Document Title

Summary of the residues in or on treated products, food and feed for fluopicolide

Data Requirement(s)

Regulation (EC) No 1107/2009 & Regulation (EU) No 283/2013

Document MCA

Section 6: Residues in or on treated products, food and feed

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

Date

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On behalf of

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Crop Science Division

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Version history

Date [yyyy-mm-dd]	Data points containing amendments or additions[1] and brief description	Document identifier and version number

[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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CA 6 RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED

Fluopicolide (AE C638206) was included in Annex I to Council Directive 91/414/EEC in 2010 (Commission Directive 2010/15/EU, Entry into Force on June 1, 2010). The expiration of approval of fluopicolide is May 31, 2023 (Commission Implementing Regulation (EU) 2017/1527). The Supplementary Dossier contains only data which were not submitted at the time of the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC and which were therefore not evaluated during the first EU review. All data which were already submitted by Bayer AG (former Bayer CropScience) for the Annex I inclusion under Council Directive 91/414/EEC are contained in the Draft Assessment Report (DAR) and its Addenda, and are included in the Baseline Dossier provided by Bayer AG.

Fluopicolide is a fungicidal active substance developed by Bayer. It is the only active substance in Europe representing a class of chemistry (pyridinylmethyl-benzamides) with a unique mode of action via delocalization of a spectrin-like protein in the Oomycetes fungi.

Fluopicolide has a long track record of safe use in a large number of targeted crops within horticulture, e.g. cucumbers, lettuce and on arable crops (e.g. potato).

Fluopicolide is active against a wide range of Oomycete fungi, the causal agents of devastating plant diseases of economic importance in EU-27 such as potato late blight (*Phytophthora infestans*) or downy mildew diseases in a broad range of crops.

It provides effective, long lasting protection at low application rates against Oomycetes diseases at different stage of development of the fungi, giving flexibility of use to the farmer.

Fluopicolide can be formulated with other active ingredients in different types of formulations to optimise and complete its activity.

The development of resistances of Oomycetes against existing, well-established fungicide groups represent a threat for European farmers by increasing the complexity of their plant protection programs leading to severe economic impacts. With Fluopicolide, farmers in EU-27 have access to a modern tool for their integrated crop protection programs, contributing to effective and sustainable management of resistance development and preserving high level of protection against Oomycete diseases.

By reducing the Oomycete damages, applications of Fluopicolide on target crops contribute to the achievement of optimum yield and quality, thus securing sufficient supply of high-quality potatoes and horticultural produces for European consumer destinations and markets abroad, being it fresh or for the processing industry.

CA 6.1 Storage stability of residues

Risk assessment residue definition (EFSA Journal 2019;17(7):5748)

- in food of plant origin: Definition 1: Fluopicolide
  Definition 2: Metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01)
- in food of animal origin: Definition 1: Fluopicolide
  Definition 2: Metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01)

Additional analytical targets in field residues trials (see chapter CA 6.3):

- **Rotational crops:** M-02, M-04, M-05, M-06 and M-09

Storage stability of residues in plants and animal products

Data on the storage stability of fluopicolide in plant matrices was submitted and reviewed for the first inclusion of fluopicolide into Annex I of Council Directive 91/414/EEC. The studies described in the DAR and the addendum to the DAR are still considered adequate to address this endpoint.

New storage stability studies, including all analytical targets, have been conducted in various plant matrices. These studies have been conducted to cover all commodity groups. The available data are summarised within the following table.

Fluopicolide, M-01 and M-02 are stable within high water, high acid, high starch plant matrices for periods of up to 30 months and for periods of up to 25 months in high oil matrices and miscellaneous matrices (green material). Fluopicolide and M-01 were found to be stable for periods of up to 41 months in cereal straw (miscellaneous matrix). Both fluopicolide and M-01 are stable within honey for up to 6 months.

M-04 and M-05 are stable in high water, high acid and high oil plant matrices for up to 18 months, and 25 months for wheat grain and in wheat straw. For wheat green material, M-04 is stable for up to 25 months, while M-05 the stability was only demonstrated for 3 months.

M-06 is stable for up to 18 months in barley grain (a high starch commodity).

M-09 is stable within high oil, high protein, high acid, high water and high starch plant matrices for up to 24 months.

The stability of fluopicolide, M-01 and M-02 in livestock products was also considered. These compounds were found to remain stable in bovine matrices for at least 2 months in milk, 4 months in fat and muscle and 9 months in liver and kidney.

Table 6.1- 1: Summary of stability data achieved at ≤-18 ºC (unless stated otherwise) in plant products

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Fluopicolide			
Wheat grain	High starch	30 months	[redacted] 2004; M-237350-01-1
Grapes	High acid	30 months	[redacted] 2004; M-237350-01-1
Potatoes	High starch	30 months	[redacted] 2004; M-237350-01-1
Cabbage	High water	30 months	[redacted] 2004; M-237350-01-1
Wheat grain	High starch	25 months	[redacted] 2007; M-274729-02-1
Wheat green material	High water	25 months	[redacted] 2007; M-274729-02-1
Wheat straw	Miscellaneous	41 months	[redacted] 2007; M-274729-02-1
Sunflower seed	High oil	25 months	[redacted] 2013; M-439984-02-1
Metabolite M-01			
Wheat grain	High starch	30 months	[redacted] 2004; M-237350-01-1
Grapes	High acid	30 months	[redacted] 2004; M-237350-01-1
Potatoes	High starch	30 months	[redacted] 2004; M-237350-01-1
Cabbage	High water	30 months	[redacted] 2004; M-237350-01-1
Wheat grain	High starch	25 months	[redacted] 2007; M-274729-02-1
Wheat green material	High water	25 months	[redacted] 2007; M-274729-02-1
Wheat straw	Miscellaneous	41 months	[redacted] 2007; M-274729-02-1
Sunflower seed	High oil	25 months	[redacted] 2013; M-439984-02-1

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Metabolite M-02			
Wheat grain	High starch	30 months	[redacted] 2004; M-237350-01-1
Grapes	High acid	30 months	[redacted] 2004; M-237350-01-1
Potatoes	High starch	30 months	[redacted] 2004; M-237350-01-1
Cabbage	High water	30 months	[redacted] 2004; M-237350-01-1
Wheat grain	High starch	25 months	[redacted] 2007; M-274729-02-1
Wheat green material	High water	25 months	[redacted] 2007; M-274729-02-1
Wheat straw	Miscellaneous	25 months	[redacted] 2007; M-274729-02-1
Sunflower seed	High oil	25 months	[redacted] 2013; M-439984-02-1
Metabolite M-04			
Wheat grain	High starch	25 months	[redacted]; 2007; M-274729-02-1
Wheat green material	High water	25 months	[redacted] 2007; M-274729-02-1
Wheat straw	Miscellaneous	25 months	[redacted] 2007; M-274729-02-1
Sunflower seed	High oil	18 months	[redacted] 2020; M-685332-01-1
Dry bean seed	High protein	18 months	[redacted] 2020; M-685332-01-1
Cucumber	High water	18 months	[redacted] 2020; M-685332-01-1
Barley grain	High starch	18 months	[redacted] 2020; M-685332-01-1
Strawberries	High acid	18 months	[redacted] 2020; M-685332-01-1

