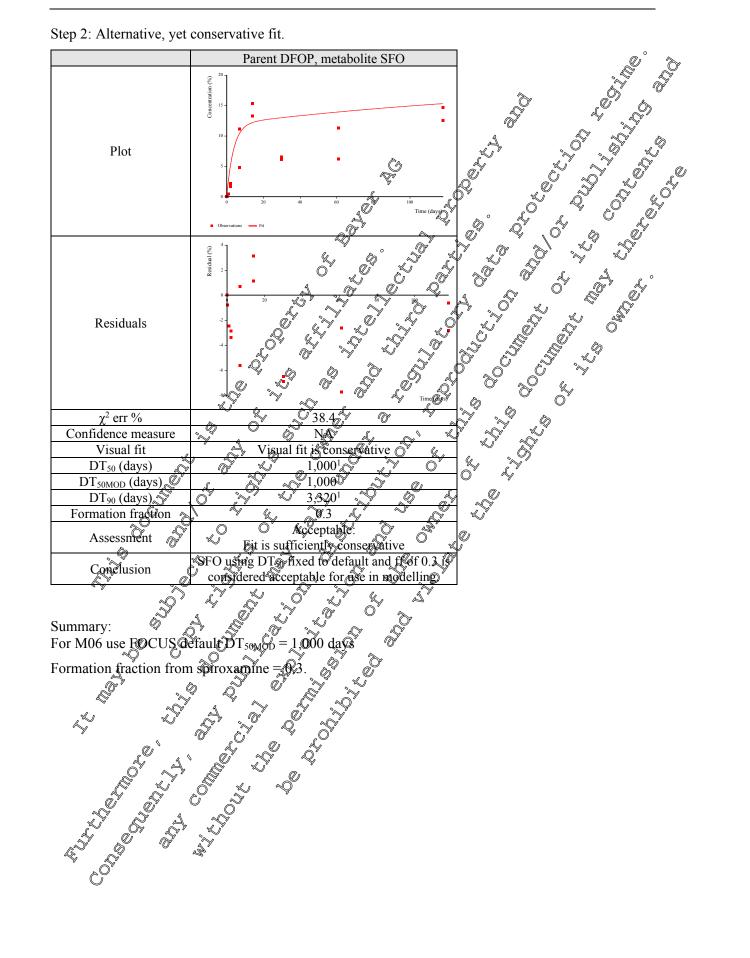


Appendix 5.2.4.2. Degradation of M06 in Hoenniger total system (KCA 7.2.2.3/04 (M-303324-01-1))



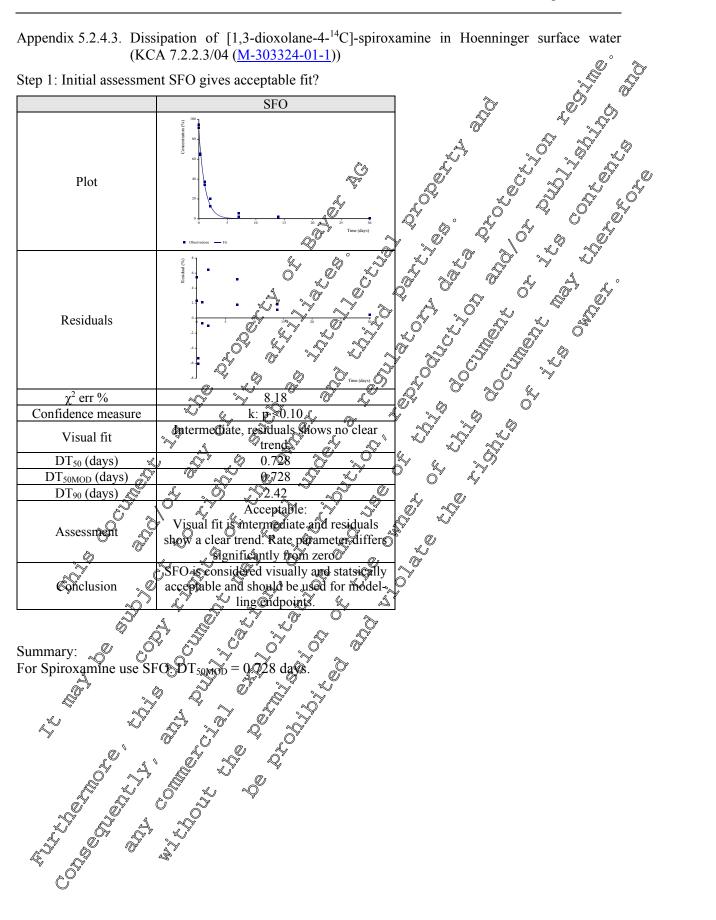


Step 2: Alternative, yet conservative fit.



