Document Title

Summary of the fate and behaviour in the environment Spiroxamine EC 500 (500 g/L)

Data Requirement(s)

Regulation (EC) No 1107/2009 & Regulation (EU) No 284/2013
Document MCP
Section 9: Fate and behaviour in the environment

According to the Guidance Document SANCO/10181/2013 for applicants on preparing dossiers for the approval of a chemical active substance

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On behalf of Bayer AG
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1 It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4, 'How to revise an Assessment Report'.

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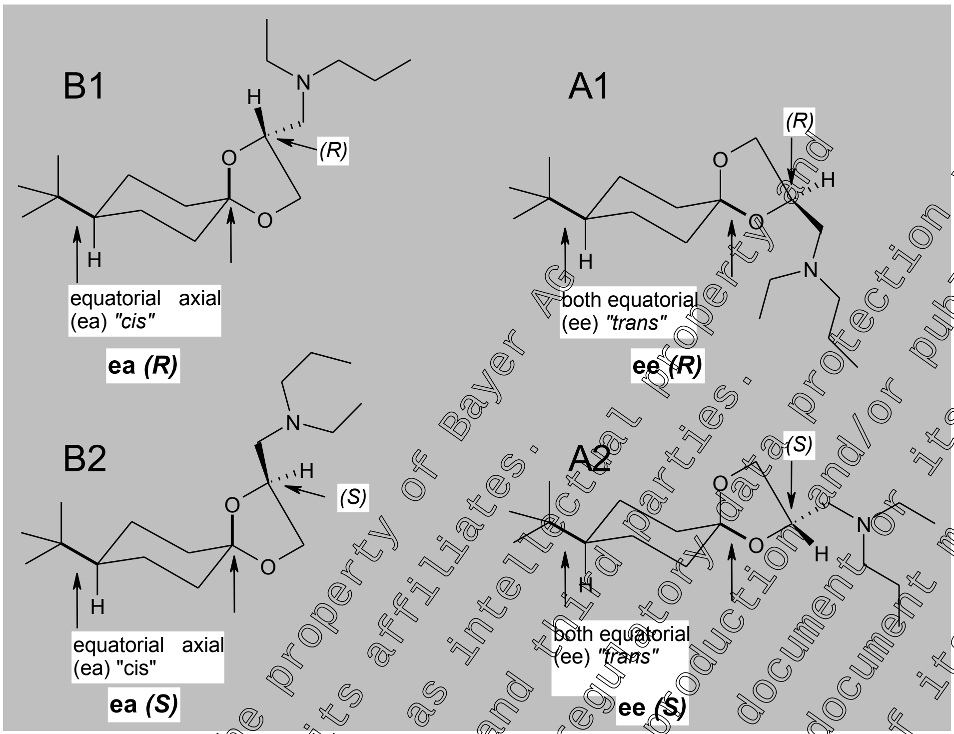
CP 9 FATE AND BEHAVIOUR IN THE ENVIRONMENT

Spiroxamine was included in Annex I to Council Directive 91/414/EEC in 1999 (Directive 1999/73/EC, Entry into Force on 1 September 1999). Spiroxamine was then renewed in 2012; the rapporteur Member State was Germany and the co-rapporteur Member State was Hungary. This Supplementary Dossier contains data which were not submitted at the time of the Annex I inclusion of spiroxamine under Council Directive 91/414/EEC and which were therefore not evaluated during the first EU review. 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 are provided in the appropriate dossier section. However, where studies do not meet relevant validity criteria and are not considered acceptable, less detailed summaries may have been provided alongside a discussion of potential 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 first renewal submissions.

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

The formulation Spiroxamine EC 500 (500 g/L), abbreviation Spiroxamine EC 500, is an emulsifiable concentrate formulation containing 160 g/L of prothioconazole and 300 g/L of spiroxamine. This formulation is registered throughout Europe under trade names such as BATAM, HOGGAR, IMPULSE EC 500, PROSPER, PROSPER 500 EC. Spiroxamine EC 500 already a representative formulation of Bayer AG for the Annex I inclusion and first renewal of spiroxamine under Council Directive 91/414/EEC.

Spiroxamine consists of four isomers (two diastereomers, 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 A/B and corresponding trans/cis notation due to a discrepancy in referencing, which is discussed in detail in position paper M-761468-01-1 (see CA 1.7/01). The stereo assignments depicted here, together with the A and B notation will be used exclusively going forward to ensure continuity of information throughout the dossier. 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 (UF) in Doc N5, at a later date (estimate September 2021).



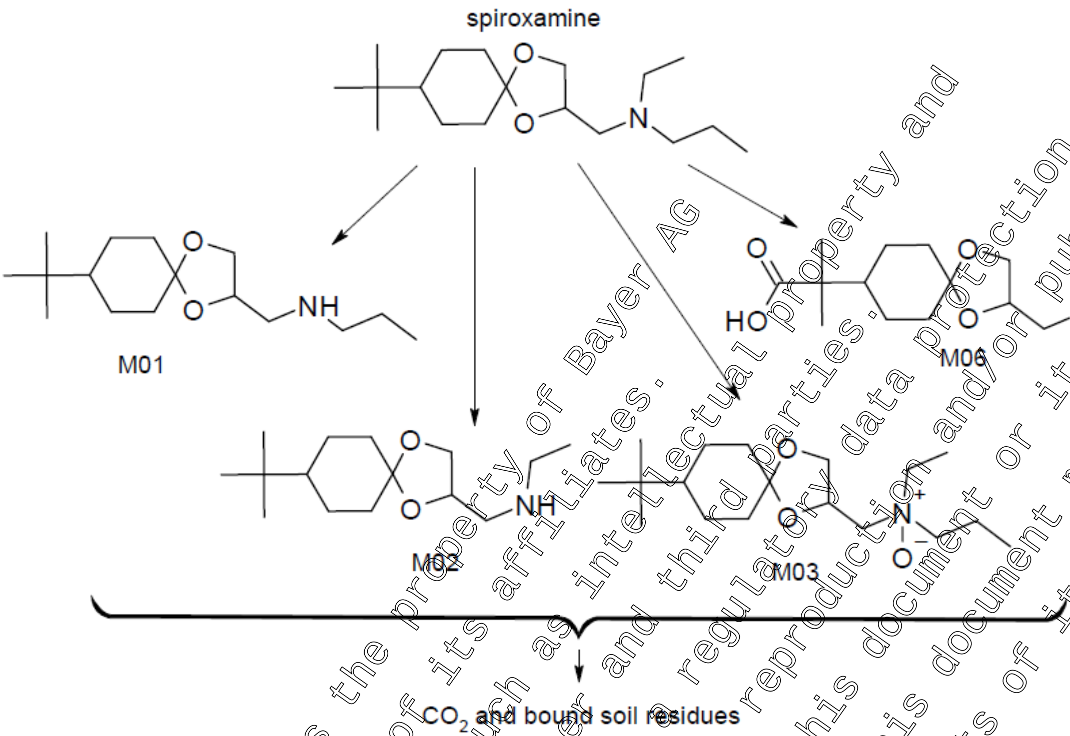
CP 9.1 Fate and behaviour in soil

Use of the representative formulated product Spiroxamine EC 500 (500 g/L) can potentially lead to measurable amounts reaching soil, therefore, the fate and behaviour in soil of Spiroxamine EC 500 (500 g/L) is addressed.

The formulated product Spiroxamine EC 500 (500 g/L), containing the active substance spiroxamine (500 g/L), is applied as a broadcast foliar spray to various crops. Consequently, the fate and behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) can be extrapolated from the studies on the active substance itself and therefore no additional laboratory studies on the fate and behaviour have been performed on the formulation.

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 9.1-1). 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% previously; the most recent data show M06 at a maximum of 5.3% AR at the final time point in the Refesol-02A soil thus triggering further evaluation and risk assessment. Studies to define the modelling parameters for M06 are currently on-going and conservative endpoints are used to provide a preliminary view of potential M06 exposure but will be updated upon study completion.

Figure 9.1-1: Aerobic soil degradation pathway for Spiroxamine



CP 9.1.1 Rate of degradation in soil

For information on the rate of degradation in soil please refer to Document MCA, Section 7.1.2. An assessment of the statistical difference of the kinetic evaluation of the lab and field studies was performed using the EFSA endpoint XL. This assessment determined that the field studies were statistically different to the lab dataset and as such modelling endpoints are taken from the field studies in isolation

CP 9.1.1.1 Laboratory studies

The rate of degradation in soil of the active substance spiroxamine and its major metabolites, as defined in CA 7.4.1 (i.e. metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid)), in laboratory studies is evaluated under CA 7.1.2.1 of the corresponding active substance dossier. As it is possible to extrapolate the behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) from the study on the active substance itself, additional laboratory studies investigating the rate of degradation in soil have not been performed.

A summary of the fate and behaviour of the active substance and associated significant metabolites in laboratory soil degradation studies is presented under CA 7.1.2.

CP 9.1.1.2 Field studies

CP 9.1.1.2.1 Soil dissipation studies

Soil dissipation behaviour of the representative formulation Spiroxamine EC 500 (500 g/L) can be extrapolated from the studies designed to evaluate the active substance addressed under CA 7.1.2.2.1. The dissipation rate of spiroxamine has been determined in five studies across eighteen European sites. Full details of the studies and derivation of the rate of dissipation according to the latest guidance is available under CA 7.1.2.2.1.

CP 9.1.1.2.2 Soil accumulation studies

Soil accumulation studies with the representative formulation Spiroxamine EC 500 (500 g/L) have not been conducted as behaviour can adequately addressed in the same manner as for the active substance and relevant metabolites (i.e. metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) as described under CA 7.1.2.2.2.

CP 9.1.2 Mobility in the soil

CP 9.1.2.1 Laboratory studies

Studies investigating the soil sorption properties of the active substance spiroxamine and major metabolites as defined in CA 7.4.1 (i.e. metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid)), are evaluated under CA 7.1.3.1 of the corresponding active substance dossier. As it is possible to extrapolate the behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) from the studies on the active substance and metabolites themselves, additional soil sorption studies have not been performed.

The high sorption displayed by spiroxamine 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 soil column studies, aged residues of spiroxamine did not significantly leach to the column percolate with only 0.2 %AR being found in the leachate.

A summary of the behaviour of the active substance and its metabolites (addressed under CA 7.1.3.1.1 and CA 7.1.3.1.2, respectively) in soil sorption studies is presented under CA 7.1.3.1.

CP 9.1.2.2 Lysimeter studies

Lysimeter studies with the representative formulation Spiroxamine EC 500 (500 g/L) were not conducted as lysimeter studies with the active substance are not triggered (CA 7.1.4.2).

Adequate soil sorption parameters for the active substance spiroxamine 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 environmental concentration in groundwater conducted under Point CP 9.2.4 do not indicate groundwater concentrations exceeding the relevant trigger levels, consequently lysimeter and/or field leaching studies with the active substance or any metabolites are not required.

CP 9.1.2.3 Field leaching studies

Field leaching studies with the representative formulation Spiroxamine EC 500 (500 g/L) have not been conducted as behaviour can be extrapolated from the active substance studies and in any case field leaching studies with the active substance have not been triggered (CA 7.1.4.3).

CP 9.1.3 Estimation of concentrations in soil

The Predicted Environmental Concentrations in soil (PECs) have been calculated for the active substance spiroxamine and major metabolite, as defined in CA 7.4.1, along with the intact formulation itself following foliar applications of Spiroxamine EC 500 (500 g/L) in accordance with the representative GAP.

The critical Good Agricultural Practice (GAP) for the representative formulation Spiroxamine EC 500 (500 g/L) is presented in document D1, with relevant agronomic parameters are summarised in Table 9.1.3-1.

Table 9.1.3-1: GAP for Spiroxamine EC 500 (500 g/L)

GAP details			Application timing			
			Early		Late	
Crop	Appln rate (g as/ha)	Growth stage	Crop interception (%)[a)]	Effective appln rate (g/ha)[a)]	Crop interception (%)[a)]	Effective appln rate (g/ha)[a)]
Vines	2x 200-300 (10 d min interval)	13-85	50 (GS13+)	2x 150	75 (GS71+)	2x 75

a) Representative of the worst case application rate.

The predicted environmental concentration in soil was calculated based upon the maximum proposed use rate following the recommendations of the FOCUS Soils Group (FOCUS 1997[1]). Calculations assume any substance reaching the soil surface is distributed uniformly to a depth of 5 cm (with no mechanical incorporation). The bulk density of soil is assumed to be 1.5 g/cm^3.

Predicted environmental concentrations in soil (PEC$_S$) – formulation

The initial predicted environmental concentration in soil of the representative formulated product Spiroxamine EC 500 (500 g/L) is presented in Table 9.1.3-2. Since the formulation metabolite other than the active substance will dissipate rapidly in the environment, it is only necessary to consider the initial concentration for Spiroxamine EC 500 (500 g/L).

Table 9.1.3-2: Worst-case initial PECs for Spiroxamine EC 500 (500 g/L) needed for environmental risk assessment

Crop	Formulation application rate (L/ha)	Application timing (growth stage)	Crop interception (%)	Soil concentration (mg Spiroxamine EC 500 (500 g/L)/kg dw soil)
Vines, 2x 300 g a.s./ha (	0.6 L/ha Spiroxamine EC 500 (500 g/L) (equivalent to 601.8 g/ha)[A]	13-85	50 minimum	0.401
Vines, 2x 200 g a.s./ha	0.4 L/ha Spiroxamine EC 500 (500 g/L) (equivalent to 401.2 g/ha)[A]	13-85	50 minimum	0.267

A Based on a Spiroxamine EC 500 (500 g/L) formulation relative density of 1.003 g/ml, see CP 2.6

The maximum initial concentration of the formulated product Spiroxamine EC 500 (500 g/L) in soil following application is 0.401 µg formulation/kg dw soil.

Predicted environmental concentrations in soil (PEC$_S$) – active substance and metabolites

The predicted environmental concentrations in soil of the active substance and of major metabolites, as defined under Point 7.4.1 (on the basis of the studies investigating the fate and behaviour of the active substance in soil under Point 7.1.1), have been calculated below based on the key endpoints presented in Table 9.1.3-3 and the uses of the representative formulation Spiroxamine EC 500 (500 g/L) described in Table 9.1.3-1.