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Metabolite M-05			
Wheat grain	High starch	25 months	[redacted] 2007; M-274729-02-1
Wheat green material	High water	3 months	[redacted] 2007; M-274729-02-1
Wheat straw	Miscellaneous	25 months	[redacted].; 2007; M-274729-02-1
Sunflower seed	High oil	18 months	[redacted] 2020; M-685332-01-1
Dry bean seed	High protein	18 months	[redacted] 2020; M-685332-01-1
Cucumber	High water	18 months	[redacted] 2020; M-685332-01-1
Barley grain	High starch	18 months	[redacted] 2020; M-685332-01-1
Strawberries	High acid	18 months	[redacted] 2020; M-685332-01-1
Metabolite M-06			
Barley grain	High starch content	18 months	[redacted] 2020; M-685332-01-1
Metabolite M-09			
Sunflower seed	High oil content	24 months	[redacted] 2020; M-681941-01-1
Dry bean seed	High protein	24 months	[redacted].; 2020; M-681941-01-1
Grapes	High acid	24 months	[redacted] 2020; M-681941-01-1
Lettuce	High water	24 months	[redacted] 2020; M-681941-01-1
Barley grain	High starch	24 months	[redacted] 2020; M-681941-01-1

Table 6.1- 2: Summary of stability data achieved at ≤-18 °C (unless stated otherwise) in livestock products

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Fluopicolide			
Bovine milk	Animal milk	2 months	[redacted] 2004; M-219457-01-2
Bovine muscle	Animal muscle	4 months	[redacted] 2004; M-219457-01-2
Bovine fat	Animal fat	4 months	[redacted] 2004; M-219457-01-2
Bovine liver	Animal liver	9 months	[redacted] 2004; M-219457-01-2
Bovine kidney	Animal kidney	9 months	[redacted] 2004; M-219457-01-2
Honey	Honey / high sugar	6 months	[redacted] 2020; M-680827-02-1
Metabolite M-01			
Bovine milk	Animal milk	2 months	[redacted] 2004; M-219457-01-2
Bovine muscle	Animal muscle	4 months	[redacted] 2004; M-219457-01-2
Bovine fat	Animal fat	4 months	[redacted] 2004; M-219457-01-2
Bovine liver	Animal liver	9 months	[redacted] 2004; M-219457-01-2
Bovine kidney	Animal kidney	9 months	[redacted] 2004; M-219457-01-2
Honey	Honey / high sugar	6 months	[redacted] 2020; M-680827-02-1
Metabolite M-02			
Bovine milk	Animal milk	2 months	[redacted] 2004; M-219457-01-2
Bovine muscle	Animal muscle	4 months	[redacted] 2004; M-219457-01-2
Bovine fat	Animal fat	4 months	[redacted] 2004; M-219457-01-2
Bovine liver	Animal liver	9 months	[redacted].; 2004; M-219457-01-2
Bovine kidney	Animal kidney	9 months	[redacted].; 2004; M-219457-01-2

The stability periods of fluopicolide and metabolites M-01, M-02, M-04, M-05 and M-06 in various matrices, when stored deep-frozen at ≤ -18 °C, are summarized in the following table.

Table 6.1- 3: Summary of the deep-frozen storage stability periods for each commodity type, for each analytical target

Analytes	Commodity Categories	Acceptable Maximum Storage duration
Fluopicolide	Plant - high water content	30 months
	Plant - high oil content	25 months
	Plant - high protein content	-
	Plant - high starch content	30 months
	Plant -high acid content	30 months
	High sugar content	6 months
	Livestock milk	2 months
	Livestock muscle	4 months
	Livestock fat	4 months
	Livestock liver	9 months
	Livestock kidney	9 months
M-01	Plant - high water content	30 months
	Plant - high oil content	25 months
	Plant - high protein content	-
	Plant - high starch content	30 months
	Plant -high acid content	30 months
	High sugar content	6 months
	Livestock milk	2 months
	Livestock muscle	4 months
	Livestock fat	4 months
	Livestock liver	9 months
	Livestock kidney	9 months
M-02	Plant - high water content	30 months
	Plant - high oil content	25 months
	Plant - high protein content	-
	Plant - high starch content	30 months
	Plant -high acid content	30 months
	Livestock milk	2 months
	Livestock muscle	4 months
	Livestock fat	4 months
	Livestock liver	9 months
	Livestock kidney	9 months
M-04	Plant - high water content	25 months
	Plant - high oil content	18 months
	Plant - high protein content	18 months

Analytes	Commodity Categories	Acceptable Maximum Storage duration
	Plant - high starch content	25 months
	Plant -high acid content	18 months
M-05	Plant - high water content	18 months
	Plant - high oil content	18 months
	Plant - high protein content	18 months
	Plant - high starch content	25 months
	Plant -high acid content	18 months
M-06	Plant - high starch content	18 months
M-09	Plant - high oil content	24 months
	Plant - high protein content	24 months
	Plant - high acid content	24 months
	Plant - high water content	24 months
	Plant - high starch content	24 months

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.1/02
Report Author:	[redacted]
Report Year:	2004
Report Title:	Final report - Determination of the storage stability of AE C638206 and the metabolites AE C653711 (BAM) and AE C657188 (PCA) in grape, potato, cabbage, and wheat grain
Report No:	C045739
Document No:	M-237350-01-1
Guideline(s) followed in study:	OPPTS 860.1380
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Document M-237350-01-1 supersedes document M-229687-01-1 (which is an interim report for the storage stability study, which was evaluated previously within the DAR).

Executive summary

The study investigated the stability of fluopicolide (AE C638206) and its metabolites, M-01 (AEC653711) and M-02 (AEC657188) in grapes, potatoes, cabbage, and wheat grain under storage conditions at < -18 °C for a period of 30 months and residues were considered to be sufficiently stable over this period.

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for the fluopicolide, M-01 and M-02. The substrates were wheat grain, grapes, potato tubers and cabbage leaves (head).

The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg. The fortified specimens were stored in a freezer at < -18 °C.

Fluopicolide and its metabolites were analysed according to the method IF-101/05424-00. The limit of quantification was 0.01 mg/kg for each analyte. The validity of the method was verified by analysing freshly fortified specimens concurrently with each set of stored specimens – these procedural recoveries were considered to be acceptably to support the results obtained from the stored samples.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	• Fluopicolide (FLC) • Metabolite M-01 • Metabolite M-02
	Batch no.:	• R001737 (FLC), MOY4627 (FLC) • R001724 (M-01), 8808018 (M-01), 08018ET (M-01) • RAW244055/1 (M-02)
	Active Ingredient / Purity:	• R001737 (99.6%), MOY4627 (98.9%) • R001724 (97.0%), 8808018 (97.0%), 08018ET (96.2%) • RAW244055/1 (97.2%)
	Storage:	• Fluopicolide: + 5 ±5 °C • Metabolite M-01: - 20 ±5 °C • Metabolite M-02: - 20 ±5 °C
	Expiry date:	• R001737 (Feb 2005), MOY4627 (Sep 2005) • R001724 (Aug 2003), 8808018 (May 2004), 08018ET (Sep 2007) • RAW244055/1 (Apr 2006)
2.	**Test commodity:**	Wheat, grapes, potatoes, and cabbages
	Crop part:	Wheat grain, grapes (berries), potato tubers and cabbage leaves

B. STUDY DESIGN AND METHODS

Study design:

A storage stability study was conducted to investigate the stability of fluopicolide (AE C638206) and its metabolites M-01 (AEC653711) and M-02 (AEC657188) in grapes, potatoes, cabbage, and wheat grain under storage conditions at < - 18 °C for a period of 30 months.

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for the parent fluopicolide and the metabolites M-01 and M-02. The substrates were wheat grain, grapes, potato tubers and cabbage leaves (head).

The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg. The fortified specimens were stored in a freezer at < - 18 °C.