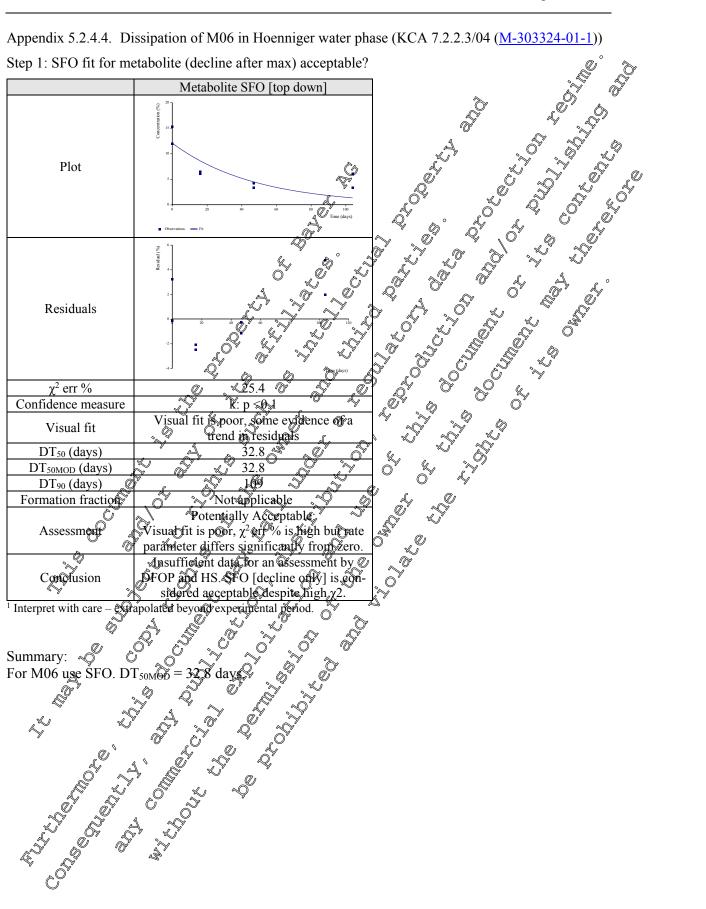


Appendix 5.2.4.3. Dissipation of [1,3-dioxolane-4-14C]-spiroxamine in Hoenninger surface water (KCA 7.2.2.3/04 (M-303324-01-1))