[1] FOCUS (1997). Soil persistence models and EU registration. European Commission Document 7617/VI/96.

Table 9.1.3-3: Summary of parameters used for determination of PECs

Component	Endpoint	Value	Comment
Spiroxamine (mw 297.5 g/mol),	Aerobic DT_{50} / DT_{90} soil (days)	56.6 / 393 (FOMC: α=1.297; β=80.06)	Worst case persistence field DT values from KCA 7.1.2.2.1/12 see Table 7.1.2.2
	$DT_{90field}$ > 1 year	Yes	i.e. PECs accumulation required
Metabolite M01 (spirox-amine-desethyl, (mw 269.4 g/mol, molar ratio 0.906))	Aerobic DT_{50} / DT_{90} soil (days)	223 / 742 (SFO)	Worst case persistence field DT values from KCA 7.1.2.2.1/12 see Table 7.1.2.2.1-71
	Maximum occurrence in soil (%)	12.0	See Table 7.4.1-1
	$DT_{90field}$ > 1 year	Yes	i.e. PECs accumulation required
Metabolite M02 (spirox-amine- despropyl, (mw 255.4 g/mol, molar ratio 0.858))	Aerobic DT_{50} / DT_{90} soil (days)	161 / 533 (SFO)	Worst case persistence field DT values from KCA 7.1.2.2.1/12 see Table 7.1.2.2.1-71
	Maximum occurrence in soil (%)	9.2	See Table 7.4.1-1
	$DT_{90field}$ > 1 year	Yes	i.e. PECs accumulation required
Metabolite M03 (spirox-amine- N-oxide, (mw 313.5 g/mol, molar ratio 1.054))	Aerobic DT_{50} / DT_{90} soil (days)	107 / 358 (SFO)	Worst case persistence lab DT values from KCA 7.1.2.1.1/09 see Table 7.1.2.1.1-1
	Maximum occurrence in soil (%)	7.9	See Table 7.4.1-1
	$DT_{90field}$ > 1 year	Yes	i.e. PECs accumulation required
Metabolite M06 (spirox-amine-acid, (mw 327.5 g/mol, molar ratio 1.101))	Aerobic DT_{50} / DT_{90} soil (days)	1000 / 3320 (SFO)	Worst case persistence lab DT values from KCA 7.1.2.1.1/09 see Table 7.1.2.1.1-1.*
	Maximum occurrence in soil (%)	5.3	See Table 7.4.1-1
	$DT_{90field}$ > 1 year	Yes	i.e. PECs accumulation required

* PECsoil for M06 are calculated using a default worst case DT50 and will be refined at a later date

The predicted environmental concentrations in soil of each metabolite was calculated using a pseudo application rate per crop using the following equation:

$$A_{metabolite}(g/ha) = A_{parent} \times \frac{\text{maximum metabolite observed (\%)}}{100} \times \text{molar correction factor}$$

Where:

A_{parent} = Total loading of the parent to soil (g a.s./ha)

$A_{metabolite}$ = Equivalent application rate of the metabolite (g a.s./ha)

The calculation of pseudo application rates for the metabolites for each use are shown in Table 9.1.3-4. The application rate that represents the worst case scenario for spiroxamine is an application to vines at 300 g a.s./ha.

Table 9.1.3-4: Pseudo application rates for metabolites of spiroxamine used in the PEC_{SOIL} calculations

Crop / application rate	Metabolite	Max. soil load per application (g a.s./ha)	Maximum observed in soil (%)	Molar correction factor	Pseudo application rate per application (g a.s./ha)
Vines/300 g a.s./ha	M01	150	12.0	0.906	16.38
Vines/300 g a.s./ha	M02	150	9.2	0.858	11.87
Vines/300 g a.s./ha	M03	150	7.9	1.054	12.44
Vines/300 g a.s./ha	M06	150	5.3	1.101	8.75

The initial predicted environmental concentration for parent in soil after application was calculated using the following equation, assuming the soil deposit is uniformly distributed in the top 5 cm soil layer and that the soil bulk density is 1.5 g/cm³ (FOCUS 1997):

$$PEC_{SOIL}\ (mg/kg) = \frac{A \times (1 - F)}{100 \times d \times \rho}$$

Where:
A = Application rate (g a.s./ha)
F = Fraction intercepted by crop
d = Depth of field soil layer (5 cm)
ρ = Dry bulk density (1.5 g/cm³)

For the metabolites, the effective dose was calculated accounting for molecular weight and maximum observed occurrence in soil. Short and long-term (seasonal) predicted concentrations in soil of the active substance spiroxamine metabolites were calculated using SFO kinetics based on worst-case persistence DT50 values (see Table 9.1.3-3) using the following equation:

$$PEC_{actual\ t} = \text{Initial } PEC_{SOIL} \text{ after application } \times e^{-kt}$$

Where:
Initial PEC_{SOIL} = Soil PEC immediately after application
k = first order degradation/dissipation rate constant (ln(2)/half-life)
t = specified time point after application (days)

For the active substance Spiroxamine, short and long-term (seasonal) predicted concentrations in soil were calculated using FOMC kinetics based on worst-case persistence DT_{50} values (see Table 9.1.3-3) using the following equation:

$$M = \frac{M_0}{\left(\frac{t}{\beta} + 1\right)^{\alpha}}$$

where
M = total amount of chemical present at time t
M_0 = total amount of chemical present at time $t = 0$
α = shape parameter determined by coefficient of variation of k values
β = location parameter

For metabolite concentrations, degradation between applications was not taken into account (worst-case).

$PECs_{accumulation}$

In addition to the seasonal PEC_S calculations, the potential accumulation ($PEC_{S,accumulation}$) in soil following repeated annual applications was calculated for metabolite where $DT_{90field}$ > 1 year i.e. the active substance spiroxamine and metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid).

For parent spiroxamine, accumulation calculations were based on application every year as a worst case. The decay of each annual application was modelled on a daily basis for up to 100 years from first application using FOMC degradation kinetics. The total daily residue was the sum of the individual residues from each application. The calculation was carried out for 100 years, assuming incorporation to 5 cm depth and with no tillage. Although soil residues are technically still increasing due to the use of FOMC kinetics, a 100 years of repeated annual applications is considered sufficiently worst-case.

For parent spiroxamine metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid), accumulation calculations were similarly conducted but using SFO kinetics and a shorter time period. Accumulation PECs for M06 are provided based on the default DT_{50} and is considered worst case; an ongoing OECD307 study is being conducted to provide realistic DT_{50} and refine the presented conservative assessment.

$PEC_{S,accumulation}$ was calculated as the sum of the $PEC_{S,plateau}$ concentration before the first annual application in the last year and the $PEC_{S,ini}$ (calculated for 5 cm soil depth) immediately after the last application:

$$PEC_{S,ini} = \frac{\max_{n \in \{1,\ldots,365\}} L_n}{100 d_{inc} \rho}$$

$$PEC_{S,accumulation} = PEC_{S,plateau} + PEC_{S,ini}$$

Where:

d_{inc} Depth of the field soil layer for incorporation (5 cm)

ρ Dry bulk density (1.5 g/cm^3)

The resulting worst-case predicted environmental concentrations in soil of the active substance are presented in Table 9.1.3-5 and for the metabolites in Table 9.1.3-6 to Table 9.1.3-9.

Table 9.1.3-5: Worst-case PECs (initial, short/long-term and TWA) for spiroxamine following application of Spiroxamine EC 500 (500 g/L) to vines

Time		Concentration in soil (mg as/kg soil dw)			
		1 x 300g a.s./ha		2 x 300 g a.s./ha [A]	
		Actual	TWA	Actual	TWA
Initial (after last appln)		0.200	-	0.372	
Short term	24h	0.197	0.198	0.366	0.369
	2d	0.194	0.197	0.361	0.366
	4d	0.188	0.194	0.350	0.361
Long term	7d	0.179	0.189	0.335	0.353
	14d	0.162	0.180	0.305	0.336
	21d	0.148	0.172	0.279	0.321
	28d	0.136	0.164	0.256	0.308
	50d	0.107	0.145	0.203	0.274
	100d	0.070	0.115	0.135	0.244
Plateau concentration (5 cm)		0.077	-	0.155	-
$PEC_{accumulation}$ (PEC_{act} +$PEC_{soil\ plateau}$)		0.277 (after 100 yrs)	-	0.527 (after 100 yrs)	-

A For concentrations of the active substance, degradation between applications was taken into account.

Table 9.1.3-6: Worst-case PECs (initial, short/long-term and TWA) for metabolite M01 following application of Spiroxamine EC 500 (500 g/L) to vines

Time		Concentration in soil (mg as/kg soil dw)			
		1 x 300g a.s./ha		2 x 300 g a.s./ha [A]	
		Actual	TWA	Actual	TWA
Initial		0.022	-	0.044	-
Short term	24h	0.022	0.022	0.044	0.044
	2d	0.022	0.022	0.043	0.044
	4d	0.022	0.022	0.043	0.043
Long term	7d	0.021	0.022	0.043	0.043
	14d	0.021	0.021	0.042	0.043
	21d	0.020	0.021	0.041	0.042
	28d	0.020	0.021	0.040	0.042
	50d	0.019	0.020	0.037	0.040
	100d	0.016	0.019	0.032	0.038
Plateau concentration (5 cm)		0.010	-	0.020	-
$PEC_{accumulation}$ (PEC_{act} +$PEC_{soil\ plateau}$)		0.032 (after 4th yr)	-	0.064 (after 4th yr)	-

A For metabolite concentrations, degradation between applications was not taken into account (worst-case).

Table 9.1.3-7: Worst-case PECs (initial, short/long-term and TWA) for metabolite M02 following application of Spiroxamine EC 500 (500 g/L) to vines

Time		Concentration in soil (mg as/kg soil dw)			
		1 x 300g a.s./ha		2 x 300 g a.s./ha [A]	
		Actual	TWA	Actual	TWA
Initial		0.016	-	0.032	
Short term	24h	0.016	0.016	0.032	0.032
	2d	0.016	0.016	0.031	0.032
	4d	0.016	0.016	0.031	0.031
Long term	7d	0.015	0.016	0.031	0.031
	14d	0.015	0.015	0.030	0.031
	21d	0.014	0.015	0.029	0.030
	28d	0.014	0.015	0.028	0.030
	50d	0.013	0.014	0.026	0.028
	100d	0.010	0.013	0.021	0.026
Plateau concentration (5 cm)		0.005	-	0.008	-
$PEC_{accumulation}$ (PEC_{act} + $PEC_{soil\ plateau}$)		0.021 (after 3rd yr)	-	0.040 (after 3rd yr)	-

A For metabolite concentrations, degradation between applications was not taken into account (worst-case).

Table 9.1.3-8: Worst-case PECs (initial, short/long-term and TWA) for metabolite M03 following application of Spiroxamine EC 500 (500 g/L) to vines

Time		Concentration in soil (mg as/kg soil dw)			
		1 x 300g a.s./ha		2 x 300 g a.s./ha [A]	
		Actual	TWA	Actual	TWA
Initial		0.017	-	0.033	-
Short term	24h	0.016	0.017	0.033	0.033
	2d	0.016	0.016	0.033	0.033
	4d	0.016	0.016	0.032	0.033
Long term	7d	0.016	0.016	0.032	0.032
	14d	0.015	0.016	0.030	0.032
	21d	0.014	0.016	0.029	0.031
	28d	0.014	0.015	0.028	0.030
	50d	0.012	0.014	0.024	0.028
	100d	0.009	0.012	0.017	0.024
Plateau concentration (5 cm)		0.001	-	0.004	-
$PEC_{accumulation}$ (PEC_{act} + $PEC_{soil\ plateau}$)		0.018 (after 2nd yr)	-	0.037 (after 3rd yr)	-

A For metabolite concentrations, degradation between applications was not taken into account (worst-case).

Table 9.1.3-9: Worst-case PECs (initial, short/long-term and TWA) for metabolite M06 following application of Spiroxamine EC 500 (500 g/L) to vines

Time		Concentration in soil (mg as/kg soil dw)			
		1 x 300g a.s./ha		2 x 300 g a.s./ha [A]	
		Actual	TWA	Actual	TWA
Initial		0.012	-	0.023	
Short term	24h	0.012	0.012	0.023	0.023
	2d	0.012	0.012	0.023	0.023
	4d	0.012	0.012	0.023	0.023
Long term	7d	0.012	0.012	0.023	0.023
	14d	0.012	0.012	0.023	0.023
	21d	0.011	0.012	0.023	0.023
	28d	0.011	0.012	0.023	0.023
	50d	0.011	0.011	0.023	0.023
	100d	0.011	0.011	0.022	0.023
Plateau concentration (5 cm)		0.040	-	0.081	-
$PEC_{accumulation}$ (PEC_{act} +$PEC_{soil\ plateau}$)		0.052 (after 15 yrs)	-	0.104 (after 15 yrs)	-

A For metabolite concentrations, degradation between applications was not taken into account (worst-case).