Analytical Part:

At each storage interval, fluopicolide and its metabolites, M-01 and M-02 were determined in the stored control samples and in the stored spiked samples according to the following method:

Method	IF-101/05424-00
Extraction	Extracted with acidified water and acetone – solution was separated from the solid material by centrifugation.
Detection	LC/MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: grapes, potato tubers, cabbage heads / leaves and wheat grain).

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Freshly fortified specimens with a nominal concentration of 0.1 mg/kg were analysed concurrently with each set of stored specimens. The results of these procedural recoveries are presented in the following tables for each of the tested matrices. The procedural recoveries meet the acceptability criteria: the mean recoveries are within the range 70 - 110% for each analyte / matrix combination and the %RSD values are <20% (where applicable). These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples.

Table 6.1- 4 Procedural recoveries for Fluopicolide in wheat grain

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Wheat Grain	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.096	92	96.2	6.1
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.099	96		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.093	89		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.105	101		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.107	103		
	3.2 [b]	Control	30-Jul-02	06-Aug-02	<0.01	-	-	-
	3.2 [b]	0.101	30-Jul-02	06-Aug-02	0.083	82	82	-
	3.2 [b]	0.101	30-Jul-02	06-Aug-02	0.083	82		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.075	75	76	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.077	77		
	12.1 [b]	Control	25-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.101	25-Apr-03	30-Apr-03	0.077	76	78.5	-
	12.1 [b]	0.102	25-Apr-03	30-Apr-03	0.082	81		
	18.3 [b]	Control	27-Oct-03	18-Nov-03	<0.01	-	-	-
	18.3 [b]	0.107	27-Oct-03	18-Nov-03	0.086	81	83.5	-
	18.3 [b]	0.107	27-Oct-03	18-Nov-03	0.091	86		
	24.4 [c]	Control	26-Apr-04	30-Apr-04	<0.01	-	-	-
	24.4 [c]	0.100	26-Apr-04	30-Apr-04	0.097	97	98.5	-
	24.4 [c]	0.099	26-Apr-04	30-Apr-04	0.100	100		
	30.4 [c]	Control	25-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.099	25-Oct-04	29-Oct-04	0.084	85	86	-
	30.4 [c]	0.099	25-Oct-04	29-Oct-04	0.087	87		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 5 Procedural recoveries for Metabolite M-01 (AE C653711, BAM) in wheat grain

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Wheat Grain	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.088	86	90.6	3.9
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.092	90		
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.095	93		
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.091	89		
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.096	95		
	3.2 [b]	Control	30-Jul-02	06-Aug-02	0.01	-	-	-
	3.2 [b]	0.100	30-Jul-02	06-Aug-02	0.093	92	91	-
	3.2 [b]	0.100	30-Jul-02	06-Aug-02	0.090	90		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.100	100	100.5	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.102	101		
	12.1 [b]	Control	25-Apr-03	06-May-03	<0.01	-	-	-
	12.1 [b]	0.098	25-Apr-03	06-May-03	0.093	95	97.5	-
	12.1 [b]	0.099	25-Apr-03	06-May-03	0.099	100		
	18.3 [b]	Control	27-Oct-03	17-Nov-03	<0.01	-	-	-
	18.3 [b]	0.100	27-Oct-03	17-Nov-03	0.100	100	100.5	-
	18.3 [b]	0.100	27-Oct-03	17-Nov-03	0.101	101		
	24.4 [c]	Control	26-Apr-04	30-Apr-04	<0.01	-	-	-
	24.4 [c]	0.094	26-Apr-04	30-Apr-04	0.097	104	103	-
	24.4 [c]	0.094	26-Apr-04	30-Apr-04	0.095	102		
	30.4 [c]	Control	25-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.096	96	105	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.114	114		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 6 Procedural recoveries for Metabolite M-02 (AE C657188, PCA) in wheat grain

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Wheat Grain	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.093	89	90	4.0
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.098	94		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.097	93		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.088	85		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.093	89		
	3.2 [b]	Control	30-Jul-02	06-Aug-02	0.01	-	-	-
	3.2 [b]	0.105	30-Jul-02	06-Aug-02	0.085	81	79.5	-
	3.2 [b]	0.104	30-Jul-02	06-Aug-02	0.081	78		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.099	28-Oct-02	01-Nov-02	0.072	73	76.5	-
	6.2 [b]	0.099	28-Oct-02	01-Nov-02	0.079	80		
	12.1 [b]	Control	25-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.097	25-Apr-03	30-Apr-03	0.083	86	84.5	-
	12.1 [b]	0.098	25-Apr-03	30-Apr-03	0.081	83		
	18.3 [b]	Control	27-Oct-03	18-Nov-03	<0.01	-	-	-
	18.3 [b]	0.103	27-Oct-03	18-Nov-03	0.077	75	76	-
	18.3 [b]	0.105	27-Oct-03	18-Nov-03	0.080	77		
	24.4 [c]	Control	26-Apr-04	30-Apr-04	<0.01	-	-	-
	24.4 [c]	0.093	26-Apr-04	30-Apr-04	0.071	76	75	-
	24.4 [c]	0.093	26-Apr-04	30-Apr-04	0.069	74		
	30.4 [c]	Control	25-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.098	25-Oct-04	29-Oct-04	0.076	78	76.5	-
	30.4 [c]	0.098	25-Oct-04	29-Oct-04	0.073	75		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 7 Procedural recoveries for Fluopicolide in red grapes

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Red Grape	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.103	29-Apr-02	30-Apr-02	0.091	89	89.2	14.7
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.085	82		
	0 [b]	0.103	29-Apr-02	30-Apr-02	0.094	91		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.096	92		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.095	92		
	3.2 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.2 [b]	0.101	31-Jul-02	07-Aug-02	0.085	84	84.5	-
	3.2 [b]	0.101	31-Jul-02	07-Aug-02	0.086	85		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.078	78	84.5	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.091	91		
	12.1 [b]	Control	25-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.102	25-Apr-03	30-Apr-03	0.082	81	85	-
	12.1 [b]	0.101	25-Apr-03	30-Apr-03	0.090	89		
	18.3 [b]	Control	27-Oct-03	18-Nov-03	<0.01	-	-	-
	18.3 [b]	0.107	27-Oct-03	18-Nov-03	0.083	77	78	-
	18.3 [b]	0.106	27-Oct-03	18-Nov-03	0.084	79		
	24.4 [c]	Control	26-Apr-04	30-Apr-04	<0.01	-	-	-
	24.4 [c]	0.100	26-Apr-04	30-Apr-04	0.081	82	81.5	-
	24.4 [c]	0.099	26-Apr-04	30-Apr-04	0.081	81		
	30.4 [c]	Control	25-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.081	82	103	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.124	124		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 8 Procedural recoveries for Metabolite M-01 (AE C653711, BAM) in red grapes

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Red Grape	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.101	29-Apr-02	30-Apr-02	0.090	88	84.2	8.4
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.073	72		
	0 [b]	0.101	29-Apr-02	30-Apr-02	0.086	85		
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.092	90		
	0 [b]	0.102	29-Apr-02	30-Apr-02	0.087	86		
	3.2 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.2 [b]	0.100	31-Jul-02	07-Aug-02	0.091	91	90.5	-
	3.2 [b]	0.100	31-Jul-02	07-Aug-02	0.090	90		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.099	98	108.5	-
	6.2 [b]	0.100	28-Oct-02	01-Nov-02	0.119	119		
	12.1 [b]	Control	25-Apr-03	06-May-03	<0.01	-	-	-
	12.1 [b]	0.099	25-Apr-03	06-May-03	0.094	95	96	-
	12.1 [b]	0.098	25-Apr-03	06-May-03	0.095	97		
	18.3 [b]	Control	27-Oct-03	17-Nov-03	<0.01	-	-	-
	18.3 [b]	0.100	27-Oct-03	17-Nov-03	0.099	99	99	-
	18.3 [b]	0.099	27-Oct-03	17-Nov-03	0.099	99		
	24.4 [c]	Control	26-Apr-04	30-Apr-04	<0.01	-	-	-
	24.4 [c]	0.094	26-Apr-04	30-Apr-04	0.082	87	86	-
	24.4 [c]	0.094	26-Apr-04	30-Apr-04	0.079	85		
	30.4 [c]	Control	25-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.095	94	99	-
	30.4 [c]	0.100	25-Oct-04	29-Oct-04	0.104	104		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 9 Procedural recoveries for Metabolite M-02 (AE C657188, PCA) in red grapes