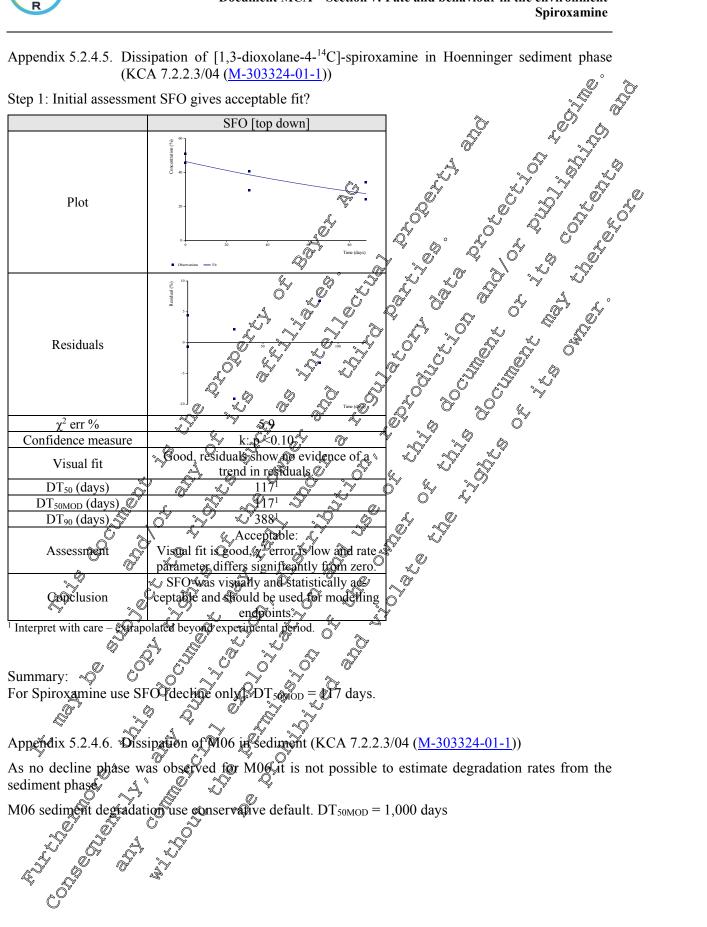


Appendix 5.2.4.4. Dissipation of M06 in Hoenniger water phase (KCA 7.2.2.3/04 (M-303324-01-1)) Step 1: SFO fit for metabolite (decline after max) acceptable?





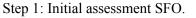
Appendix 5.2.4.5. Dissipation of [1,3-dioxolane-4-¹⁴C]-spiroxamine in Hoenninger sediment phase (KCA 7.2.2.3/04 (M-303324-01-1))