Table 9.1.3-10: Overview of initial PECs following single (1x 300 g/ha), multiple (2x 300 g/ha) and repeated annual applications for a period of 100 years of 2x 300 g/ha to vines

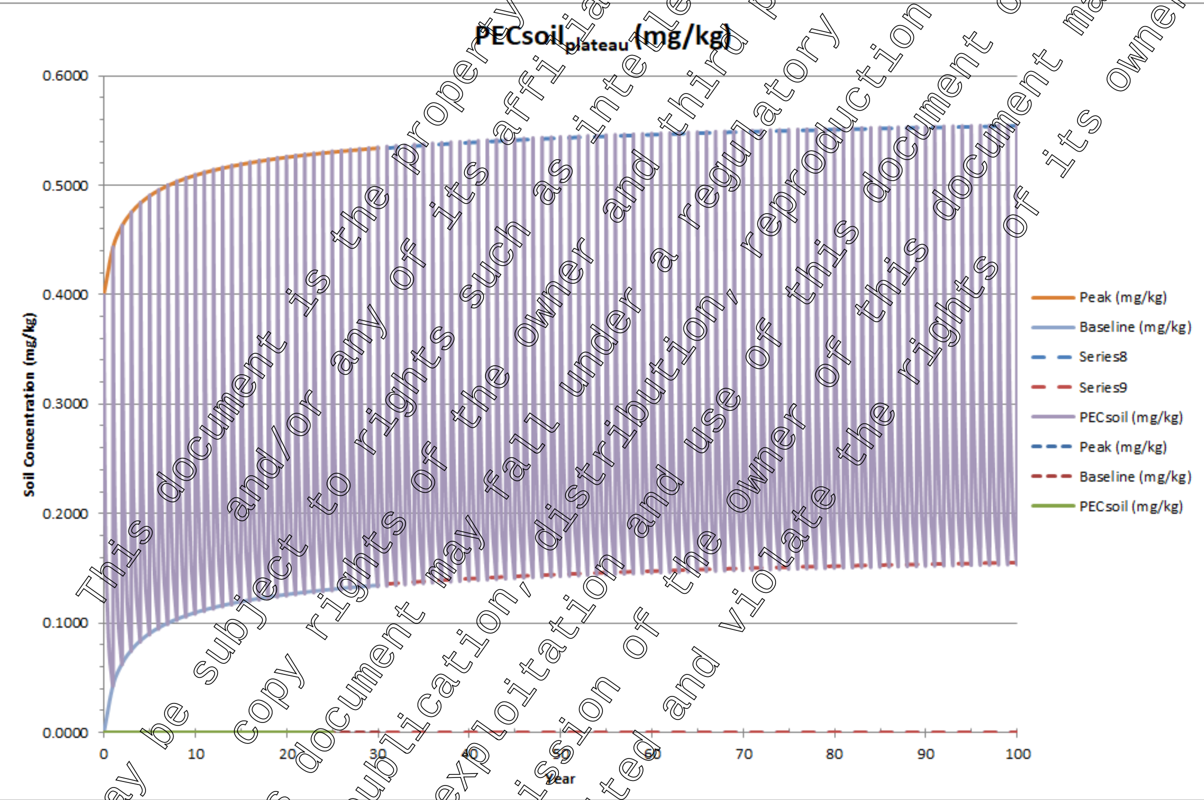
Substance	Concentration in soil (mg as/kg soil dw)		
	1x 300 g/ha	2 x 300 g a.s./ha [A,B]	Repeated annual application of 2x 300 g/ha
Spiroxamine	0.200	0.372	0.155 (background) 0.555 (peak) after 100 yrs annual use
M01 (spiroxamine-desethyl)	0.022	0.044	0.020 (background) 0.064 (peak) plateau after 4 yrs annual use
M02 (spiroxamine-despropyl),	0.016	0.032	0.008 (background) 0.040 (peak) plateau after 3 yrs annual use
M03 (spiroxamine-N-oxide)	0.017	0.033	0.004 (background) 0.037 (peak) plateau after 3 yrs annual use

Substance	Concentration in soil (mg as/kg soil dw)		
	1x 300 g/ha	2 x 300 g a.s./ha [A,B]	Repeated annual application of 2x 300 g/ha
M06 (spiroxamine-acid)	0.012	0.023	0.081 (background) 0.104 (peak) plateau after 20 yrs annual use

A For concentrations of the active substance, degradation between applications was taken into account.
B For metabolite concentrations, degradation between applications was not taken into account (worst-case).

The predicted accumulation of spiroxamine in soil over a 100-year period after application to vines is illustrated in Figure 9.1.3-1.

Figure 9.1.3-1: Accumulation of spiroxamine in soil following repeated annual application to grape vines (2x 300 g/ha annually)



Following application of 2x 300 g/ha to vines, worst-case PEC in soil of the active substance spiroxamine and metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) were 0.372, 0.044, 0.032, 0.033 and 0.023 mg/kg soil dw. Following worst-case repeated annual applications to vines (i.e. 2x 300 g/ha annually), worst-case peak accumulated PEC in soil were 0.555, 0.064, 0.040, 0.037 and 0.104 mg/kg soil dw.

For procedural reasons studies listed in the Table CP 9.1.3-1 below are included in the current dossier as available data or information previously submitted but not necessarily evaluated. However, these reports have been fully superseded by newer studies. Consequently, no summaries of the reports have been included in the dossier.

Table CP 9.1.3-1: Studies previously submitted and not relied upon for the risk assessment

Data Point	Document No.	Date	Title
KCP 9.1.3/01	M-304048-02-1	2008	Predicted environmental concentrations of spiroxamine in soil (PECsoil) - Use in vines in Europe

CP 9.2 Fate and behaviour in water and sediment

Use of the representative formulated product Spiroxamine EC 500 (500 g/L) can potentially lead to amounts reaching surface water during treatments by spray drift or *via* soil drainage and run-off, therefore the fate and behaviour in water and sediment of Spiroxamine EC 500 (500 g/L) is addressed.

CP 9.2.1 Aerobic mineralisation in surface water

As it is possible to extrapolate the behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) from the study on the active substance itself, additional laboratory studies investigating the aerobic mineralisation in surface water of Spiroxamine EC 500 (500 g/L) have not been performed.

CP 9.2.2 Water/sediment study

As it is possible to extrapolate the behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) from the study on the active substance itself, additional laboratory studies investigating the behaviour of Spiroxamine EC 500 (500 g/L) in water/sediment studies have not been performed.

CP 9.2.3 Irradiated water/sediment study

As it is possible to extrapolate the behaviour of the active substance resulting from use of the formulated product Spiroxamine EC 500 (500 g/L) from the study on the active substance itself, additional laboratory studies investigating the behaviour of Spiroxamine EC 500 (500 g/L) in irradiated water/sediment studies have not been performed.

CP 9.2.4 Estimation of concentrations in groundwater

CP 9.2.4.1 Calculation of concentrations in groundwater

The Predicted Environmental Concentrations in groundwater (PEC_{GW}) following foliar applications of Spiroxamine EC 500 (500 g/L) have been calculated for the active substance spiroxamine and major metabolite, as defined in CA 7.4.1, in accordance with the representative GAP.

The predicted environmental concentration of the active substance spiroxamine and significant metabolite in groundwater (PEC_{GW}) is determined using the standardised recommendations of the FOCUS working group on surface water scenarios (FOCUS 2000[2], 2014[3] and EC 2014[4]). The PECs are provided in one existing study included in the last evaluation which is therefore included for completeness but

[2] FOCUS (2000). FOCUS groundwater scenarios in the EU review of active substances. Report of the FOCUS groundwater scenarios workgroup, EC Document Reference Sanco/321/2000 rev. 2.

[3] FOCUS (2014). Generic guidance for Tier 1 FOCUS groundwater assessments, version 2.2. FOCUS groundwater scenarios working group.

[4] EC (2014). Assessing Potential for Movement of Active Substances and their Metabolites to Ground Water in the EU, Report of the FOCUS Ground Water Work Group, EC Document Reference Sanco/13144/2010 version 3, 613 pp.

which has been superseded by a new modelling report conducted to modern requirements CP 9.2.4.1/02 (M-763142-01-1).

Substance	Report reference	Document no.	Comment
Spiroxamine	KCP 9.2.4.1/01	M-304012-01-1	Submitted for first renewal of spirox-amine, 2010. Reviewed under UP. Considered valid and acceptable.
Spiroxamine	KCP 9.2.4.1/02	M-763142-01-1	New data not yet reviewed under UP.

Data Point:	KCP 9.2.4.1/01
Report Author:	[redacted]; [redacted]
Report Year:	2008
Report Title:	Predicted environmental concentrations of spiroxamine in groundwater recharge (PECgw) based on calculations with FOCUS-PEARL and FOCUS-PELMO - Use in vines in Europe
Report No:	MEF-08/269
Document No:	M-304012-01-1
Guideline(s) followed in study:	FOCUS (2000)
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted RAR (2010)
GLP/Officially recognised testing facilities:	No, not conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

This study was previous considered during the evaluation of spiroxamine (RAR (2010)) and is therefore included again for completeness. This study presents the PEC modelling conducted on the representative for the last evaluation, however, the PEC modelling reported in this study is superseded by the new PEC modelling performed in study KCP1 9.2.4.1/02 (M-763142-01-1).

Data Point:	KCP 9.2.4.1/02
Report Author:	[redacted]
Report Year:	2021
Report Title:	A modelling assessment of spiroxamine and its metabolites applied to vines in groundwater
Report No:	0471836-GW1
Document No:	M-763142-01-1
Guideline(s) followed in study:	FOCUS (2000, 2014), EFSA (2014)
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	not applicable
Acceptability/Reliability:	Yes

Executive summary

The leaching behaviour of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spirox-amine-despropyl) and M03 (spiroxamine-N-oxide) following application of the spiroxamine Spirox-amine EC 500 (500 g/L) formulation to grape vines was examined in accordance with the FOCUS groundwater scenarios workshop guidelines (FOCUS, 2000 and 2014) and the EFSA guidance for protected crops (EFSA, 2014).

The following field uses were simulated in accordance with the supported uses of the Spiroxamine EC 500 (500 g/L) formulation:

Two applications (BBCH 13 onwards) at a rate of 300g a.s./ha to vines

Two applications (BBCH 13 onwards) at a rate of 200g a.s./ha to vines

Simulations for the field uses were conducted using the FOCUS groundwater scenarios in the FOCUS PEARL (version 4.4.4), FOCUS PELMO (version 5.5.3) and FOCUS MACRO (version 5.5.4) models.

The input parameters for the calculations are defined Table 9.2.4.1-1 and were selected based on recommendations from FOCUS (FOCUS, 2000 and 2014).

These results demonstrate that spiroxamine can be used safely as proposed without the risk of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) exceeding acceptable levels in groundwater.

The predicted 80th percentile average annual concentrations for spiroxamine following application to vines were lower than the 0.1 µg/L regulatory threshold in groundwater at 1 m depth for all crop / scenario combinations. The PEC_{GW} values for metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) following annual application spiroxamine to crops were <0.001 µg/L, which is expected due to the high K_{OC} of spiroxamine and its metabolites, as well as being in accordance to values submitted previously. All values are below the 0.1 µg/L regulatory threshold in groundwater at 1 m depth for all the available crop / scenario combinations.

Simulations for the field uses were conducted using the FOCUS groundwater scenarios in the FOCUS PEARL (version 4.4.4), FOCUS PELMO (version 5.5.3) and FOCUS MACRO (version 5.5.4) models.

Study design

The purpose of this study was to assess the potential for leaching of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) following application of the Spiroxamine EC 500 (500 g/L) formulation to grape vines in accordance with the EU representative GAP.

The predicted environmental concentrations in groundwater (PEC_{GW}) for the field uses were determined using the FOCUS PEARL (version 4.4.4), FOCUS PELMO (version 5.5.3) and FOCUS MACRO (version 5.5.4) groundwater models and scenarios in accordance with the FOCUS groundwater scenarios workgroup guidelines (FOCUS, 2000 and 2014).

The input parameters used in the modelling for spiroxamine and its metabolites are summarised in Table 9.2.4.1-1 to Table 9.2.4.1-2. The representative use is summarised in Table 9.2.4.1-3.

Table 9.2.4.1-1: Physico-chemical parameters used in modelling for spiroxamine

Parameter	Value	Remarks
Physico-chemical		
Molecular weight (g/mol)	297.5	MCA Renewal of Approval dossier, see CA 1.7
Water solubility at 20°C (mg/L)	470	MCA Renewal of Approval dossier, see CA 2.5
Vapour pressure at 20°C (Pa)	4.5×10^{-3}	MCA Renewal of Approval dossier, see CA 2.2
Molar enthalpy of vaporization (kJ/mol)	95	FOCUS recommendation
Diffusion coefficient in water (m²/d) (m²/s)	4.3 x 10-5 (20°C) (PEARL)	
Diffusion coefficient in gas (m²/d)	0.43 (20°C)	
Degradation in soil		
DT_{50} soil (d)	43.8	Geometric mean of uncropped field data (n= 8), submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.2.1-72
Temperature correction function Reference temperature (°C) PELMO: Q10 (-) PEARL: (kJ/mol)	 20 2.58 65.4	FOCUS recommendation
Moisture correction function Reference moisture (-) PEARL/PELMO: moisture exponent (-)	pF 2 0.7 0.49	
Sorption to soil		
K_{FOC} (mL/g)	4111	Geometric mean (n= 8) calculated from individual values, see data point CA 7.1.3.1, Table 7.1.3.1-1
K_{FOM} (mL/g)	2384	Calculated K_{FOC} / 1.724
Freundlich exponent 1/n (-)	0.892	Arithmetic mean (n=8) calculated from individual values submitted in MCA Renewal of Approval dossier see CA 7.1.3.1
Crop/management related parameters		
Crop uptake factor (-)	0.47	Crop uptake factor calculate by Briggs equation, see Appendix 2
Washoff Factor (1/m) (PEARL)	0.0001	Default
Washoff Factor (1/m) (MACRO)	0.05	Default
Foliar DT_{50} (d)	10	Default

Table 9.2.4.1-2: Input parameters used in groundwater modelling for the metabolites of spiroxamine

Parameter	M01 (spiroxamine-desethyl)		M02 (spiroxamine-despropyl)		M03 (spiroxamine-N-oxide)	
	Value	Remarks	Value	Remarks	Value	Remarks
Molecular weight (g/mol)	269.4	Based on structure	269.4	Based on structure	313.5	Based on structure
Water solubility at 20°C (mg/L)	14.8	MCA Renewal of Approval dossier, see CA 2.5	46.6	MCA Renewal of Approval dossier, see CA 2.5	1000	MCA Renewal of Approval dossier, see CA 2.5
Vapour pressure at 20°C (Pa)	0	Default value (FOCUS, 2014)	0	Default value (FOCUS, 2014)	0	Default value (FOCUS, 2014)
K_{FOC} (mL/g)	3271	Geometric mean (n=4) submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1	2695	Geometric mean (n=4) submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1	1677	Geometric mean (n=4) submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1
1/n	0.848	Arithmetic mean (n=4) submitted in MCA Renewal of Approval dossier see CA 7.1.3.1	0.878	Arithmetic mean (n=4) submitted in MCA Renewal of Approval dossier see CA 7.1.3.1	0.900	Arithmetic mean (n=4) submitted in MCA Renewal of Approval dossier see CA 7.1.3.1
DT_{50} soil @ 20°C & pF2 (days)	168.6	Geometric mean (n=10) of laboratory values, submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2	219.1	Geometric mean (n=10) of laboratory values, submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2	46.4	Geometric mean (n=7) of laboratory values, submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2
Plant uptake factor	0	Default value	0	Default value	0	Default value