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Red Grape	0 [b]	Control	29-Apr-02	30-Apr-02	<0.01	-	-	-
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.094	90	90.4	5.8
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.085	82		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.097	93		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.100	96		
	0 [b]	0.104	29-Apr-02	30-Apr-02	0.095	91		
	3.2 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.2 [b]	0.105	31-Jul-02	07-Aug-02	0.083	78	79	-
	3.2 [b]	0.104	31-Jul-02	07-Aug-02	0.083	80		
	6.2 [b]	Control	28-Oct-02	01-Nov-02	<0.01	-	-	-
	6.2 [b]	0.099	28-Oct-02	01-Nov-02	0.067	68	72.5	-
	6.2 [b]	0.099	28-Oct-02	01-Nov-02	0.076	77		
	12.1 [b]	Control	25-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.098	25-Apr-03	30-Apr-03	0.085	87	88	-
	12.1 [b]	0.097	25-Apr-03	30-Apr-03	0.086	89		
	18.3 [b]	Control	27-Oct-03	18-Nov-03	<0.01	-	-	-
	18.3 [b]	0.103	27-Oct-03	18-Nov-03	0.077	75	75.5	-
	18.3 [b]	0.105	27-Oct-03	18-Nov-03	0.078	76		
	24.4 [c]	Control	26-Apr-04	04-May-04	<0.01	-	-	-
	24.4 [c]	0.094	26-Apr-04	04-May-04	0.070	75	75	-
	24.4 [c]	0.093	26-Apr-04	04-May-04	0.070	75		
	30.4 [c]	Control	25-Oct-04	08-Nov-04	<0.01	-	-	-
	30.4 [c]	0.098	25-Oct-04	08-Nov-04	0.091	92	88	-
	30.4 [c]	0.098	25-Oct-04	08-Nov-04	0.082	84		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 10 Procedural recoveries for Fluopicolide in potato tubers

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Potato Tubers	0 [b]	Control	06-May-02	10-May-02	<0.01	-	-	-
	0 [b]	0.104	06-May-02	10-May-02	0.110	106	106.6	11.4
	0 [b]	0.103	06-May-02	10-May-02	0.130	126		
	0 [b]	0.103	06-May-02	10-May-02	0.098	95		
	0 [b]	0.103	06-May-02	10-May-02	0.101	98		
	0 [b]	0.103	06-May-02	10-May-02	0.111	108		
	3.1 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.1 [b]	0.101	31-Jul-02	07-Aug-02	0.094	93	92.5	-
	3.1 [b]	0.101	31-Jul-02	07-Aug-02	0.093	92		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.091	91	91.5	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.092	92		
	12.1 [b]	Control	28-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.102	28-Apr-03	30-Apr-03	0.087	86	85	-
	12.1 [b]	0.102	28-Apr-03	30-Apr-03	0.086	84		
	18.2 [b]	Control	28-Oct-03	18-Nov-03	<0.01	-	-	-
	18.2 [b]	0.107	28-Oct-03	18-Nov-03	0.091	85	87.5	-
	18.2 [b]	0.107	28-Oct-03	18-Nov-03	0.096	90		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.100	27-Apr-04	30-Apr-04	0.101	101	99	-
	24.3 [c]	0.099	27-Apr-04	30-Apr-04	0.096	97		
	30.3 [c]	Control	26-Oct-04	29-Oct-04	<0.01	-	-	-
	30.3 [c]	0.099	26-Oct-04	29-Oct-04	0.097	97	100	-
	30.3 [c]	0.099	26-Oct-04	29-Oct-04	0.103	103		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 11 Procedural recoveries for Metabolite M-01 (AE C653711, BAM) in potato tubers

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Potato Tubers	0 [b]	Control	06-May-02	21-Sep-02	<0.01	-	-	-
	0 [b]	0.102	06-May-02	21-Sep-02	0.083	82	84	2.8
	0 [b]	0.102	06-May-02	21-Sep-02	0.084	83		
	0 [b]	0.102	06-May-02	21-Sep-02	0.088	86		
	0 [b]	0.102	06-May-02	21-Sep-02	0.089	87		
	0 [b]	0.102	06-May-02	21-Sep-02	0.083	82		
	3.1 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.1 [b]	0.100	31-Jul-02	07-Aug-02	0.086	86	86	-
	3.1 [b]	0.100	31-Jul-02	07-Aug-02	0.086	86		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.109	109	104	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.099	99		
	12.1 [b]	Control	28-Apr-03	06-May-03	<0.01	-	-	-
	12.1 [b]	0.099	28-Apr-03	06-May-03	0.096	97	95	-
	12.1 [b]	0.099	28-Apr-03	06-May-03	0.092	93		
	18.2 [b]	Control	28-Oct-03	17-Nov-03	<0.01	-	-	-
	18.2 [b]	0.100	28-Oct-03	17-Nov-03	0.091	91	94	-
	18.2 [b]	0.100	28-Oct-03	17-Nov-03	0.097	97		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.094	27-Apr-04	30-Apr-04	0.097	103	103.5	-
	24.3 [c]	0.094	27-Apr-04	30-Apr-04	0.097	104		
	30.3 [c]	Control	26-Oct-04	29-Oct-04	<0.01	-	-	-
	30.3 [c]	0.100	26-Oct-04	29-Oct-04	0.099	99	97	-
	30.3 [c]	0.100	26-Oct-04	29-Oct-04	0.095	95		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 12 Procedural recoveries for Metabolite M-02 (AE C657188, PCA) in potato tubers

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Potato Tubers	0 [b]	Control	06-May-02	10-May-02	<0.01	-	-	-
	0 [b]	0.104	06-May-02	10-May-02	0.074	71	82.5	8.8
	0 [b]	0.104	06-May-02	10-May-02	0.086	83		
	0 [b]	0.104	06-May-02	10-May-02	0.090	87		
	0 [b]	0.104	06-May-02	10-May-02	0.094	90		
	0 [b]	0.104	06-May-02	10-May-02	0.084	81		
	3.1 [b]	Control	31-Jul-02	07-Aug-02	0.01	-	-	-
	3.1 [b]	0.104	31-Jul-02	07-Aug-02	0.075	72	72	-
	3.1 [b]	0.104	31-Jul-02	07-Aug-02	0.075	72		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.099	29-Oct-02	01-Nov-02	0.078	79	83	-
	6.1 [b]	0.099	29-Oct-02	01-Nov-02	0.086	87		
	12.1 [b]	Control	28-Apr-03	13-May-03	<0.01	-	-	-
	12.1 [b]	0.098	28-Apr-03	13-May-03	0.094	96	89.5	-
	12.1 [b]	0.098	28-Apr-03	13-May-03	0.081	83		
	18.2 [b]	Control	28-Oct-03	18-Nov-03	<0.01	-	-	-
	18.2 [b]	0.103	28-Oct-03	18-Nov-03	0.073	71	76	-
	18.2 [b]	0.103	28-Oct-03	18-Nov-03	0.083	81		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.093	27-Apr-04	30-Apr-04	0.068	73	70.5	-
	24.3 [c]	0.093	27-Apr-04	30-Apr-04	0.064	68		
	30.3 [c]	Control	26-Oct-04	08-Nov-04	<0.01	-	-	-
	30.3 [c]	0.098	26-Oct-04	08-Nov-04	0.085	86	87.5	-
	30.3 [c]	0.098	26-Oct-04	08-Nov-04	0.087	89		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 13 Procedural recoveries for Fluopicolide in cabbage leaves (head)