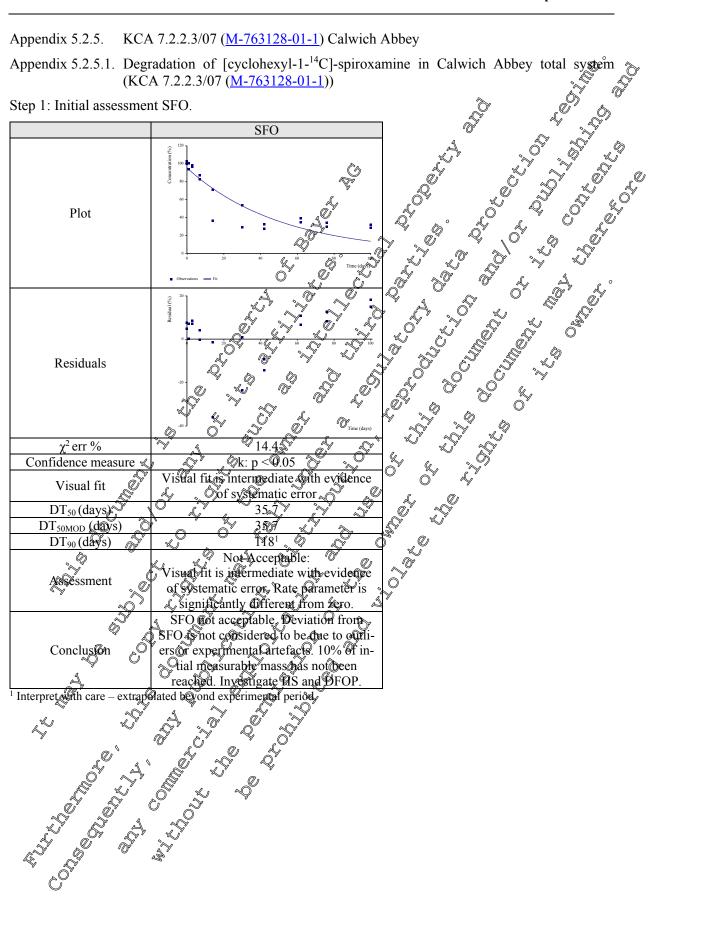




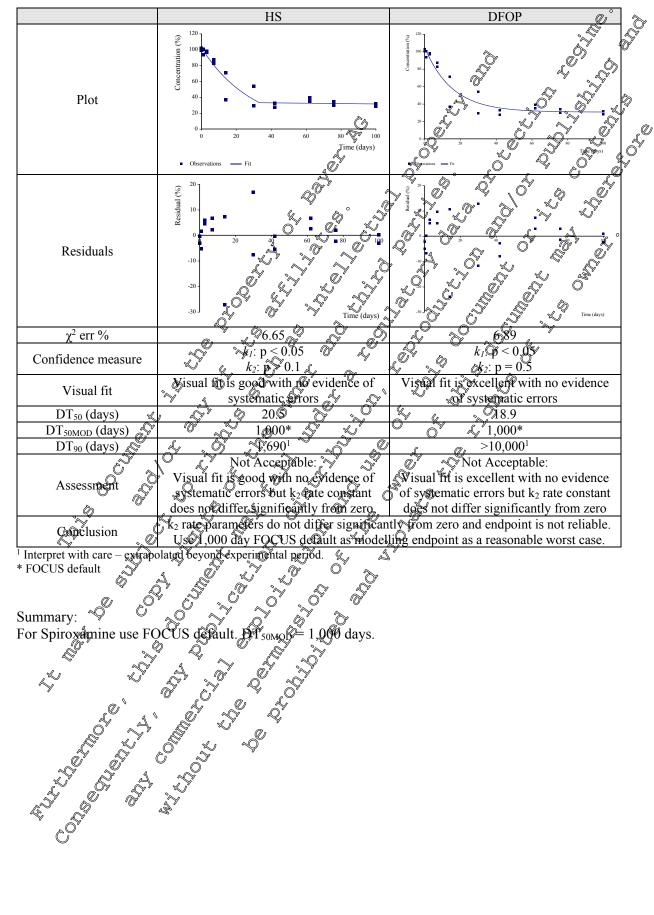
Appendix 5.2.5. KCA 7.2.2.3/07 (M-763128-01-1) Calwich Abbey

Appendix 5.2.5.1. Degradation of [cyclohexyl-1-14C]-spiroxamine in Calwich Abbey total system (KCA 7.2.2.3/07 (M-763128-01-1))





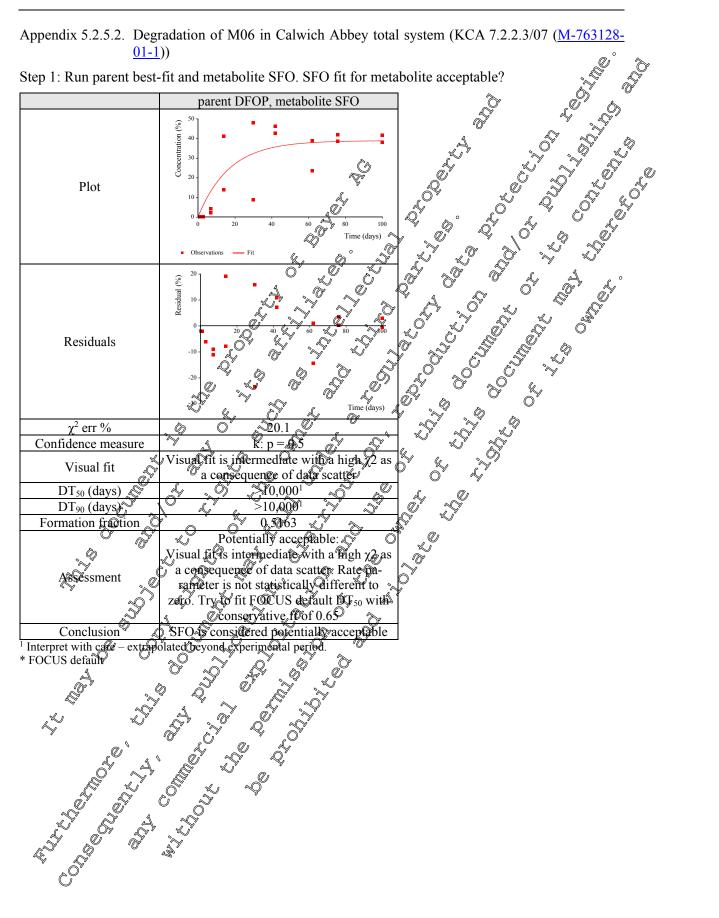




Step 3: 10% of initially measured mass has not been reached, run HS and/or DFOP:



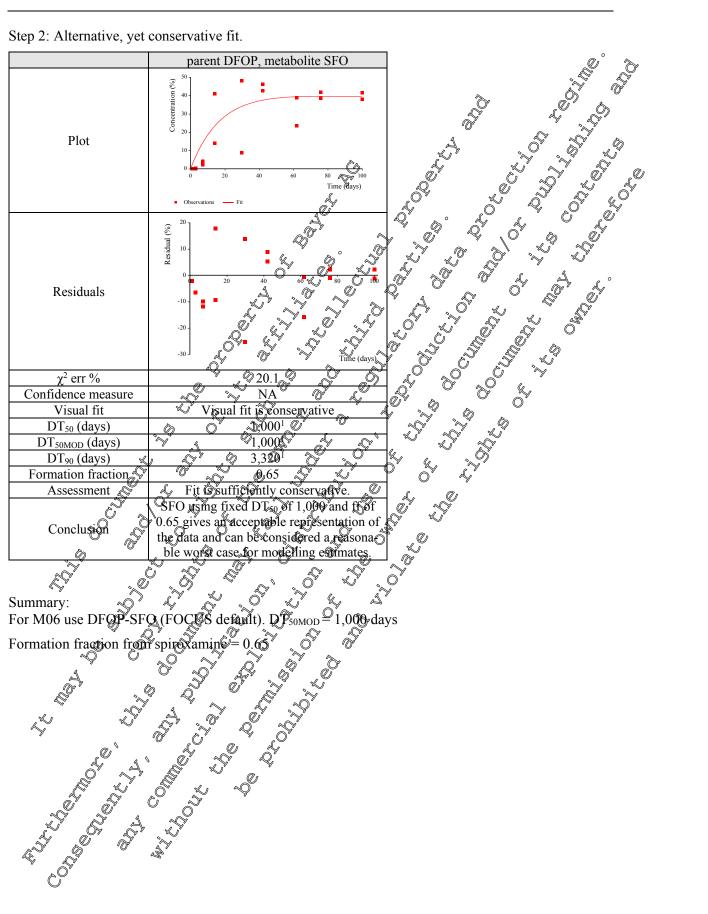
Appendix 5.2.5.2. Degradation of M06 in Calwich Abbey total system (KCA 7.2.2.3/07 (M-763128-(01-1))



Step 1: Run parent best-fit and metabolite SFO. SFO fit for metabolite acceptable?

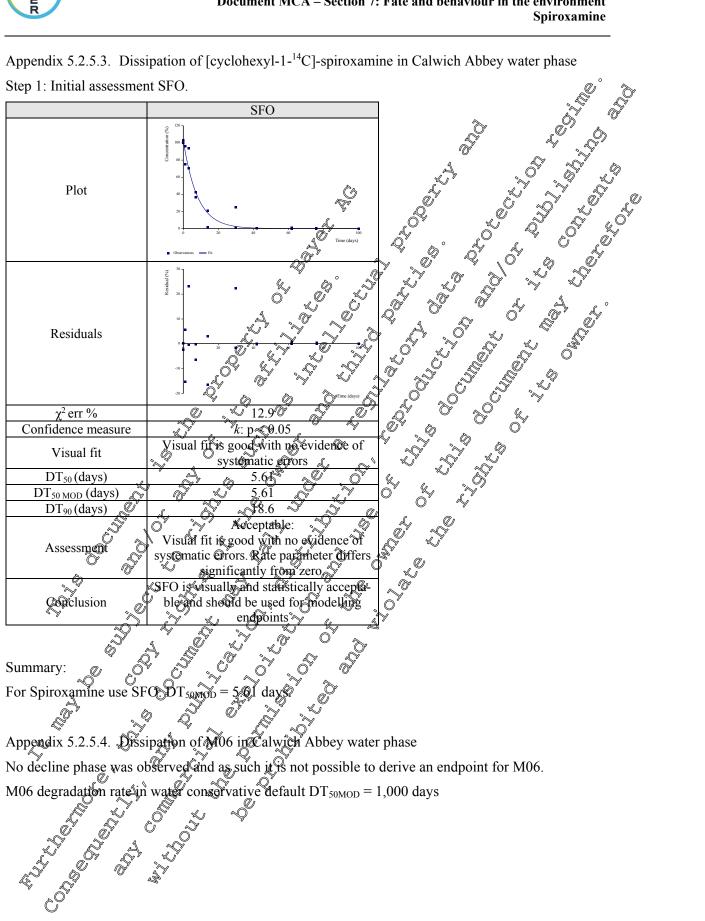


Step 2: Alternative, yet conservative fit.