Parameter	M01 (spiroxamine-desethyl)		M02 (spiroxamine-despropyl)		M03 (spiroxamine-N-oxide)	
	Value	Remarks	Value	Remarks	Value	Remarks
Formation fraction	0.183	Arithmetic mean (n=10), of laboratory values; submitted in MCA Renewal of Approval dossier, see CA 7.1.2	0.138	Arithmetic mean (n=10), of laboratory values;) submitted in MCA Renewal of Approval dossier see CA 7.1.2	0.149	Arithmetic mean (n= 7), of laboratory values; submitted in MCA Renewal of Approval dossier see CA 7.1.2
MACRO conversion fraction	0.1657	0.183 (ff x (MWmetabolite/ MWparent)	1.185×10^{-3}	0.138 (ff x (MWmetabolite/ MWparent)	0.157	0.149 (ff x (MWmetabolite/ MWparent)
Washoff Factor (1/m) (PEARL)	0.0001	Default	0.0001	Default	0.0001	Default
Foliar DT_{50} (d)	10	Default	10	Default	10	Default

Table 9.2.4.1-3: Supported use of Spiroxamine EC 500 (500 g/L) formulation

GAP details			Early application		Late application	
Crop	Appln rate (g as/ha)	Growth stage (PHI)	Int. (%)	Effective appln rate (g as/ha)	Int. (%)	Effective appln rate (g as/ha)
Vines	2x 200-300 (10 d min interval)	13-85	50 (GS13+)	2x 150	75 (GS71+)	2x 75

Applications made to vines were simulated using the relevant FOCUS scenarios in FOCUS PEARL (version 4.4.4) and FOCUS PELMO (version 5.5.3). In FOCUS MACRO (version 5.5.4), simulations were performed using the Châteaudun scenario.

The groundwater models account for crop interception using different methods. For consistency, the internal interception routines of the models were disabled and the application rates were manually adjusted for crop interception, in accordance with FOCUS recommendation (FOCUS, 2000 and 2014).

The calculation of the adjusted application rates is shown in Table 9.2.4.1-4.

Table 9.2.4.1-4: Calculation of exposure to soil for use in groundwater simulations

Scenario	FOCUS dates for emergence/ harvest	Application timing	
		Early	Late
Grapes (FOCUS vines), 2x 300 g as/ha (10 d min interval) GS13-85, min PHI 14 d			
Châteaudun (C)	1-Apr/1-Nov	14-Apr (104), 24-Apr (114)	29-Sep (272), 9-Oct (282)
Hamburg (H)	1-May/30-Oct	9-May (129) , 19-May (139)	23-Sep (266), 3-Oct (276)
Kremsmünster (K)	1-May/30-Oct	9-May (129) , 19-May (139)	23-Sep (266), 3-Oct (276)
Piacenza (P)	1-Apr/1-Nov	14-Apr (104), 24-Apr (114)	29-Sep (272), 9-Oct (282)
Porto (O)	15-Mar/30-Sep	30-Mar (89), 9-Apr (99)	05-Sep (248), 15-Sep (258)
Sevilla (S)	31-Mar/30-Nov	9-Apr (99), 19-Apr (109)	09-Oct (282), 19-Oct (292)
Thiva (T)	15-Mar/20-Oct	27-Mar (86), 6-Apr (96)	12-Sep (255), 22-Sep (265)
		Earliest appln @GS13 with 2nd appln 10 days later	2nd appln @GS85 with 1st appln 10 days prior

Results and discussion

The PEC_{GW} (80^{th} percentile annual average leachate concentration at 1 m soil depth) values, modelled using FOCUS PEARL, PELMO and MACRO for spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) following application of the Spiroxamine EC 500 (500 g/L)formulation to grape vines, are provided in Table 9.2.4.1-5 to Table 9.2.4.1-8.

Table 9.2.4.1-5: PEC_{GW} following annual application of spiroxamine in accordance with the GAP, using the FOCUS PEARL model and early application

Crop	Scenario	80th Percentile PEC_{GW} at 1 m Soil Depth (µg/L)			
		Spiroxamine	M01 (spirox-amine-desethyl)	M02 (spirox-amine-despro-pyl)	M03 (spirox-amine-N-oxide)
Vines (early applica-tion)	Châteaudun	<0.001	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001	<0.001
	Kremsmünster	<0.001	<0.001	<0.001	<0.001
	Piacenza	<0.001	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001

Table 9.2.4.1-6: PEC_{GW} following annual application of spiroxamine in accordance with the GAP, using the FOCUS PEARL model and late application

Crop	Scenario	80th Percentile PEC_{GW} at 1 m Soil Depth (µg/L)			
		Spiroxamine	M01 (spirox-amine-desethyl)	M02 (spirox-amine-despro-pyl)	M03 (spirox-amine-N-oxide)
Vines (late ap-plica-tion)	Châteaudun	<0.001	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001	<0.001
	Kremsmünster	<0.001	<0.001	<0.001	<0.001
	Piacenza	<0.001	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001

Table 9.2.4.1-7: PEC_{GW} following annual application of spiroxamine in accordance with the GAP, using the FOCUS PELMO model and early application

Crop	Scenario	80th Percentile PEC_{GW} at 1 m Soil Depth (µg/L)			
		Spiroxamine	M01 (spi-roxamine-desethyl)	M02 (spi-roxamine-despropyl)	M03 (spi-roxamine-N-oxide)
Vines (early application)	Châteaudun	<0.001	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001	<0.001
	Kremsmünster	<0.001	<0.001	<0.001	<0.001
	Piacenza	<0.001	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001

Table 9.2.4.1-8: PEC$_{GW}$ following annual application of spiroxamine in accordance with the GAP, using the FOCUS PELMO model and late application

Crop	Scenario	80th Percentile PEC$_{GW}$ at 1 m Soil Depth (µg/L)			
		Spirox-amine	M01 (spirox-amine-de-sethyl)	M02 (spirox-amine-despropyl)	M03 (spirox-amine-N-oxide)
Vines (late application)	Châteaudun	<0.001	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001	<0.001
	Kremsmünster	<0.001	<0.001	<0.001	<0.001
	Piacenza	<0.001	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001	<0.001

Table 9.2.4.1-9: PEC$_{GW}$ following annual application of spiroxamine in accordance with the GAP, using the FOCUS MACRO model application to Châteaudun

Crop	Application window	80th Percentile PEC$_{GW}$ at 1 m Soil Depth (µg/L)			
		Spiroxamine	M01 (spirox-amine-de-sethyl)	M02 (spirox-amine-despropyl)	M03 (spirox-amine-N-oxide)
Vines	Early	<0.01	<0.01	<0.01	<0.01
	Late	<0.01	<0.01	<0.01	<0.01

Conclusions

Predicted environmental concentrations of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) in groundwater have been generated in accordance with FOCUS guidelines FOCUS (2000 and 2014) and in accordance with the EU representative uses of the Spiroxamine EC 500 (500 g/L) formulation on grape vines.

The predicted 80th percentile average annual concentrations for spiroxamine following application to grape vines were lower than the 0.1 µg/L regulatory threshold in groundwater at 1 m depth for all crop / scenario combinations. The PEC$_{GW}$ values for metabolites M01, M02 and M03 following annual application spiroxamine to crops were also lower than the 0.1 µg/L regulatory threshold in groundwater at 1 m depth for all the available crop / scenario combinations.

These results demonstrate that spiroxamine can be used safely as proposed without the risk of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) exceeding acceptable levels in groundwater.

Assessment and conclusion by applicant:
The study was conducted to guideline(s) FOCUS (2000, 2014) and EFSA (2014) (required guidelines). The study is considered valid for use in the risk assessment.

PEC$_{GW}$ calculations for M06 have not been presented as critical studies to define modelling inputs are currently on-going. In studies investigating the route of degradation of the active substance spiroxamine in soil (presented under CA 7.1.1.1), the metabolite M06 is only observed >5% AR in one out of ten soils and only at the very last sampling point (in all other soils and all other sampling points the observed level of metabolite M06 was <5%). Due to the low levels of M06 observed, it was difficult to obtain reliable degradation rate constants from the parent applied studies. Consequently, estimated PEC$_{GW}$

from conservative input parameters were found to be provide unreasonable estimates of leaching when compared to the outcome of the soil column studies (see KCA 7.1.4.1) where only 0.2% of AR were observed in leachate. PEC_{GW} for M06 will be provided upon completion of the studies.

CP 9.2.4.2 Additional field tests

Based on the results of the FOCUS groundwater modelling assessment (Document M-CP, Section 9.2.4.1), additional field testing is not required.

CP 9.2.5 Estimation of concentrations in surface water and sediment

The Predicted Environmental Concentrations in surface water (PEC_{SW}) have been calculated for the active substance spiroxamine and major metabolite, as defined in CA 7.4.1, along with the formulation following foliar applications of Spiroxamine EC 500 (500 g/L) in accordance with the representative GAP.

The predicted environmental concentration of the formulated product Spiroxamine EC 500 (500 g/L), the active substance spiroxamine and significant metabolite in surface water (PECsw) is determined using the standardised recommendations of the FOCUS working group on surface water scenarios (FOCUS 2001[5], 2007[6], 2011[7], 2012[8] and 2015[9]). The PECs are provided in one existing study included in the last evaluation which is therefore included for completeness but which has been superseded by two new modelling reports conducted to modern requirements CP 9.2.5/02 (M-763144-01-1) and CP 9.2.5/03 (M-763145-01-1).

Substance	Report reference	Document no.	Comment
Spiroxamine	KCP 9.2.5/01	M-304024-01-1	Submitted for first renewal of spiroxamine, 2010. Reviewed under UP. Considered valid and acceptable.
Spiroxamine	KCP 9.2.5/02	M-763144-01-1	New data not yet reviewed under UP.
Spiroxamine	KCP 9.2.5/03	M-763145-01-1	

PECsw formulation

The initial predicted environmental concentration in surface water of the representative formulated product Spiroxamine EC 500 (500 g/L) is presented in Table 9.2.5-1. Since the formulation metabolite other than the active are assumed to dissipate rapidly in the environment, it is only necessary to consider the initial concentration for Spiroxamine EC 500 (500 g/L).

[5] FOCUS (2001). FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.
[6] FOCUS (2007). Landscape and Mitigation Factors in Aquatic Ecological Risk Assessment. Volume 1. Extended Summary and Recommendations. SANCO/10422/2005, version 2.0, September 2007.
[7] FOCUS (2011). Generic Guidance for FOCUS surface water Scenarios. Version 1. January 2011.
[8] FOCUS (2012). Generic guidance for FOCUS surface water scenarios. Version 1.2, December 2012.
[9] FOCUS (2015). Generic Guidance for FOCUS surface water Scenarios. Version 1.4. May 2015.

Table 9.2.5-1: Worst-case initial PECsw for Spiroxamine EC 500 (500 g/L) needed for environmental risk assessment

Crop	Formulation application rate	Mitigation distance (m)	PECsw (µg Spiroxamine EC 500 (500 g/L)/L)[A]		
			Water body type Ditch	Water body type Pond	Water body type Stream
Vines, 2x 300 g a.s./ha	0.6 L/ha Spiroxamine EC 500 (500 g/L) (equivalent to 601.8 g/ha)[B]	Default	10.38	0.3684	8.612
		5	6.274	0.4277	6.274
		10	2.273	0.2355	2.273
Vines, 2x 200 g a.s./ha	0.4 L/ha Spiroxamine EC 500 (500 g/L) (equivalent to 401.2 g/ha)[B]	Default	6.918	0.2456	5.741
		5	4.183	0.2851	4.183
		10	1.515	0.1570	1.515

A Calculated using the FOCUS drift calculator (v.1 Apr 2001) with the vines, late applns drift loadings and considering a worst-case single application
B Based on a Spiroxamine EC 500 (500 g/L) formulation relative density of 1.003 g/ml, see CP 2.6

The maximum initial concentration of the formulated product Spiroxamine EC 500 (500 g/L) in surface water following application with no applied mitigation and in consideration of no spray buffer zones of 5 and 10 m is 10.38, 6.274 and 2.273 µg formulation/L, respectively.

PECsw FOCUS steps 1-2

Data Point:	KCP 9.2.5/01
Report Author:	[redacted]; [redacted]
Report Year:	2008
Report Title:	Predicted environmental concentrations of spiroxamine in surface water and sediment (PECsw, PECsed) based on the tiered FOCUSsw approach - Use in vines in Europe
Report No:	MEF-08/270
Document No:	M-304024-01-1
Guideline(s) followed in study:	FOCUS (2003)
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted RAR (2010)
GLP/Officially recognised testing facilities:	No, not conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

This study was previous considered during the evaluation of spiroxamine (RAR (2010)) and is therefore included again for completeness. This study presents the PEC modelling conducted on the representative for the last evaluation, however, the PEC modelling reported in this study is superseded by the new PEC modelling performed in study KCP1 9.2.5/02 (M-763144-01-1) and KCP1 9.2.5/03 (M-763145-01-1).

Data Point:	KCP 9.2.5/02
Report Author:	[redacted]
Report Year:	2021
Report Title:	A modelling assessment of spiroxamine and its metabolites in surface water using FOCUS surface water steps 1 & 2
Report No:	0471836-SW1
Document No:	M-763144-01-1
Guideline(s) followed in study:	FOCUS (2000, 2014), EFSA (2014)
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	not applicable
Acceptability/Reliability:	Yes

Executive summary

The potential for spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) to reach surface water and sediment, following application to grape vines was investigated. Reported below are PEC values relating to vines only.