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Cabbage Leaves (Head)	0 [b]	Control	06-May-02	10-May-02	<0.01	-	-	-
	0 [b]	0.104	06-May-02	10-May-02	0.101	98	92.6	6.4
	0 [b]	0.103	06-May-02	10-May-02	0.099	96		
	0 [b]	0.103	06-May-02	10-May-02	0.087	84		
	0 [b]	0.104	06-May-02	10-May-02	0.092	89		
	0 [b]	0.103	06-May-02	10-May-02	0.100	96		
	3.1 [b]	Control	30-Jul-02	06-Aug-02	<0.01	-	-	-
	3.1 [b]	0.101	30-Jul-02	06-Aug-02	0.087	87	87.5	-
	3.1 [b]	0.101	30-Jul-02	06-Aug-02	0.089	88		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.085	84	81.5	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.080	79		
	12.1 [b]	Control	28-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.101	28-Apr-03	30-Apr-03	0.078	77	79.5	-
	12.1 [b]	0.101	28-Apr-03	30-Apr-03	0.083	82		
	18.2 [b]	Control	28-Oct-03	18-Nov-03	<0.01	-	-	-
	18.2 [b]	0.107	28-Oct-03	18-Nov-03	0.089	84	85.5	-
	18.2 [b]	0.101	28-Oct-03	18-Nov-03	0.093	87		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.100	27-Apr-04	30-Apr-04	0.093	93	93	-
	24.3 [c]	0.100	27-Apr-04	30-Apr-04	0.093	93		
	30.4 [c]	Control	26-Oct-04	29-Oct-04	<0.01nd	-	-	-
	30.4 [c]	0.100	26-Oct-04	29-Oct-04	0.096	97	98.5	-
	30.4 [c]	0.099	26-Oct-04	29-Oct-04	0.099	100		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 14 Procedural recoveries for Metabolite M-01 (AE C653711, BAM) in cabbage leaves (head)

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Cabbage Leaves (Head)	0 [b]	Control	06-May-02	21-Sep-02	<0.01	-	-	-
	0 [b]	0.102	06-May-02	21-Sep-02	0.086	85	86.2	3.5
	0 [b]	0.102	06-May-02	21-Sep-02	0.086	85		
	0 [b]	0.102	06-May-02	21-Sep-02	0.092	91		
	0 [b]	0.102	06-May-02	21-Sep-02	0.085	83		
	0 [b]	0.102	06-May-02	21-Sep-02	0.088	87		
	3.1 [b]	Control	30-Jul-02	06-Aug-02	<0.01	-	-	-
	3.1 [b]	0.100	30-Jul-02	06-Aug-02	0.103	104	97.5	-
	3.1 [b]	0.100	30-Jul-02	06-Aug-02	0.091	91		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.100	29-Oct-02	01-Nov-02	0.120	119	102	-
	6.1 [b]	0.101	29-Oct-02	01-Nov-02	0.085	85		
	12.1 [b]	Control	28-Apr-03	06-May-03	<0.01	-	-	-
	12.1 [b]	0.098	28-Apr-03	06-May-03	0.092	93	94	-
	12.1 [b]	0.099	28-Apr-03	06-May-03	0.093	95		
	18.2 [b]	Control	28-Oct-03	17-Nov-03	<0.01	-	-	-
	18.2 [b]	0.100	28-Oct-03	17-Nov-03	0.092	92	93	-
	18.2 [b]	0.100	28-Oct-03	17-Nov-03	0.093	94		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.094	27-Apr-04	30-Apr-04	0.096	103	104.5	-
	24.3 [c]	0.094	27-Apr-04	30-Apr-04	0.099	106		
	30.4 [c]	Control	26-Oct-04	29-Oct-04	<0.01	-	-	-
	30.4 [c]	0.100	26-Oct-04	29-Oct-04	0.098	98	102.5	-
	30.4 [c]	0.100	26-Oct-04	29-Oct-04	0.107	107		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

Table 6.1- 15 Procedural recoveries for Metabolite M-02 (AE C657188, PCA) in cabbage leaves (head)

Sample matrix	Period [a] (Months)	Fortification level (mg/kg)	Date of extraction	Date of analysis	Recovery values (mg/kg)	Recovery values (%)	Mean Recovery (%)	% RSD
Cabbage Leaves (Head)	0 [b]	Control	06-May-02	10-May-02	<0.01	-	-	-
	0 [b]	0.104	06-May-02	10-May-02	0.088	85	90.6	6.6
	0 [b]	0.104	06-May-02	10-May-02	0.087	84		
	0 [b]	0.104	06-May-02	10-May-02	0.096	93		
	0 [b]	0.104	06-May-02	10-May-02	0.102	98		
	0 [b]	0.104	06-May-02	10-May-02	0.097	93		
	3.1 [b]	Control	30-Jul-02	22-Aug-02	<0.01	-	-	-
	3.1 [b]	0.104	30-Jul-02	22-Aug-02	0.077	74	72	-
	3.1 [b]	0.104	30-Jul-02	22-Aug-02	0.073	70		
	6.1 [b]	Control	29-Oct-02	01-Nov-02	<0.01	-	-	-
	6.1 [b]	0.099	29-Oct-02	01-Nov-02	0.074	75	74.5	-
	6.1 [b]	0.099	29-Oct-02	01-Nov-02	0.073	74		
	12.1 [b]	Control	28-Apr-03	30-Apr-03	<0.01	-	-	-
	12.1 [b]	0.097	28-Apr-03	30-Apr-03	0.075	77	75	-
	12.1 [b]	0.098	28-Apr-03	30-Apr-03	0.071	73		
	18.2 [b]	Control	28-Oct-03	18-Nov-03	<0.01	-	-	-
	18.2 [b]	0.103	28-Oct-03	18-Nov-03	0.074	71	72	-
	18.2 [b]	0.103	28-Oct-03	18-Nov-03	0.075	73		
	24.3 [c]	Control	27-Apr-04	30-Apr-04	<0.01	-	-	-
	24.3 [c]	0.093	27-Apr-04	30-Apr-04	0.067	72	74.5	-
	24.3 [c]	0.093	27-Apr-04	30-Apr-04	0.072	77		
	30.4 [c]	Control	26-Oct-04	08-Nov-04	<0.01	-	-	-
	30.4 [c]	0.098	26-Oct-04	08-Nov-04	0.077	78	79.5	-
	30.4 [c]	0.098	26-Oct-04	08-Nov-04	0.079	81		

a) The freshly fortified specimens were analysed concurrently with specimens that were stored for the given period.
b) Results were first reported in [redacted] 2004, Report C040897 (M-229687-01-1)
c) Results were reported in [redacted] 2004, Report C045739 (M-237350-01-1)

II. RESULTS AND DISCUSSION

The following table summarises the amount of fluopicolide, M-01 and M-02 recovered in the stored samples after the various storage intervals, as well as the procedural recoveries from samples freshly fortified at the respective sampling points.