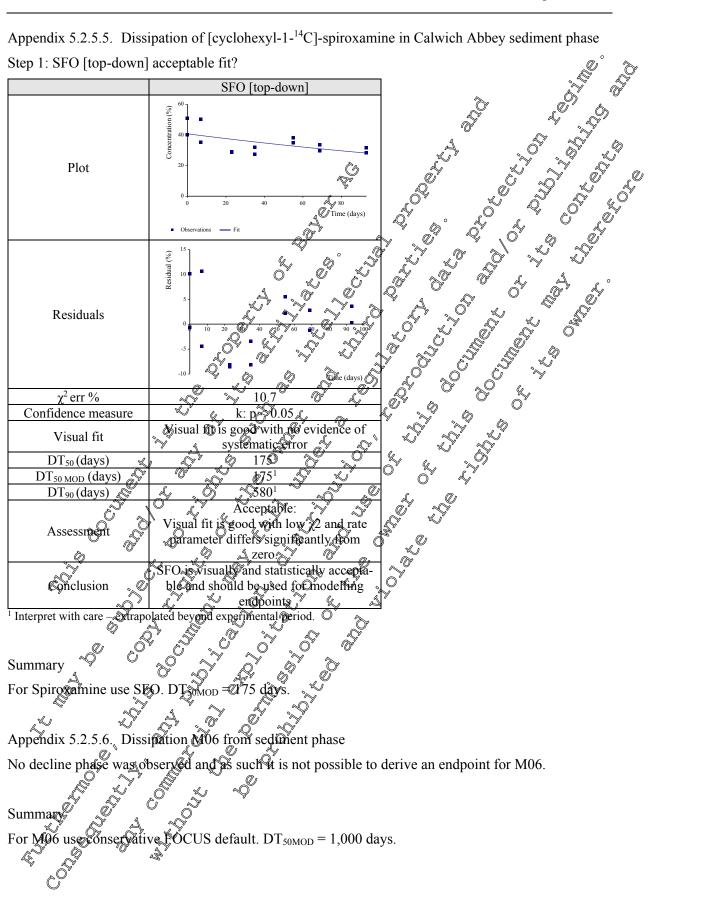




Appendix 5.2.5.3. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Calwich Abbey water phase Step 1: Initial assessment SFO.







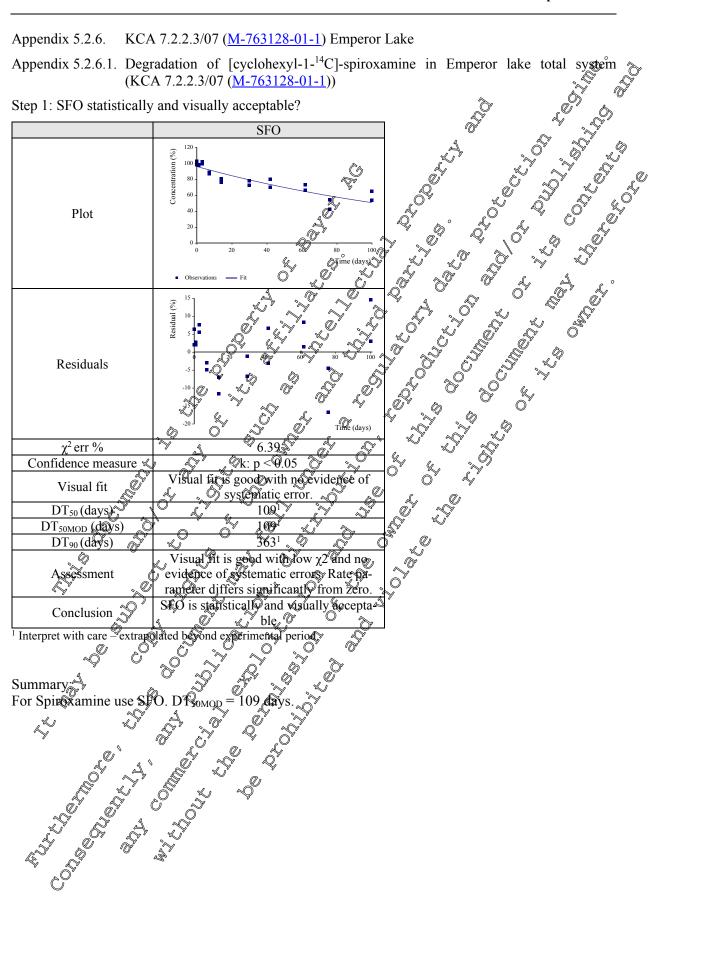
Appendix 5.2.5.5. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Calwich Abbey sediment phase Step 1: SFO [top-down] acceptable fit?