The following open field uses were simulated in accordance with the supported uses of the Spiroxamine EC 500 (500 g/L) formulation:

- Two applications (BBCH 13-85) at a maximum rate of 300 g a.s./ha to grape vines

Simulations for the open field uses of the Spiroxamine EC 500 (500 g/L) formulation were conducted using Steps 1-2 in FOCUS in accordance with the FOCUS guidance for surface water modelling (FOCUS, 2001 and 2015). A refinement of the values generated at Steps 1-2 to more realistic concentrations was performed for spiroxamine using FOCUS Step 3 and Step 4 in another study (see CP 9.2.5/03).

The input parameters for the calculations were selected based on recommendations from FOCUS (FOCUS 2001, 2007, 2011, 2012, 2015) and EFSA (2004), and studies submitted with the MCA 7 renewal of approval dossier.

The global maximum PEC_{SW} and PEC_{SED} values for spiroxamine and its metabolites at Step 2 are provided in Table 9.2.5-2. Detailed values and time weighted averages (TWA) are provided in the surface water report (M-763144-01-1).

Table 9.2.5-2: Global maximum PEC_{SW} and PEC_{SED} for spiroxamine and its metabolites

Crop	Compound	Global maximum at Step 2	
		PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
Grape vines 2x 300 g/ha, GS13-85	Spiroxamine	8.602	250.316
	M01 (spiroxamine-desethyl)	1.084	34.983
	M02 (spiroxamine-despropyl)	0.917	24.409
	M03 (spiroxamine-N-oxide)	2.420	39.636
	M06 (spiroxamine-acid)	21.656	0.691

Study design

The purpose of this study was to predict the environmental concentrations of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) in surface water and sediment following application to grape vines made in accordance with the EU representative GAP.

Conservative predicted environmental concentrations for spiroxamine and its metabolites in surface water and sediment (PEC_{SW} and PEC_{SED}) following application to open field crops were simulated using Steps 1-2 in FOCUS (version 3.2). A refinement of these values generated at Steps1-2 to more realistic concentrations were calculated for spiroxamine using the FOCUS Step 3 surface water scenarios with the FOCUS suite of surface water models was performed in in another study (see CP 9.2.5/03). The modelling simulations were carried out in accordance with the FOCUS guidance for surface water modelling (FOCUS, 2001 and 2015).

The input parameters used in the modelling for spiroxamine and its metabolites are summarised in Table 9.2.5-3 to Table 9.2.5-4.

Table 9.2.5-3: Physico-chemical parameters used in modelling for spiroxamine

Parameter	Value	Remarks
Physico-chemical		
Molecular weight (g/mol)	297.5	MCA Renewal of Approval dossier, see CA 1.7
Water solubility (mg/L)	470	MCA Renewal of Approval dossier, see CA 2.5
Vapour pressure (Pa)	$2.84x10^{-9}$ (20°C)	MCA Renewal of Approval dossier, see CA 2.2
Degradation in soil		
DT_{50} soil (d)	43.8	Geometric mean of uncropped field data (n= 8), submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.2.1-72
Sorption to soil		
K_{FOC} (mL/g)	4111	Geometric mean (n= 8) calculated from individual values, see data point CA 7.1.3.1, Table 7.1.3.1-1
K_{FOM} (mL/g)	2384	Calculated K_{Foc} / 1.724
Degradation in aquatic systems		
DT_{50} whole system (Step 1)	157.9	Geometric mean (n=6) submitted in MCA Renewal of Approval dossier, see data point CA 7.2.2.3, Table 7.2.2.3-23.
DT_{50} water (d) (Step 2)	1000	FOCUS recommendation, water set to conservative assumption
DT_{50} sediment (d) (Step 2)	157.9	FOCUS recommendation, sediment set to whole system degradation value.

Table 9.2.5-4: Input parameters used in STEPs 1-2 for the metabolites of spiroxamine

Parameter	M01 (spiroxamine-desethyl)		M02 (spiroxamine-despropyl)		M03 (spiroxamine-N-oxide)		M06 (spiroxamine-acid)	
	Value	Remarks	Value	Remarks	Value	Remarks	Value	Remarks
Molecular weight (g/mol)	269.4	Based on structure	255.4	Based on structure	313.5	Based on structure	327.5	Based on structure
Water solubility (mg/L)	14.8	MCA Renewal of Approval dossier, see CA 2.5	46.6	MCA Renewal of Approval dossier, see CA 2.5	1000	Default value	1000	Default value
K_{FOC} (mL/g)	3271	Geometric mean (n=4) submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1	2695	Geometric mean (n=4), submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1	1677	Geometric mean (n=4), submitted in MCA Renewal of Approval dossier, see data point CA 7.1.3.1.2, Table 7.1.3.1.2-1	3.2	Preliminary value, submitted in MCA Renewal of Approval dossier see CA 7.1.3.1
DT_{50} soil @ 20°C & pF2 (days)	168.6	Geometric mean (n=10) of laboratory values submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2	219.1	Geometric mean (n=10) of laboratory values submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2	46.4	Geometric mean (n=7) of laboratory values submitted in MCA Renewal of Approval dossier, see data point CA 7.1.2.1.1, Table 7.1.2.1.1-2	479.6	Geometric mean (n=4) of laboratory values submitted in MCA Renewal of Approval dossier, see CA 7.1.2.1.1
Max % observed in soil	12.0	From MCA Renewal of Approval dossier, see Table 7.4.1-1	9.2	From MCA Renewal of Approval dossier, see Table 7.4.1-1	7.2	From MCA Renewal of Approval dossier, see Table 7.4.1-1	5.3 (aerobic)	From MCA Renewal of Approval dossier, see Table 7.4.1-1
DT_{50} water (d)	1000	FOCUS default value (worst-case)	1000	FOCUS default value (worst-case)	1000	FOCUS default value (worst-case)	293.6	FOCUS recommendation, water set to whole system degradation value
DT_{50} sediment (d)	1000		1000		1000		1000	FOCUS recommendation, sediment set to conservative assumption

Parameter	M01 (spiroxamine-desethyl)		M02 (spiroxamine-despropyl)		M03 (spiroxamine-N-oxide)		M06 (spiroxamine-acid)	
	Value	Remarks	Value	Remarks	Value	Remarks	Value	Remarks
DT_{50} total system (d)	1000		1000		1000		293.6	Geometric mean (n=5) submitted in MCA Renewal of Approval dossier, see data point CA 7.2.2.3, Table 7.2.2.3-23
Max % observed in water/sediment	4.3	From MCA Renewal of Approval dossier, see Table 7.4.1-1	3.2	From MCA Renewal of Approval dossier, see Table 7.4.1-1	11.3	From MCA Renewal of Approval dossier, see Table 7.4.1-1	44.5	From MCA Renewal of Approval dossier, see Table 7.4.1-1

Table 9.2.5-5: Supported use of the Spiroxamine EC 500 (500 g/L) formulation

Crop	Application rate (g a.s./ha)	Number of applications	Interval between applications	BBCH growth stage at application
Grape vines	300	2	10 days	13-85
Grape vines	200	2	10 days	13-85

At Step 2, seasons of application were estimated based on the earliest and latest likely dates that applications would be made, in accordance with the BBCH growth ranges proposed in the EU representative GAP. In accordance with FOCUS guidance (FOCUS, 2001 and 2015), where there are multiple applications, Step 2 simulations were performed based on both the multiple and the respective single application rates and the worst-case PEC_{SW} and PEC_{SED} values were selected for input into the environmental risk assessment. The regions of use and seasons for application used in the Step 2 modelling are presented in Table 9.2.5-6.

Table 9.2.5-6: Model parameters used in FOCUS Step 2 surface water modelling for vines

Crop	Zone (Step 2)	Season	Interception
Grape vines	North Europe	Mar-May	Average (20%)
		Jun-Sep	Full (70%)
	South Europe	Mar-May	Average (20%)
		Jun-Sep	Full (70%)

Results and discussion

Summaries of the maximum PEC_{SW} and PEC_{SED} values for spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) at FOCUS Steps 1 and 2, as calculated by the FOCUS surface water models, are provided in Table 9.2.5-7 and Table 9.2.5-8 for PEC_{SW} and PEC_{SED} values, respectively. Detailed values and time weighted averages (TWA) are provided in the surface water report (M-763144-01-1).

Table 9.2.5-7: Maximum PEC_{SW} for spiroxamine and its metabolites - FOCUS Step 1-2

FOCUS Step	Area	Application timing	Multiple appln (µg/L)					Single appln (µg/L)				
			spx	M01	M02	M03	M06	spx	M01	M02	M03	M06
Vines, 2x 300 g/ha, GS13-85												
1	-	-	46.914	6.131	5.076	14.417	117.043	-	-	-	-	-
2	N	Mar-May, average int. (20%), early vines drift	3.741	0.567	0.479	1.329	12.022	2.699	0.295	0.242	0.717	6.462
2	N	Jun-Sep, full int. (70%), late vines drift	8.602	0.556	0.466	1.551	14.517	8.028	0.313	0.246	0.956	8.010
2	S	Mar-May, average int. (20%), early vines drift	6.425	1.084	0.917	2.420	21.656	3.484	0.562	0.474	1.305	11.619
2	S	Jun-Sep, full int. (70%), late vines drift	8.602	0.763	0.641	1.988	18.370	8.028	0.402	0.337	1.090	10.072
-	-	**Maximum (step 2)**	**8.602**	**1.084**	**0.917**	**2.4200**	**21.656**	**8.028**	**0.562**	**0.474**	**1.305**	**11.619**
Vines, 2x 200 g/ha, GS13-85												
1	-	-	31.276	4.088	3.384	9.611	78.029	-	-	-	-	-
2	N	Mar-May, average int. (20%), early vines drift	2.494	0.387	0.139	0.886	8.015	1.799	0.197	0.165	0.478	4.308
2	N	Jun-Sep, full int. (70%), late vines drift	5.735	0.723	0.311	1.034	14.437	5.352	0.375	0.164	0.637	7.746
2	S	Mar-May, average int. (20%), early vines drift	4.284	0.371	0.611	1.614	9.678	2.323	0.208	0.316	0.870	5.340
2	S	Jun-Sep, full int. (70%), late vines drift	5.735	0.508	0.427	1.325	12.247	5.352	0.268	0.224	0.726	6.715
-	-	**Maximum (step 2)**	**5.735**	**0.723**	**0.611**	**1.614**	**14.437**	**5.352**	**0.375**	**0.316**	**0.870**	**7.746**

Table 9.2.5-8: Maximum PEC_{SED} for spiroxamine and its metabolites - FOCUS Step 1-2

FOCUS Step	Area	Application timing	Multiple appln (µg/L)					Single appln (µg/L)				
			spx	M01	M02	M03	M06	spx	M01	M02	M03	M06
Vines, 2x 300 g/ha, GS13-85												
1	-	-	1360.000	183.796	127.415	219.460	3.736	-	-	-	-	-
2	N	Mar-May, average int. (20%), early vines drift	140.439	18.080	12.604	21.348	0.384	76.097	9.385	6.518	11.509	0.206
2	N	Jun-Sep, full int. (70%), late vines drift	175.067	16.881	11.723	23.356	0.463	97.452	8.897	6.157	12.817	0.256
2	S	Mar-May, average int. (20%), early vines drift	250.316	34.983	24.409	39.636	0.691	135.374	18.130	12.602	21.359	0.371
2	S	Jun-Sep, full int. (70%), late vines drift	219.018	23.642	16.445	30.672	0.586	121.163	12.395	8.591	16.756	0.321
-	-	**Maximum (step 2)**	**250.316**	**34.983**	**24.409**	**39.636**	**0.691**	**135.374**	**18.130**	**12.602**	**21.359**	**0.371**
Vines, 2x 200 g/ha, GS13-85												
1	-	-	909.603	122.531	84.943	146.307	2.490	-	-	-	-	-
2	N	Mar-May, average int. (20%), early vines drift	93.626	12.053	8.403	14.232	0.256	50.731	6.256	4.345	7.673	0.138
2	N	Jun-Sep, full int. (70%), late vines drift	116.712	23.322	7.816	15.571	0.462	64.968	12.087	4.105	8.544	0.248
2	S	Mar-May, average int. (20%), early vines drift	166.878	11.254	16.273	26.424	0.309	90.249	5.931	8.402	14.239	0.171
2	S	Jun-Sep, full int. (70%), late vines drift	146.012	15.761	10.964	20.448	0.391	80.775	8.264	5.727	11.171	0.215
-	-	**Maximum (step 2)**	**166.878**	**23.322**	**16.273**	**26.424**	**0.462**	**90.249**	**12.087**	**8.402**	**14.239**	**0.248**

Conclusions

Predicted environmental concentrations of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) in surface water and sediment have been generated in accordance with FOCUS and EFSA guidance, for the use of Spiroxamine EC 500 (500 g/L) on grape vines.

The maximum PEC_{SW} values for the metabolites at Step 2 for vines were 1.084 µg/L for M01 (spiroxamine-desethyl), 0.917 µg/L for M02 (spiroxamine-despropyl), 2.420 µg/L for M03 (spiroxamine-N-oxide), and 21.656 µg/L for M06 (spiroxamine-acid).

The global maximum PEC_{SW} and PEC_{SED} values for spiroxamine and its metabolites at Step 2 are provided in Table 9.2.5-9.

Table 9.2.5-9: Global maximum PEC_{SW} and PEC_{SED} for spiroxamine and its metabolites - FOCUS Step 2

Crop	Compound	Global maximum at Step 2[a]	
		PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
Grape vines 2x 300 g/ha, GS13-85	Spiroxamine	8.602	250.316
	M01 (spiroxamine-desethyl)	1.084	34.983
	M02 (spiroxamine-despropyl)	0.917	24.409
	M03 (spiroxamine-N-oxide)	2.420	39.636
	M06 (spiroxamine-acid)	21.656	0.691

[a] Maximum value resulted from duplicate application

Assessment and conclusion by applicant:

The study was conducted to guideline(s) FOCUS 2001, 2015 (required guideline). The study is considered valid for use in the risk assessment.