Table 6.1- 16 Residues stability of fluopicolide and its metabolites (M-01 and M-02) in various plant matrices following storage at -18°C

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Fluopicolide				
Grapes	0.103 – 0.104	0	0.085, 0.091, 0.094, 0.095, 0.096 **[Mean = 0.092]**	82, 88, 91, 92, 92 **[Mean = 89]**
Grapes	0.103	3.2	0.081, 0.084 **[Mean = 0.083]**	79, 82 **[Mean = 81]**
Grapes	0.103 – 0.104	6.2	0.085, 0.086 **[Mean = 0.083]**	82, 83 **[Mean = 83]**
Grapes	0.103 – 0.104	12.1	0.085, 0.094 **[Mean = 0.090]**	90, 83 **[Mean = 86]**
Grapes	0.103 – 0.104	18.3	0.079, 0.081 **[Mean = 0.080]**	77, 78 **[Mean = 77]**
Grapes	0.103	24.4	0.078, 0.082 **[Mean = 0.080]**	76, 80 **[Mean = 78]**
Grapes	0.104	30.4	0.085, 0.094 **[Mean = 0.090]**	82, 90 **[Mean = 86]**
Potatoes	0.103 – 0.104	0	0.098, 0.101, 0.11, 0.111, 0.13 **[Mean = 0.110]**	95, 98, 106, 108, 126 **[Mean = 106]**
Potatoes	0.103 – 0.104	3.1	0.091, 0.091 **[Mean = 0.091]**	88. 89 **[Mean = 88]**
Potatoes	0.103 – 0.104	6.1	0.082, 0.092 **[Mean = 0.087]**	80. 89 **[Mean = 84]**
Potatoes	0.103 – 0.104	12.1	0.093, 0.095 **[Mean = 0.094]**	90. 91 **[Mean = 91]**
Potatoes	0.103 – 0.104	18.2	0.082, 0.085 **[Mean = 0.084]**	79. 82 **[Mean = 81]**
Potatoes	0.103	24.3	0.090, 0.094 **[Mean = 0.092]**	87, 91 **[Mean = 89]**
Potatoes	0.104	30.3	0.096, 0.096 **[Mean = 0.096]**	92, 93 **[Mean = 93]**
Cabbage	0.103 – 0.104	0	0.087, 0.092, 0.099, 0.100, 0.101 **[Mean = 0.096]**	84, 89, 96, 96, 98 **[Mean = 92]**
Cabbage	0.103 – 0.104	3.1	0.081, 0.083 **[Mean = 79]**	78, 80 **[Mean = 79]**
Cabbage	0.103	6.1	0.079, 0.081 **[Mean = 0.080]**	76, 78 **[Mean = 77]**

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Cabbage	0.103 – 0.104	12.1	0.082, 0.082 **[Mean = 0.082]**	80, 80 **[Mean = 80]**
Cabbage	0.103	18.2	0.082, 0.082 **[Mean = 0.082]**	79, 79 **[Mean = 79]**
Cabbage	0.103	24.3	0.084, 0.086 **[Mean = 0.085]**	81, 84 **[Mean = 83]**
Cabbage	0.103	30.4	0.084, 0.085 **[Mean = 0.085]**	81, 82 **[Mean = 81]**
Wheat grain	0.104	0	0.093, 0.096, 0.099, 0.105, 0.107 **[Mean = 0.100]**	89, 92, 95, 101, 103 **[Mean = 96]**
Wheat grain	0.103 0.104	3.2	0.086 0.083 **[Mean = 0.085]**	83 81 **[Mean = 82]**
Wheat grain	0.103	6.2	0.072, 0.077 **[Mean = 0.075]**	70, 75 **[Mean = 72]**
Wheat grain	0.104 0.103	12.1	0.087 0.085 **[Mean = 0.086]**	84 83 **[Mean = 84]**
Wheat grain	0.104 0.103	18.3	0.087 0.085 **[Mean = 0.086]**	84 83 **[Mean = 84]**
Wheat grain	0.104	24.4	0.113, 0.100 **[Mean = 0.107]**	109, 97 **[Mean = 103]**
Wheat grain	0.103	30.4	0.091, 0.095 **[Mean = 0.093]**	88, 92 **[Mean = 90]**
Metabolite M-01				
Grapes	0.101 – 0.102	0	0.073, 0.086, 0.087, 0.09, 0.092 **[Mean = 0.086]**	72, 85, 85, 89, 90 **[Mean = 84]**
Grapes	0.102	3.2	0.091, 0.093 **[Mean = 0.092]**	89, 91 **[Mean = 90]**
Grapes	0.101 – 0.102	6.2	0.097, 0.099 **[Mean = 0.098]**	96, 97 **[Mean = 97]**
Grapes	0.101	12.1	0.096, 0.098 **[Mean = 0.097]**	95, 97 **[Mean = 96]**
Grapes	0.101	18.3	0.103, 0.103 **[Mean = 0.103]**	102, 102 **[Mean = 102]**
Grapes	0.102	24.4	0.087, 0.087 **[Mean = 0.087]**	85, 85 **[Mean = 85]**
Grapes	0.101 – 0.102	30.4	0.100, 0.103 **[Mean = 0.102]**	98, 102 **[Mean = 100]**
Potatoes	0.102	0	0.083, 0.083, 0.084, 0.088, 0.089 **[Mean = 0.085]**	82, 82, 83, 86, 87 **[Mean = 84]**

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Potatoes	0.102	3.1	0.089, 0.108 **[Mean = 0.099]**	88, 106 **[Mean = 97]**
Potatoes	0.102	6.1	0.094, 0.095 **[Mean = 0.094]**	93, 94 **[Mean = 93]**
Potatoes	0.102	12.1	0.097, 0.097 **[Mean = 0.097]**	96, 96 **[Mean = 96]**
Potatoes	0.102	18.2	0.092, 0.096 **[Mean = 0.094]**	90, 95 **[Mean = 92]**
Potatoes	0.102	24.3	0.101, 0.106 **[Mean = 0.104]**	99, 104 **[Mean = 102]**
Potatoes	0.101 – 0.102	30.3	0.099, 0.100 **[Mean = 0.100]**	98, 98 **[Mean = 98]**
Cabbage	0.102	0	0.085, 0.086, 0.086, 0.088, 0.092 **[Mean = 0.087]**	83, 85, 85, 87, 91 **[Mean = 86]**
Cabbage	0.102	3.1	0.089, 0.091 **[Mean = 0.090]**	88, 89 **[Mean = 88]**
Cabbage	0.102	6.1	0.096, 0.098 **[Mean = 0.097]**	95, 97 **[Mean = 96]**
Cabbage	0.102	12.1	0.098, 0.098 **[Mean = 0.098]**	96, 97 **[Mean = 97]**
Cabbage	0.101 – 0.102	18.2	0.097, 0.103 **[Mean = 0.100]**	96, 102 **[Mean = 99]**
Cabbage	0.102	24.3	0.098, 0.106 **[Mean = 0.106]**	97, 104 **[Mean = 100]**
Cabbage	0.101 – 0.102	30.4	0.093, 0.100 **[Mean = 0.097]**	92, 99 **[Mean = 95]**
Wheat grain	0.102	0	0.088, 0.091, 0.092, 0.095, 0.096 **[Mean = 0.092]**	86, 89, 90, 93, 94 **[Mean = 91]**
Wheat grain	0.102	3.2	0.092, 0.096 **[Mean = 0.094]**	91, 95 **[Mean = 93]**
Wheat grain	0.102	6.2	0.087, 0.103 **[Mean = 95]**	86, 101 **[Mean = 94]**
Wheat grain	0.102 - 0.101	12.1	0.101, 0.125 **[Mean = 0.113]**	99, 123 **[Mean = 111]**
Wheat grain	0.101 - 0.102	18.3	0.102, 0.105 **[Mean = 104]**	100, 103 **[Mean = 102]**
Wheat grain	0.102	24.4	0.097, 0.099 **[Mean = 0.098]**	95, 97 **[Mean = 96]**
Wheat grain	0.102	30.4	0.097, 0.098 **[Mean = 0.098]**	95, 97 **[Mean = 96]**