Appendix 5.2.6. KCA 7.2.2.3/07 (M-763128-01-1) Emperor Lake

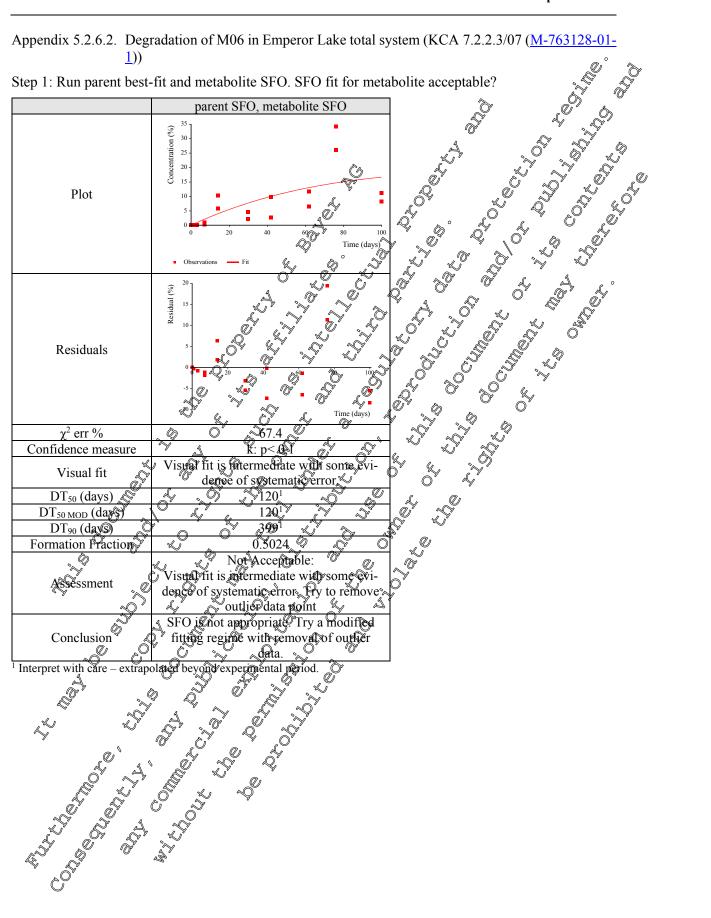
Appendix 5.2.6.1. Degradation of [cyclohexyl-1-¹⁴C]-spiroxamine in Emperor lake total system (KCA 7.2.2.3/07 (M-763128-01-1))

Step 1: SFO statistically and visually acceptable?