PECsw FOCUS steps 3-4

Data Point:	KCP 9.2.5/03
Report Author:	[redacted]
Report Year:	2021
Report Title:	A modelling assessment of spiroxamine using FOCUS surface water steps 3 & 4 - Application of SPX EC 500 (500 g/L) to vines
Report No:	0471836-SW2
Document No:	M-763145-01-1
Guideline(s) followed in study:	FOCUS (2000, 2014), EFSA (2014)
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	not applicable
Acceptability/Reliability:	Yes

Executive summary

The potential to refine values generated at Step 1-2 (see CP 9.2.5/02) for spiroxamine to more realistic concentrations was performed using FOCUS Step 3 and Step 4.

The requested uses were simulated in accordance with the supported uses of the Spiroxamine EC 500 (500 g/L) formulation:

- Two applications (BBCH 13 - 85) at a rate of 300 g a.s./ha to grape vines
- Two applications (BBCH 13 - 85) at a rate of 200 g a.s./ha to grape vines

The input parameters for the calculations were selected based on recommendations from FOCUS (FOCUS 2001, 2007, 2011, 2012, 2015) and EFSA (2004), and studies submitted in the appropriate section of the MCA 7.

The global maximum PEC_{SW} and PEC_{SED} values for spiroxamine at Step 3 and 4 are provided in Table 9.2.5-10 and Table 9.2.5-11.

Table 9.2.5-10: Global maximum PEC_{SW} and PEC_{SED} for spiroxamine – FOCUS Step 3

Use	Maximum PEC_{SW} (µg/L)
Vines, early 2 x 300 g a.s./ha	5.263[a)]
Vines, late, 2 x 300 g a.s./ha	5.309
Vines, early 2 x 200 g/ha	3.508[a)]
Vines, late 2 x 200 g a.s./ha	3.531

[a)] Maximum value resulted from single application

The maximum PEC_{SW} values for spiroxamine at FOCUS Step 4 are presented in Table 9.2.5-11.

Table 9.2.5-11: Global maximum PEC_{SW} and PEC_{SED} for spiroxamine – FOCUS Step 4

Use	Mitigation	Maximum PEC_{SW} (µg/L)
Vines, early 2 x 300 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.399
Vines, late, 2 x 300 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.376
Vines, early 2 x 200 g/ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.330[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.255
Vines, late 2 x 200 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.331[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.250

[a)] Maximum value resulted from single application
VFS = vegetated filter strip, SDBZ = spray drift buffer zone, SDRT = spray drift reduction technology

Study design

The purpose of this study was to predict the environmental concentrations of spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) in surface water and sediment following application to grape vines made in accordance with the EU representative GAP.

A refinement of values generated at Steps1-2 to more realistic concentrations were calculated for spiroxamine using the FOCUS Step 3 surface water scenarios with the FOCUS suite of surface water models (MACRO version 5.5.4, PRZM version 4.3.1, SPIN version 2.2 and TOXSWA version 5.5.3) in the SWASH version 5.3 shell. Mitigation was added at Step 4 using the SWAN version 5.0.0 tool. The modelling simulations were carried out in accordance with the FOCUS guidance for surface water modelling (FOCUS, 2001 and 2015).

The input parameters used in the modelling for spiroxamine are summarised in Table 9.2.5-12.

Table 9.2.5-12: Physico-chemical parameters used in modelling for spiroxamine

Parameter	Value	Remarks
	Physico-chemical	
Molecular weight (g/mol)	297.5	From CA 1.7
Water solubility (mg/L)	470	From CA 2.25
Vapour pressure (Pa)	0.0047 (20°C)	From CA 2.2
	Degradation in soil	
DT_{50} soil (d)	43.8	Geometric mean of uncropped field data (n=8), under CA 7.1.2.2.1/12, see Table 7.1.2.2.1-72
Temperature correction function Reference temperature (°C) MACRO: (K^{-1}) PRZM: Q_{10} (-)	 20 0.095 2.58	FOCUS recommendation
Moisture correction function Reference moisture (-) PRZM/MACRO: moisture exponent (-)	 pF2 0.7	
	Sorption to soil	
K_{FOC} (mL/g)	4110	Geometric mean (n=8) calculated from individual values summarised under CA 7.1.3.1, See Table 7.1.3.1.1-1
K_{FOM} (mL/g)	2384	Calculated K_{FOC} / 1.724
Freundlich exponent 1/n (-)	0.892	Arithmetic mean (n=8) calculated from individual values summarised under CA 7.1.3.1, see Table 7.1.3.1.1-1
	Degradation in aquatic systems	
DT_{50} whole system	157.9	Geometric mean (n=6) under CA 7.2.2.2/08, see Table 7.2.2.3-23
DT_{50} water (d)	1000	FOCUS recommendation, water set to conservative assumption
DT_{50} sediment (d)	157.9	FOCUS recommendation, sediment set to whole system degradation value
DT_{50} crop (d)	10	FOCUS recommendation
Temperature correction function Reference temperature (°C) TOXSWA: activation energy (J/mol)	 20 65400	
Crop uptake factor (-)	0.47	Based on Briggs equation and measured $logK_{OW}$ [A]
Wash off coefficient PRZM: (cm^{-1}) MACRO: (mm^{-1})	 0.5 0.05	FOCUS recommendation

A According to EFSA (2013), European Commission (2014) and FOCUS (2014), the Briggs relation can be used to derive the Plant Uptake Factor (PUF) from experimentally measured $logK_{OW}$ values at neutral pH:

$$PUF = 0.784\ \exp\left(-\frac{(\log(Kow) - 1.78)^2}{2.44}\right)$$

For spiroxamine, $\log(K_{OW})$ values of 2.79 (diastereomer A) and 2.98 (diastereomer B) were determined at pH 7 (Krohn, 1995). Using Briggs' relation, this corresponds to a PUF of 0.52 (diastereomer A) and 0.43 (diastereomer B). As the molar masses are identical for both isomers, the mole fractions are 0.53 for diastereomer A and 0.46 for diastereomer B (Krohn, 1994). Therefore: PUF_{SPX} = 0.53 * 0.52 + 0.43 * 0.46 = 0.47.
A PUF of 0.47 is used for spiroxamine in the risk assessment.

Table 9.2.5-12: Supported use of the Spiroxamine EC 500 (500 g/L) formulation

Crop	F G or I [a]	Number of applications	Application rate (g a.s./ha)	Interval between applications (days)	Range of growth stages / season	PHI
Grape vines	F	2	300	10	BBCH 13-85	14 d minimum
Grape vines	F	2	200	10	BBCH 13-85	14 d minimum

[a] Outdoor of field use (F), greenhouse application (G) or indoor application (I)

The foliar application method was selected so that a crop interception value would be determined by the model based on the growth stage.

In accordance with FOCUS guidance, where there are multiple applications, Step 3 simulations were performed based on both the multiple and the respective single application rates and the worst-case PEC_{SW} and PEC_{SED} values were selected for input into the environmental risk assessment.

Due to the wide range of BBCH stages within the requested GAP, several potential application periods have been used for modelling, based on timings from AppDate v3.06 (2019). In accordance with guidance, an application window starting at various growth stages was therefore set up for each scenario, as specified in Table 9.2.5-13. The actual application dates were then determined automatically in PRZM and MACRO using the Pesticide Application Timing calculator (PAT).

The application timings for selected for the beginning (early) and end (late) of the application windows are provided in Table 9.2.5-13.

Table 9.2.5-13: Application timings for field uses on grape vines in surface water simulations

Scenario details		FOCUS default dates		SWASH application window (start date)											
				Early season						Late season					
				Window 1 (a)		Window 2 (b)		Window 3 (c)		Window 1 (d)		Window 2 (e)		Window 3 (f)	
Sce-nario	**Crop no.**	**Emer-gence**	**Harvest**	**Start**	**End**	**Start**	**End**	**Start**	**End**	**Start**	**End**	**Start**	**End**	**Start**	**End**
Grapes (FOCUS crop vines early), 2x 300 g as/ha (10 d min int) GS13-85, min PHI 14 d [Original dates]															
D6	n.a.	1-Feb	10-Nov	11-Feb (42)	23-Mar (82)	20-Feb (51)	1-Apr (91)	n.a.	n.a.	12-Mar (71)	21-Apr (111)	15-Aug (227)	24-Sep (267)	23-Sep (266)	2-Nov (306)
R1	n.a.	15-Apr	30-Oct	24-Apr (114)	3-Jun (154)	1-May (121)	10-Jun (161)	n.a.	n.a.	19-May (139)	28-Jun (179)	6-Sep (249)	16-Oct (289)	30-Sep (273)	9-Nov (313)
R2	n.a.	15-Mar	30-Sep	30-Mar (89)	9-May (129)	12-Apr (102)	22-May (142)	n.a.	n.a.	14-May (134)	23-Jun (174)	3-Sep (246)	13-Oct (286)	15-Sep (258)	25-Oct (298)
R3	n.a.	1-Apr	1-Nov	14-Apr (104)	24-May (144)	26-Apr (116)	5-Jun (156)	n.a.	n.a.	24-May (144)	3-Jul (184)	20-Sep (263)	30-Oct (303)	9-Oct (282)	18-Nov (322)
R4	n.a.	10-Mar	20-Sep	24-Mar (83)	3-May (123)	6-Apr (96)	16-May (136)	n.a.	n.a.	7-May (127)	16-Jun (167)	23-Aug (235)	2-Oct (275)	5-Sep (248)	15-Oct (288)

Notes: 2x 300 g a.s./ha (10d min interval), application method airblast, PRZM input (CAM2, application foliar linear, depth incorporated 4 cm)
Codes used within modelling runs:
t1 : 2x 300 g/ha
t5 : 2x 200 g/ha
Application windows based on AppDate (v3.06).
Early season – window 1/starting GS13; window 2/starting GS16
Late season – window 1/starting GS53; window 2/starting GS81; window 3/starting GS85.
Using the minimum application window (30 days + (no. of applications – 1) x minimum application interval, i.e. 40 days). Treatments were conducted every year. FOCUS crop vines/early were used for all applications <GS16, FOCUS crop vines/late were used for all applications ≥GS16.
n.a.: not applicable

The length of the application windows were calculated using the equation below:

$$\text{Length of window (days)} = 30 + \left((n - 1) \times \text{interval between applications (days)}\right)$$

Where:
n = number of applications

Step 4 – application of mitigation measures

The Swan (version 5.0.0) tool was used to apply mitigation measures in the form of vegetative filter strips (VFS) and no spray buffer zones (NSBZ).

Results and discussion

Summaries of the maximum PEC_{SW} and PEC_{SED} values for spiroxamine at FOCUS Step 3 and 4, as calculated by the FOCUS surface water models, are provided in Table 9.2.5-14 to Table 9.2.5-17.

Table 9.2.5-14: Maximum PEC_{SW} and PEC_{SED} following application of 2 x 300 g a.s./ha spiroxamine to Grape vines – FOCUS Step 3

Scenario	Water body	PEC_{SW} (µg/L)							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)
Multiple application 2x 300 g/ha									
D6	Ditch	5.021	Spray drift	0.517	6.177	5.309	Spray drift	2.627	21.530
R1	Pond	0.265	Spray drift	0.213	2.799	0.272	Spray drift	0.218	3.118
R1	Stream	3.670	Spray drift	0.047	1.086	3.755	Spray drift	0.066	1.253
R2	Stream	4.942	Spray drift	0.038	1.835	5.034	Spray drift	0.055	6.388
R3	Stream	5.263	Spray drift	0.075	1.301	5.294	Spray drift	0.166	5.688
R4	Stream	3.683	Spray drift	0.157	5.070	3.754	Spray drift	0.189	5.383
Single application 1x 300 g/ha									
D6	Ditch	5.021	Spray drift	0.517	6.177	5.120	Spray drift	1.584	14.110
R1	Pond	0.265	Spray drift	0.213	2.799	0.183	Spray drift	0.139	1.763
R1	Stream	3.670	Spray drift	0.047	1.086	3.755	Spray drift	0.045	0.780
R2	Stream	4.942	Spray drift	0.038	1.835	5.034	Spray drift	0.032	3.250
R3	Stream	5.263	Spray drift	0.075	1.301	5.294	Spray drift	0.135	5.688
R4	Stream	3.683	Spray drift	0.157	5.070	3.754	Spray drift	0.097	2.835

Table 9.2.5-15: Maximum PEC_{SW} and PEC_{SED} following application of 2 x 200 g a.s./ha spiroxamine to Grape vines - FOCUS Step 3

Scenario	Water body	PEC_{SW} (µg/L)							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)
Multiple application 2x 200 g/ha									
D6	Ditch	3.346	Spray drift	0.344	4.151	3.531	Spray drift	1.744	14.550
R1	Pond	0.176	Spray drift	0.141	1.889	0.181	Spray drift	0.144	2.103
R1	Stream	2.446	Spray drift	0.031	0.729	2.503	Spray drift	0.044	0.835
R2	Stream	3.294	Spray drift	0.026	1.238	3.355	Spray drift	0.036	4.451
R3	Stream	3.508	Spray drift	0.050	0.875	3.528	Spray drift	0.110	3.897
R4	Stream	2.455	Spray drift	0.101	3.406	2.502	Spray drift	0.123	3.625
Single application 1x 200 g/ha									
D6	Ditch	3.346	Spray drift	0.077	1.141	3.413	Spray drift	1.051	9.508
R1	Pond	0.121	Spray drift	0.091	1.098	0.122	Spray drift	0.092	1.190
R1	Stream	2.446	Spray drift	0.017	0.331	2.503	Spray drift	0.030	0.521
R2	Stream	3.294	Spray drift	0.013	0.563	3.355	Spray drift	0.021	2.260
R3	Stream	3.508	Spray drift	0.050	0.787	3.528	Spray drift	0.088	3.897
R4	Stream	2.455	Spray drift	0.045	1.374	2.502	Spray drift	0.063	1.911

Summaries of the PE_{SW} and PEC_{SED} values for spiroxamine following application of mitigation measures at Step 4 are provided in Table 9.2.5-15.