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Metabolite M-02				
Grapes	0.104	0	0.085, 0.094, 0.095 0.097, 0.100 **[Mean = 0.094]**	82, 90, 91, 93, 96 **[Mean = 91]**
Grapes	0.104	3.2	0.085, 0.090 **[Mean = 0.088]**	82, 87 **[Mean = 84]**
Grapes	0.104	6.2	0.089, 0.091 **[Mean = 0.090]**	86, 88 **[Mean = 87]**
Grapes	0.104	12.1	0.087, 0.091 **[Mean = 0.089]**	84, 88 **[Mean = 86]**
Grapes	0.104	18.3	0.077, 0.079 **[Mean = 0.078]**	74, 76 **[Mean = 75]**
Grapes	0.104	24.4	0.090, 0.095 **[Mean = 0.093]**	87, 91 **[Mean = 89]**
Grapes	0.104	30.4	1.0**, 0.080 **[Mean = 0.080]**	991**, 77 **[Mean = 77]**
Potatoes	0.104	0	0.074, 0.084, 0.086, 0.090, 0.094 **[Mean = 0.086]**	71, 81, 83, 87, 90 **[Mean = 82]**
Potatoes	0.104	3.1	0.081, 0.086 **[Mean = 0.084]**	78, 83 **[Mean = 80]**
Potatoes	0.104	6.1	0.078, 0.081 **[Mean = 0.080]**	75, 78 **[Mean = 77]**
Potatoes	0.104	12.1	0.083, 0.086 **[Mean = 0.085]**	80, 82 **[Mean = 81]**
Potatoes	0.104	18.2	0.058, 0.062 **[Mean = 0.060]**	56, 59 **[Mean = 57]**
Potatoes	0.104	24.3	0.078, 0.082 **[Mean = 0.080]**	75, 79 **[Mean = 77]**
Potatoes	0.104	30.3	0.081, 0.082 **[Mean = 0.082]**	79, 77 **[Mean = 78]**
Cabbage	0.104	0	0.087, 0.088, 0.096, 0.097, 0.102 **[Mean = 0.094]**	84, 85, 93, 93, 98 **[Mean = 90]**
Cabbage	0.104	3.1	0.072, 0.080 **[Mean = 0.076]**	69, 77 **[Mean = 73]**
Cabbage	0.104	6.1	0.080, 0.084 **[Mean = 0.082]**	77, 81 **[Mean = 79]**
Cabbage	0.104	12.1	0.079, 0.080 **[Mean = 0.080]**	76, 76 **[Mean = 76]**
Cabbage	0.104	18.2	0.071, 0.072 **[Mean = 0.072]**	69, 69 **[Mean = 69]**
Cabbage	0.104	24.3	0.085, 0.087 **[Mean = 0.086]**	82, 83 **[Mean = 83]**

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Cabbage	0.104	30.4	0.062, 0.071 **[Mean = 0.067]**	60, 68 **[Mean = 64]**
Wheat grain	0.104	0	0.093, 0.098, 0.097, 0.088, 0.093 **[Meam = 0.094]**	85, 89, 89, 93, 94 **[Mean = 90]**
Wheat grain	0.104	3.2	0.075, 0.083 **[Mean = 0.079]**	72, 80 **[Mean = 76]**
Wheat grain	0.104	6.2	0.080, 0.082 **[Mean= 0.081]**	77, 79 **[Mean = 78]**
Wheat grain	0.104	12.1	0.089, 0.114 **[Mean = 0.102]**	86, 110 **[Mean = 97]**
Wheat grain	0.104	18.3	0.080, 0.084 **[Mean = 0.082]**	77, 81 **[Mean = 79]**
Wheat grain	0.104	24.4	0.082, 0.084 **[Mean = 0.083]**	79, 80 **[Mean = 80]**
Wheat grain	0.104	30.4	0.074, 0.079 **[Mean = 0.077]**	71, 76 **[Mean = 74]**

** The analysed concentration was unrealistic. The result was considered as an anomaly and was therefore excluded from the formal stability data.

III. CONCLUSION

Representative plant commodities (grape, potato, cabbage, wheat grain, wheat forage and wheat straw) were fortified at 0.1 mg/kg with fluopicolide and its metabolites M-01, M-02. The metabolites M-04 and M-05 were fortified in wheat matrices only. The fortified samples were stored at low temperatures at -18°C and analysed at set intervals. The recoveries show that residues of fluopicolide and its metabolites are M-01 and M-02 are stable for up to 30 months in grape, potato, wheat grain and cabbage matrices and 12 months in wheat straw and forage. Metabolites M-04 and M-05 were also stable within the tested wheat matrices for a period up to 12 months.

The study was previously considered to be acceptable during the first EU review process for inclusion of fluopicolide on Annex I. The study complies with the current testing requirements specified within OECD 506. On this basis, the study is considered to remain acceptable and support the reported frozen storage stability periods for each of the tested compounds within the respective plant matrices.

Assessment and conclusion by applicant:

Residues of fluopicolide, M-01 and M-02 are stable within wheat grain (high starch matrix), grape berries (high acid matrix), potato tubers (high starch matrix) and cabbage leaves (high water matrix) for a period of up to 30 months.

Data Point:	KCA 6.1/04
Report Author:	[redacted]
Report Year:	2007
Report Title:	Storage stability of AE C638206 and its metabolites AE C657378 (3-OH-BAM), AE C653711 (BAM) and AE 1344122 (P1x) in/on cereals (rest of plant, grain, straw) for 25 months
Report No:	MR-178/04
Document No:	M-274729-02-1
Guideline(s) followed in study:	not specified
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Document M-274729-02-1 supersedes document M-237538-01-1 (which is an interim report for the storage stability study, which was evaluated previously within the DAR).

Executive summary

The study investigated the storage stability of residues of fluopicolide and its metabolites, M-01, M-04 and M-05, in fortified control samples of plant origin (wheat straw, grain, green material) during freezer storage for 25 months and (for fluopicolide and M-01) 41 months for straw samples. The samples were fortified at a level of 0.10 mg/kg.

The samples were stored in amber glass bottles at - 18°C or below and were analysed at nominal intervals of 0, 30, 90, 180, 360, 540 and 760 days.

Residues of fluopicolide and its metabolites M-01, M-04 and M-05 in/on plant material were determined by HPLC-MS/MS according to method 00782/M001 and 00782/M002 and 00782/M003 (M-04, M-05). The Limit of Quantitation (LOQ), defined as the lowest validated fortification level, was 0.01 mg/kg for all compounds.

In the control samples, the residues of all compounds were below 30% of the LOQ. After a deep-freezer storage period of 25 months, mean recovery rates for fluopicolide and its metabolites M-01, M-04 and M-05 between 73 and 138% (normalised to day 0) were determined.