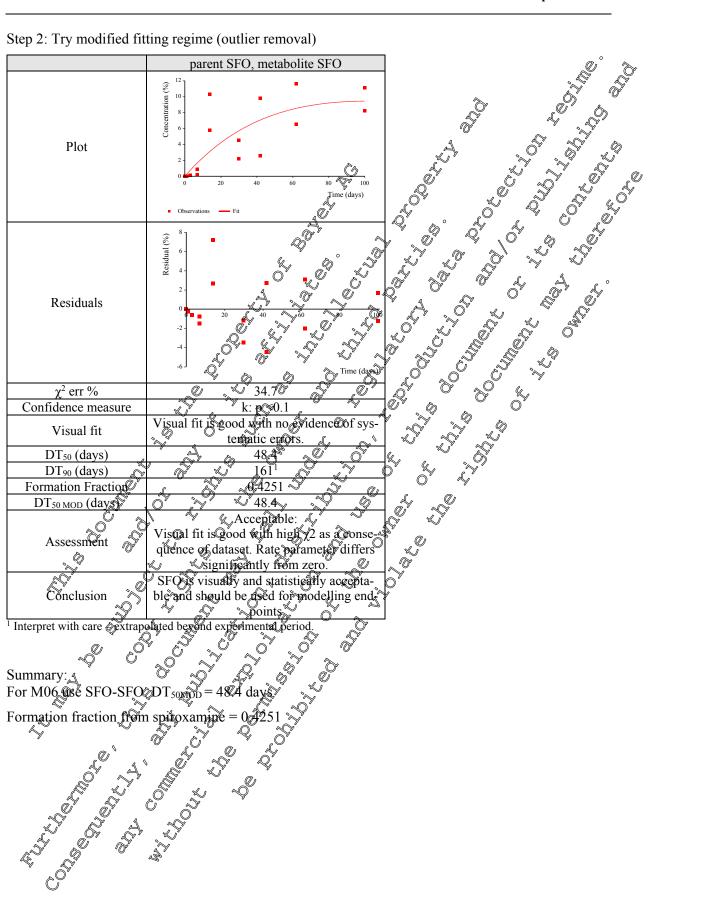


Appendix 5.2.6.2. Degradation of M06 in Emperor Lake total system (KCA 7.2.2.3/07 (M-763128-01-1))



Step 1: Run parent best-fit and metabolite SFO. SFO fit for metabolite acceptable?





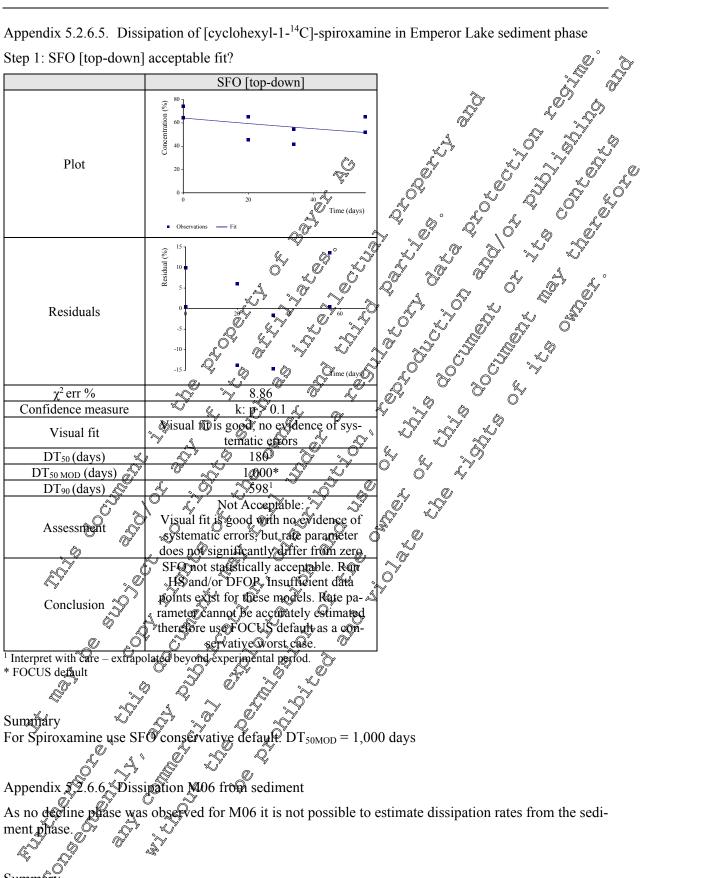
Step 2: Try modified fitting regime (outlier removal)



Step 1: Initial assessment SFO. SFO Concentration (%) Plot 20 Observations Fit Residual (%) 20 Residuals $\chi^2 \, \text{err} \, \%$ Ľ 18/ 0.0**5** Confidence measure k: p χ isual fit is good although χ^2 high. No Visual fit widence of symmetric error DT₅₀ (days) Visual fit is good atthough χ^2 high. No evidence of systematic error. Rate na-ameter difference of systematic error. DT_{50 MOD} (days) DT₉₀ (days 202 702 Assessment Conclusion FOOs statistically and visionly accepta For Spiroxamine use SFOOD STORE n and a second , N Appendix 5.2.6.4. Dissipation of M06 in Emperior Lake water phase The second second are such it is not possible to derive an endpoint for M06. Summary $\frac{1}{2}$ M06 modelling endpoint conservative default. DT_{50MOD} = 1,000 days

Appendix 5.2.6.3. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Emperor Lake water phase





Appendix 5.2.6.5. Dissipation of [cyclohexyl-1-¹⁴C]-spiroxamine in Emperor Lake sediment phase Step 1: SFO [top-down] acceptable fit?

Summary

For M06 use conservative default $DT_{50MOD} = 1,000$ days.