Table 9.2.5-16: Maximum PEC_{SW} and PEC_{SED} following application of 2 x 300 g a.s./ha spiroxamine to grape vines - FOCUS Step 4

Scenario	Water body	PEC_{SW} (µg/L)							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)
Multiple application 2x 300 g/ha; 20 m VFS + 20 m SDBZ + 0% SDRT									
D6	Ditch	0.385	Spray drift	0.052	0.650	0.478	Drainage	0.260	2.349
R1	Pond	0.111	Runoff	0.090	1.213	0.113	Runoff	0.092	1.330
R1	Stream	0.349	Spray drift	0.008	0.152	0.358	Spray drift	0.009	0.165
R2	Stream	0.467	Spray drift	0.005	0.138	0.478	Spray drift	0.008	0.415
R3	Stream	0.496	Spray drift	0.014	0.187	0.496	Spray drift	0.021	0.491
R4	Stream	0.399	Runoff	0.032	0.617	0.360	Runoff	0.037	0.661
Single application 1x 300 g/ha; 20 m VFS + 20 m SDBZ + 0% SDRT									
D6	Ditch	0.385	Spray drift	0.012	0.173	0.466	Drainage	0.154	1.495
R1	Pond	0.074	Runoff	0.057	0.693	0.074	Runoff	0.058	0.747
R1	Stream	0.349	Spray drift	0.003	0.069	0.358	Spray drift	0.007	0.098
R2	Stream	0.467	Spray drift	0.002	0.061	0.478	Spray drift	0.005	0.207
R3	Stream	0.496	Spray drift	0.010	0.155	0.496	Spray drift	0.021	0.451
R4	Stream	0.351	Spray drift	0.014	0.251	0.358	Spray drift	0.018	0.334
Multiple application 2x 300 g/ha; 20 m VFS + 25 m SDBZ + 0% SDRT									
D6	Ditch	0.297	Drainage	0.041	0.511	0.376	Drainage	0.203	1.856
R1	Pond	0.093	Runoff	0.076	1.029	0.095	Runoff	0.077	1.131
R1	Stream	0.251	Spray drift	0.007	0.148	0.259	Spray drift	0.008	0.153
R2	Stream	0.335	Spray drift	0.004	0.133	0.343	Spray drift	0.007	0.412
R3	Stream	0.357	Spray drift	0.013	0.173	0.357	Spray drift	0.018	0.470
R4	Stream	0.399	Runoff	0.031	0.606	0.360	Runoff	0.035	0.645

Scenario	Water body	PEC$_{SW}$ (µg/L)							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC$_{SED}$ (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC$_{SED}$ (µg/kg)
Single application 1x 300 g/ha; 20 m VFS + 25 m SDBZ + 0% SDRT									
D6	Ditch	0.274	Spray drift	0.009	0.136	0.364	Drainage	0.120	1.170
R1	Pond	0.062	Runoff	0.047	0.584	0.062	Runoff	0.048	0.630
R1	Stream	0.251	Spray drift	0.003	0.067	0.259	Spray drift	0.006	0.088
R2	Stream	0.335	Spray drift	0.002	0.059	0.343	Spray drift	0.004	0.206
R3	Stream	0.357	Spray drift	0.009	0.148	0.357	Spray drift	0.018	0.433
R4	Stream	0.253	Spray drift	0.013	0.246	0.259	Spray drift	0.017	0.325

VFS = vegetative filter strip, SDBZ = spray drift buffer zone, SDRT = spray drift reduction technology

Table 9.2.5-17: Maximum PEC$_{SW}$ and PEC$_{SED}$ following application of 2 x 200 g a.s./ha spiroxamine to Grape vines - FOCUS Step 4

Scenario	Water body	PEC$_{SW}$ (µg/L)							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC$_{SED}$ (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC$_{SED}$ (µg/kg)
Multiple application 2x 200 g/ha; 20 m VFS + 20 m SDBZ + 0% SDRT									
D6	Ditch	0.257	Spray drift	0.035	0.436	0.318	Drainage	0.173	1.585
R1	Pond	0.074	Runoff	0.060	0.819	0.075	Runoff	0.061	0.897
R1	Stream	0.232	Spray drift	0.005	0.100	0.239	Spray drift	0.006	0.108
R2	Stream	0.312	Spray drift	0.003	0.092	0.318	Spray drift	0.005	0.286
R3	Stream	0.330	Spray drift	0.009	0.123	0.331	Spray drift	0.014	0.327
R4	Stream	0.255	Runoff	0.021	0.404	0.239	Spray drift	0.024	0.434
Single application 1x 200 g/ha; 20 m VFS + 20 m SDBZ + 0% SDRT									
D6	Ditch	0.257	Spray drift	0.008	0.116	0.310	Drainage	0.102	1.006
R1	Pond	0.049	Runoff	0.038	0.468	0.049	Runoff	0.038	0.504
R1	Stream	0.232	Spray drift	0.002	0.046	0.239	Spray drift	0.004	0.064
R2	Stream	0.312	Spray drift	0.002	0.041	0.318	Spray drift	0.003	0.143
R3	Stream	0.330	Spray drift	0.007	0.101	0.331	Spray drift	0.014	0.303
R4	Stream	0.234	Spray drift	0.009	0.165	0.239	Spray drift	0.012	0.220

Scenario	Water body	PEC							
		Early application (GS13-53)				Late application (GS53-85)			
		Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)	Initial	Main route of entry	21-day TWA	Maximum PEC_{SED} (µg/kg)
Multiple application 2x 200 g/ha; 20 m VFS + 25 m SDBZ + 0% SDRT									
D6	Ditch	0.198	Drainage	0.027	0.343	0.250	Drainage	0.135	1.252
R1	Pond	0.062	Runoff	0.050	0.695	0.063	Runoff	0.051	0.763
R1	Stream	0.167	Spray drift	0.005	0.097	0.172	Spray drift	0.005	0.100
R2	Stream	0.223	Spray drift	0.002	0.088	0.229	Spray drift	0.005	0.283
R3	Stream	0.238	Spray drift	0.008	0.114	0.238	Spray drift	0.012	0.313
R4	Stream	0.255	Runoff	0.020	0.397	0.230	Runoff	0.022	0.423
Single application 1x 200 g/ha; 20 m VFS + 25 m SDBZ + 0% SDRT									
D6	Ditch	0.182	Spray drift	0.006	0.091	0.242	Drainage	0.079	0.787
R1	Pond	0.041	Runoff	0.032	0.394	0.041	Runoff	0.032	0.425
R1	Stream	0.167	Spray drift	0.002	0.044	0.172	Spray drift	0.004	0.058
R2	Stream	0.223	Spray drift	0.001	0.039	0.229	Spray drift	0.003	0.141
R3	Stream	0.238	Spray drift	0.006	0.096	0.238	Spray drift	0.012	0.292
R4	Stream	0.168	Spray drift	0.008	0.161	0.172	Spray drift	0.011	0.213

VFS = vegetative filter strip, SDBZ = spray drift buffer zone, SDRT = spray drift reduction technology

Conclusions

Predicted environmental concentrations of spiroxamine in surface water and sediment have been generated in accordance with FOCUS and EFSA guidance, for the use of Spiroxamine EC 500 (500 g/L) on grape vines.

The global maximum PEC_{SW} and PEC_{SED} values for spiroxamine and its metabolites at Step 3 are provided in Table 9.2.5-19 and Step 4 are presented in Table 9.2.5-19.

Table 9.2.5-18: Global maximum PEC_{SW} and PEC_{SED} for spiroxamine - FOCUS Step 3

Use	Maximum PEC_{SW} (µg/L)
Vines, early 2 x 300 g a.s./ha	5.263[a)]
Vines, late, 2 x 300 g a.s./ha	5.309
Vines, early 2 x 200 g/ha	3.508[a)]
Vines, late 2 x 200 g a.s./ha	3.531

[a)] Maximum value resulted from single application

Table 9.2.5-19: Maximum PEC_{SW} and PEC_{SED} for spiroxamine - FOCUS Step 4

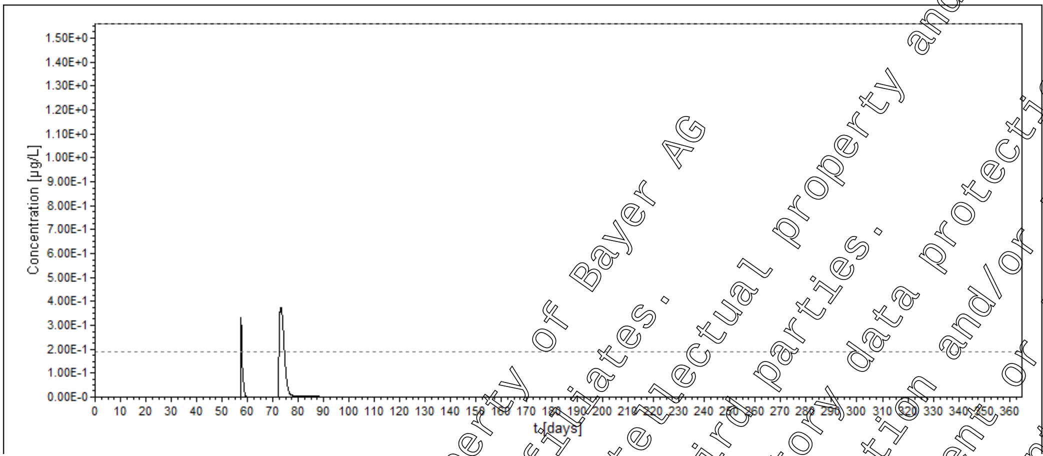
Use	Mitigation	Maximum PEC_{SW} (µg/L)
Vines, early 2 x 300 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.399
Vines, late, 2 x 300 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.376
Vines, early 2 x 200 g/ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.330[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.255
Vines, late 2 x 200 g a.s./ha	20 m VFS + 20 m SDBZ + 0% SDRT	0.331[a)]
	20 m VFS + 25 m SDBZ + 0% SDRT	0.250

[a)] Maximum value resulted from single application
VFS = vegetated filter strip, SDBZ = spray drift buffer zone, SDRT = spray drift reduction technology

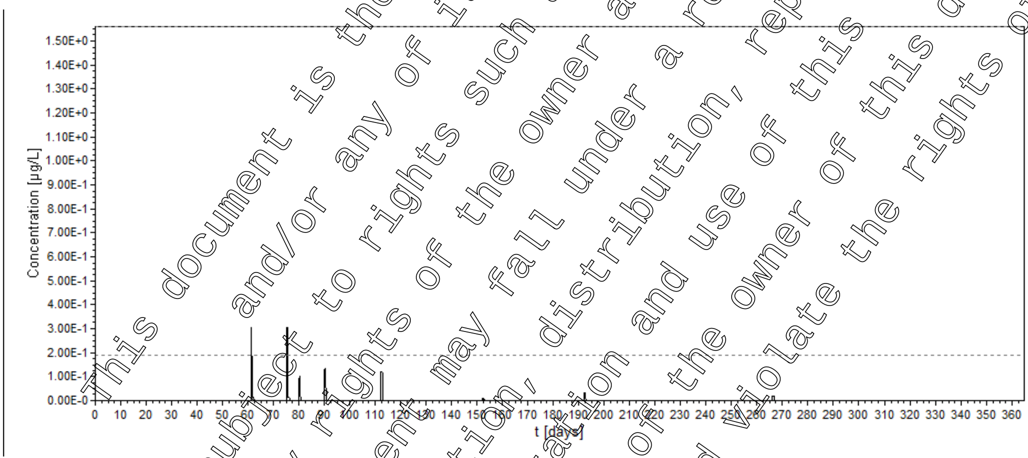
In order to provide further refinement to Step 3 and 4 SW modelling, EPAT profiles can be considered. Example EPAT profiles for are shown in Figure 9.2.5-1 below which show the exposure profile for drainage (D) and run-off (R) scenario are mainly driven by spray drift. A more detailed evaluation of the exposure profiles can be conducted, on request.

Figure 9.2.5-1: Example exposure profile following 2x 300 g/ha to vines with mitigation of 20 m VFS + 20 m SDBZ (application window b)

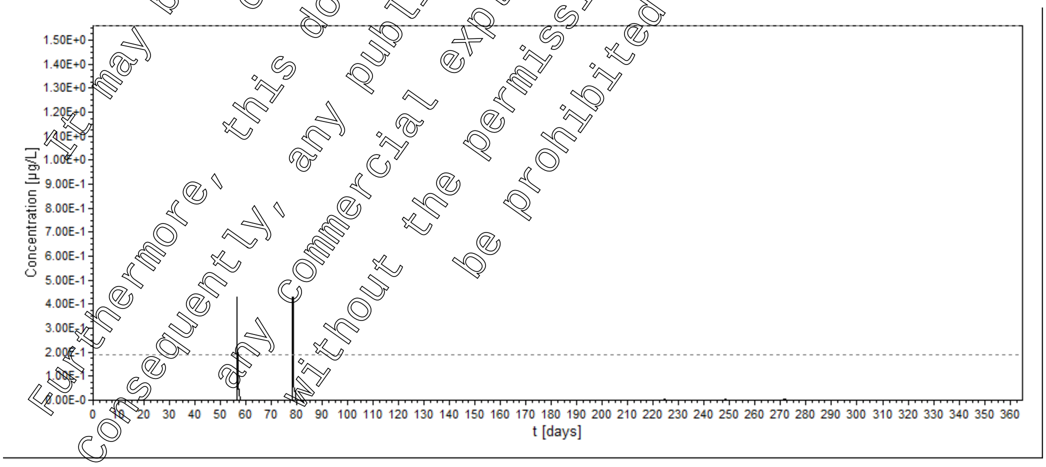
Drainage scenario (D6)



Run-off scenario (R1)



Run-off scenario (R3)



Assessment and conclusion by applicant:

The study was conducted to guideline(s) FOCUS 2001, 2015 (required guideline). The study is considered valid for use in the risk assessment.

CP 9.3 Fate and behaviour in air

CP 9.3.1 Route and rate of degradation in air and transport via air

The fate and behaviour in air of the representative formulation Spiroxamine EC 500 (500 g/L) can be extrapolated from the active substance studies addressed under CA 7.3.

Based on an overall vapour pressure value for the whole active substance (i.e. combined A and B isomers) of 4.7 x 10^{-3} Pa (20°) and individual vapour pressure values of 3.0 x 10^{-3} and 6.0 x 10^{-3} 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 m^3/mol (pH7, 20°C) and individual Henry's law constants of 2.5 x 10^{-3} and 5.0 x 10^{-3} Pa m^3/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 *ca.* 2% after 24 hrs. Any volatilisation of the active substance from the laboratory soil studies under Point CA 7.1.1. was also very low (<1% AR), although some volatilisation was observed from water surfaces in the water/sediment study (under Point CA 7.2.2.3). However, the estimated photochemical oxidative degradation half-life (using the Atkinson equation) in air of the active substance spiroxamine is <3 hours and therefore, if present, spiroxamine will not persist in the atmosphere.

Consequently, the predicted environmental concentration of the active substance in air is expected to be negligible and is not calculated.

CP 9.4 Estimation of concentrations for other routes of exposure

Use of the representative formulated product Spiroxamine EC 500 (500 g/L) can potentially lead to amounts reaching surface water during treatments by spray drift or *via* soil drainage and run-off, and therefore potentially reaching Water Treatment Plants (WTPs) where disinfection processes have the potential to modify the active substance or metabolites during treatment. In order to address the potential for harmful compounds being formed during the disinfection process, an assessment of potential exposure at WTPs is presented.

Impact of WTP Exposure

Data Point:	KCP 9.4/01
Report Author:	[redacted]
Report Year:	2021
Report Title:	Spiroxamine: Effects of water treatment on parent and metabolites in drinking water
Report No:	0471836-WT1
Document No:	M-764010-01-1
Guideline(s) followed in study:	None
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	not applicable
Acceptability/Reliability:	Yes

Executive Summary

Under Regulation (EC) No 1107/2009, it is necessary to show that active substances for use in plant protection products have no harmful effect on human or animal health through drinking water. The presence and potential levels of active substance and any metabolites in drinking water should therefore be investigated to assess the risk of formation of harmful substances such as nitrosamines, dioxins and furans during drinking water disinfection processes.

In this paper, the potential for formation of such substances resulting from treatment of water containing spiroxamine and its metabolites has been looked at. A review of the degradation pathways of spiroxamine in water and soil has been performed. Spiroxamine degrades to major metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-desthyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid), minor metabolites, bound residues and carbon dioxide in soil, either via microbial processes. In water/sediment spiroxamine degrades to major metabolites, M06 (spiroxamine-acid), minor metabolites, bound residues and carbon dioxide, via microbial processes.

Groundwater and surface water are the most common sources of drinking water in Europe. The predicted environmental concentrations (PECs) of spiroxamine and its major metabolites in surface water and groundwater have been estimated and were found to be present at very low levels. In addition, the concentrations of spiroxamine and its metabolites in surface water are estimated for small edge of field water bodies. Drinking water is abstracted from much larger waterbodies so a dilution factor for typical large waterbodies has been estimated and drinking water concentrations calculated.

Based on these concentrations and the various steps in the drinking water treatment process, an assessment has been made on the likelihood of water treatment by-products of spiroxamine or its metabolites being present in drinking water.

It is very likely that during the drinking water treatment processes prior to disinfection (sand filtration, coagulation/sedimentation/filtration and carbon filtration), spiroxamine and its metabolites will be removed due to their very high propensity to adsorb to organic material.

Since levels of spiroxamine and its metabolites will be negligible in drinking water prior to disinfection processes, it is very unlikely that disinfection by-products of spiroxamine and its metabolites will be present in drinking water.

Predicted environmental concentrations in drinking water (PEC_{DW}) and its sources

The main sources of drinking water in Europe are groundwater and surface water, with surface water combined with artificial recharge and river bank filtration only accounting for a very minor contribution. This paper has therefore focussed on groundwater and surface water as sources of drinking water.

Groundwater (PEC_{GW})

The leaching behaviour of spiroxamine and its metabolites, was examined in accordance with the FOCUS groundwater scenarios workshop guidelines (FOCUS, 2000 and 2014).

Simulations of spiroxamine and its metabolites, M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) following application to field crops were conducted with the FOCUS groundwater scenarios in FOCUS PEARL (version 4.4.4), FOCUS PELMO (version 5.5.3) and FOCUS MACRO (version 5.5.4) in accordance with the FOCUS groundwater scenarios workshop guidelines (FOCUS, 2000 and 2014).

The following uses were simulated in accordance with the supported uses of the spiroxamine, see Table 9.4-1:

Table 9.4-1: Modelled uses for Spiroxamine

Crop	FOCUS Scenario	BBCH range	Application rate per application (g a.s./ha)	Crop inter-ception (%)	Soil loading per applica-tion (g a.s./ha)
Grape vines	Vines, early	BBCH 13 on-wards	300	50	150
	Vines, late	BBCH 71 on-wards	300	75	75

The predicted 80th percentile average annual concentrations in groundwater at 1 m depth for spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl) and M03 (spiroxamine-N-oxide) were <0.001 µg/L for all uses and all scenarios; therefore, are all significantly below the 0.1 µg/L regulatory threshold. In studies investigating the route of degradation of the active substance spiroxamine in soil (presented under CA 7.1.1.1), the metabolite M06 is only observed >5% AR in one out of ten soils and only at the very last sampling point (in all other soils and all other sampling points the observed level of metabolite M06 was <5%). Due to the low levels of M06 observed, it was difficult to obtain reliable degradation rate constants from the parent applied studies. Consequently, estimated PEC_{GW} from conservative input parameters were found to be provide unreasonable estimates of leaching when compared to the outcome of the soil column studies (see KCA 7.1.4.1) where only 0.2% of AR were observed in leachate. Potential inputs via groundwater for metabolite M06 (spiroxamine-acid) are currently being defined as the studies required to define the modelling input parameters are underway and modelling using conservative assumptions result in unrealistic estimates of PEC_{GW}. It should be noted that exposure of spiroxamine and its metabolite via groundwater are not expected and that exposure of the WTP with residues would be predominantly via surface water.

Surface water (PEC_{SW})

The potential for spiroxamine and its metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide) and M06 (spiroxamine-acid) to reach surface water, was examined in accordance with FOCUS guidance for surface water modelling (FOCUS (2001 and 2015)).

Applications made to vines were simulated using Steps 1-2 in FOCUS in accordance with FOCUS guidance for surface water modelling (FOCUS (2001 and 2015)). A refinement of the values generated at Steps 1-2 to more realistic concentrations were calculated for spiroxamine only using FOCUS Step 3. FOCUS Step 4 was used to apply mitigation measures.

The maximum PEC_{SW} values for spiroxamine at FOCUS Step 4 are presented in CP 9.2.5/03 but represented in Table 9.4-2.

Table 9.4-2: Maximum PEC_{SW} values for spiroxamine – FOCUS Step 4

Use	Mitigation	Maximum PEC_{SW} (µg/L)
Grape vines, early 2 x 300 g a.s./ha	20 m VFS + 20 m NSBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m NSBZ + 0% SDRT	0.399
Grape vines, late 2 x 300 g a.s./ha	20 m VFS + 20 m NSBZ + 0% SDRT	0.496[a)]
	20 m VFS + 25 m NSBZ + 0% SDRT	0.376
Grape vines, early 2 x 200 g a.s./ha	20 m VFS + 20 m NSBZ + 0% SDRT	0.330[a)]
	20 m VFS + 25 m NSBZ + 0% SDRT	0.255
Grape vines, late 2 x 200 g a.s./ha	20 m VFS + 20 m NSBZ + 0% SDRT	0.331[a)]
	20 m VFS + 25 m NSBZ + 0% SDRT	0.250

a) Maximum value resulted from single application
VFS = vegetated filter strip, SDBZ = spray drift buffer zone, SDRT = spray drift reduction technology

The overall maximum PEC_{SW} values for the metabolites at Step 2 for the field uses are presented in CP 9.2.5/02 but re-presented in Table 9.4-3:

Table 9.4- 3: Overall maximum PECSW values for the metabolites of spiroxamine for field uses – FOCUS Step 2

Compound	Overall maximum PEC_{SW} (µg/L)
M01 (spiroxamine-desethyl)	1.084
M02 (spiroxamine-despropyl)	0.917
M03 (spiroxamine-N-oxide)	2.420
M06 (spiroxamine-acid)	21.656

Please note that assumptions at Step 2 are extremely conservative and that further reductions in PEC_{SW} would be expected at Step 3 and 4 (not presented).

Drinking water abstracted from surface water

PEC_{SW} values have been assessed with the standard FOCUS scenarios. These calculations are performed with receiving water bodies, such as ditches, ponds and streams (Table 9.4-4), however, these types of water body are generally not used as a source of drinking water in Europe. Therefore, a dilution will take place, before the substance of interest reaches major rivers or lakes serving as drinking water supplies. Characteristics of some typical European rivers and lakes are shown in Table 9.4-5.

Table 9.4-4: Water volume of small water bodies in model scenarios

Scenario	Dimensions	Volume
Ditch	Length: 100 m Depth: 0.3 m Width: 1 m	30000 L (30 m3)
Pond	Depth: 1 m Diameter: 30 m	706858 L (707 m3)
Stream	Length: 100 m Depth: 0.3 m Width: 1 m	30000 L (30 m3)

Table 9.4-5: Characteristics of European rivers and lakes

Name of waterbody	Outflow (m3/s)	Volume
Danube	6700	-
Rhine	2300	-
Elbe	870	-
Loire	930	-
Average river outflow	2700	-
Lake Constance	-	4.8 x 1010 m3

Dilution factors of 10^7 and 10^9 can be applied to PEC_{SW} for the pond scenarios and the ditch or stream scenarios, respectively if a major lake (e.g. Lake Constance) is used as a drinking water supply, as follows:

Pond scenarios dilution factor = 4.8×10^{10} m^3 / 707 m^3 = 6.8×10^7

Ditch/stream dilution factor = 4.8×10^{10} m^3 / 30 m^3 = 1.6×10^9

A dilution factor of 10^5 and 10^6 can be applied to PEC_{SW} for the pond scenarios and the ditch or stream scenarios, respectively if a river with an average outflow is used as a drinking water supply. These dilution factors are calculated as follows:

Total outflow over 7 hours = 2700 m^3/s x 7 hours x 3600 s = 6.8×10^7 m^3

Pond scenarios dilution factor = 6.8×10^7 m^3 / 707 m^3 = 9.6×10^5

Ditch/stream scenarios dilution factor = 6.8×10^7 m^3 / 30 m^3 = 2.3×10^6

Thus a dilution factor of 10^5 can be applied as a worst case assumption. However, considering the original estimated concentrations of spiroxamine or its metabolites in surface water, any consideration of dilution demonstrates an extremely low risk that transformation products of spiroxamine could cause adverse effects as they are considerably below the maximum drinking water limit of 0.1 µg/L.

Drinking water treatment processes

In Europe, groundwater generally undergoes the following treatment prior to use as drinking water:

No treatment or treatment without disinfection (*ca* 10 % all drinking water)

Treatment with disinfection (*ca* 40 % all drinking water)

When groundwater is disinfected, the most common treatment methods before disinfection are aeration with rapid sand filtration or carbon filtration.

Only 40% of drinking water from disinfected groundwater (*ca* 16% of all drinking water) is chlorine disinfected.

Almost all surface water (*ca* 45% all drinking water) is disinfected prior to use as drinking water. Surface water is most likely to undergo coagulation/sedimentation/filtration or carbon filtration prior to disinfection.

A total of 62% of drinking water from disinfected surface water (*ca* 28% of all drinking water) is chlorine disinfected

Disinfection is most commonly performed with chlorine and hypochlorite with chlorine dioxide and chloramine each accounting for less than 5% of disinfection methods.

UV treatment accounts for ca 10% of disinfection methods and only 2% of disinfection methods use ozone.

Removal of spiroxamine and its metabolites before disinfection

The K_{FOC} values for spiroxamine and its metabolites (please see CP 9.1.2) are as follows:

Table 9.4-6: K_{FOC} values for spiroxamine and its metabolites

Compound	K_{FOC} (mL/g)
Spiroxamine	4111
M01 (spiroxamine-desethyl)	3271
M02 (spiroxamine-despropyl)	2695
M03 (spiroxamine-N-oxide)	1677
M06 (spiroxamine-acid)	Study ongoing

Based on these K_{FOC} values it can be seen that all of these compounds are slightly mobile or immobile from the McCall classification. It is therefore very likely that spiroxamine and its metabolites will be removed from drinking water through the sand filtration, coagulation/sedimentation/filtration or carbon filtration process. Studies on the sorption behaviour of M06 (spiroxamine-acid) are ongoing, however, this affinity is also expected to hold true for this compound. Nevertheless, even if the experimentally derived K_{FOC} value is low, dilution and degradation will occur as discussed previously, yielding concentrations so low that any transformation products from disinfection will not pose a risk to human health.

The overall predicted concentration of spiroxamine and its metabolites in ground water and surface water indicate an overall very low risk to human health irrespective of what reaction processes occur during water treatment.

Conclusions

An assessment has been made on the likelihood of water treatment by-products of spiroxamine or its metabolites being present in drinking water. The most common sources of drinking water in Europe are groundwater and surface water.

Spiroxamine degrades to major metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide), M06 (spiroxamine-acid), minor metabolites, bound residues and carbon dioxide in soil, either via microbial or photolytic processes. In pelagic and water/sediment systems spiroxamine degrades to major metabolites M01 (spiroxamine-desethyl), M02 (spiroxamine-despropyl), M03 (spiroxamine-N-oxide), M06 (spiroxamine-acid), minor metabolites, bound residues and carbon dioxide, either via microbial or photolytic processes.

The PECs of spiroxamine and its major metabolites in surface water and groundwater have been estimated and were found to be present at very low levels. It is also very likely that during the drinking water treatment processes prior to disinfection (sand filtration, coagulation/sedimentation/filtration or carbon filtration), spiroxamine and its metabolites will be removed due to their relatively high propensity to adsorb to organic material. For those metabolites which have a low K_{FOC}, dilution and degradation will occur to levels so low that any transformation products from disinfection will not pose a risk to human health.

Since levels of spiroxamine and its metabolites will be negligible in drinking water prior to disinfection processes, it is very unlikely that disinfection by-products of spiroxamine and its metabolites will be present in drinking water.

Assessment and conclusion by applicant:
The study is considered valid for use in the risk assessment.