No degradation during the deep-freezer storage of 25 months could be observed. The recoveries from stored samples were at a similar level as those from concurrent recovery experiments. Therefore, it can be assumed that all residues of fluopicolide and its metabolites M-01, M-04 and M-05 in samples of plant origin (wheat grain and for wheat straw – M-05 and M-04) are stable for at least 25 months and 41 months (for wheat straw – fluopicolide and M-01) under deep-freezer storage conditions as shown in this study. Due to low recoveries after 3 months, M-05 can only be considered stable for up to 3 months in wheat green material – the other analytes are stable for 25 months in wheat green material.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item:
- Fluopicolide (FLC)
- Metabolite M-01
- Metabolite M-04
- Metabolite M-05

Batch no.:
- AZ 09776 (FLC), AZ 10787 (FLC), AZ 12877 (FLC)
- AZ 09918 (M-01), AZ 10191 (M-01), AZ 11993 (M-01)
- AZ 10840 (M-04)
- AZ 10446 (M-05), AZ 10191 (M-05), AZ 13163 (M-05)

Active Ingredient / Purity:
- AZ 09776 (99.3%), AZ 10787 (98.9%), AZ 12877 (98.9%)
- AZ 09918 (97.0%), AZ 10191 (96.2%), AZ 11993 (96.2%)
- AZ 10840 (96.4%)
- AZ 10446 (98.8%), AZ 10191 (98.8%), AZ 13163 (98.8%)

Storage:
- Fluopicolide: + 5 ±5 °C
- Metabolite M-01: - 20 ±5 °C
- Metabolite M-04: - 20 ±5 °C
- Metabolite M-05: - 20 ±5 °C

Expiry date:
- AZ 09776 (Feb 2005), AZ 10787 (Sep 2005), AZ 12877 (Aug 2008)
- AZ 09918 (May 2004), AZ 10191 (Oct 2004), AZ 11993 (Sep 2007)
- AZ 10840 (Jul 2006)
- AZ 10446 (Feb 2002), AZ 10191 (Jan 2006), AZ 13163 (Jan 2010)

2. Test commodity: Wheat

Crop part: Wheat grain, wheat straw and wheat green material

B. STUDY DESIGN AND METHODS

Study design:

Residues of AE C638206 and its metabolites (AE C657378, AEC653711 and AE 1344122) in fortified control samples of plant origin (wheat straw, grain, green material) during freezer storage for 25 months. The samples were fortified at a level of 0.10 mg/kg.

The samples were stored in amber glass bottles at -18°C or below and were analysed at nominal intervals of 0, 30, 90, 180, 360, 540 and 760 days.

Analytical method

Residues of fluopicolide and its metabolites, M-01, M-04 and M-05 were analysed within the residue trials samples according to the following method:

Method	00782/M001, 00782/M002 and 00782/M003
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01, M-04 and M-05, in wheat green material, grain and straw)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Freshly fortified specimens with a nominal concentration of 0.1 mg/kg were analysed concurrently with each set of stored specimens. The results of these procedural recoveries are presented in the following tables for each of the tested matrices. The majority of the procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte / matrix combination. One exception is for wheat green material (at day 551) for M-05, where a mean recovery of 117% was obtained; this is considered to be acceptable, as it maximises the levels of the residue. These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples.

Table 6.1- 17 Procedural recoveries for fluopicolide (AE C638206) in wheat straw

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat straw	0	0.10	2003-09-17	...	...
	30	0.10	2003-10-17	73,75	74
	89	0.10	2003-12-15	91, 90	91
	182	0.10	2004-03-17	90, 100	95
	363	0.10	2004-09-14	97, 95	96
	545	0.10	2005-03-15	104, 105	105
	777	0.10	2005-11-02	85,76	81
	1251	0.10	2007-02-09	90, 83	87

Table 6.1- 18 Procedural recoveries for Metabolite M-01 (AE C653711) in wheat straw

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat straw	0	0.10	2003-09-17	...	...
	30	0.10	2003-10-17	73,76	75
	89	0.10	2003-12-15	91, 88	90
	182	0.10	2004-03-17	97, 100	99
	363	0.10	2004-09-14	89, 90	85
	546	0.10	2005-03-16	91, 99	95
	782	0.10	2005-11-07	90,86	88
	1251	0.10	2007-02-09	88, 91	90

Table 6.1- 19 Procedural recoveries for Metabolite M-04 (AE C653378) in wheat straw

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat straw	0	0.10	Wheat Straw	...	...
	30	0.10	Wheat Straw	80,74	77
	89	0.10	Wheat Straw	82, 88	85
	182	0.10	Wheat Straw	85, 87	86
	363	0.10	Wheat Straw	81, 82	82
	553	0.10	Wheat Straw	105, 104	105
	770	0.10	Wheat Straw	81, 82	82

Table 6.1- 20 Procedural recoveries for Metabolite M-05 (AE 1344122) in wheat straw

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat straw	0	0.10	2003-09-17	-	-
	30	0.10	2003-10-17	75, 46*	-
	89	0.10	2003-12-15	79,79	79
	182	0.10	2004-03-17	68,72	70
	363	0.10	2004-09-14	69,73	71
	553	0.10	2005-03-23	81, 80	80
	770	0.10	2005-10-26	61,65	63

*: One concurrent recovery was excluded.

Table 6.1- 21 Procedural recoveries for Metabolite M-04 (AE C657378) in wheat grain

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat grain	0	0.10	2003-10-01	—	—
	28	0.10	2003-10-29	78, 88	83
	114	0.10	2004-01-23	89, 86	88
	168	0.10	2004-03-17	86,88	87
	349	0.10	2004-09-14	90,88	89
	552	0.10	2005-04-05	96**, ***	96
	754	0.10	2006-04-25*	108, 100	105

*: Control samples prepared on 2004-04-01 were taken for method validation (actual storage period was 754 days).

Table 6.1- 22 Procedural recoveries for Metabolite M-05 (AE 1344122) in wheat grain

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat grain	0	0.10	2003-10-01	—	—
	28	0.10	2003-10-29	74,77	76
	114	0.10	2004-01-15	85,76	81
	168	0.10	2004-03-17	88,83	86
	349	0.10	2004-09-14	82,85	84
	552	0.10	2005-04-05	75,71,68	71
	754	0.10	2006-04-25**	89,64	77

Table 6.1- 23 Procedural recoveries for Metabolite M-04 (AE C657378) in wheat green material

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat green material	0	0.10	2003-09-17	—	—
	30	0.10	2003-10-17	83, 103	93
	89	0.10	2003-12-15	98, 109	104
	182	0.10	2004-03-17	96,89	93
	363	0.10	2004-09-14	89, 88	89
	551	0.10	2005-03-21	95, 93	94
	769	0.10	2005-10-25	82, 87	85

Table 6.1- 24 Procedural recoveries for Metabolite M-05 (AE 1344122) in wheat green material

Sample matrix	Storage Interval (days)	Fortification level (mg/kg)	Date of extraction (yyyy-mm-dd)	Recovery values (%)	Mean Recovery (%)
Wheat green material	0	0.10	2003-09-17	—	—
	30	0.10	2003-10-17	76,78	77
	89	0.10	2003-12-15	95, 87	91
	182	0.10	2004-03-17	65,67	66
	363	0.10	2004-09-14	83, 86	84
	551	0.10	2005-03-21	117, 118	117
	769	0.10	2005-10-25	67,65	66

*: Not used for calculation.

II. RESULTS AND DISCUSSION

The following table summarises the amount of fluopicolide, M-01, M-04 and M-05 recovered in the stored samples after the various storage intervals, as well as the procedural recoveries from samples freshly fortified at the respective sampling points.

Table 6.1- 25 Residues stability of fluopicolide and its metabolites (M-01, M-04 and M-05) in various plant matrices following storage at -18ºC

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recoveries (%)
Fluopicolide (AE C638206)			
Wheat straw	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat straw	0.10	0	77, 84, 81, 87,75 **[Mean = 81]**
Wheat straw	0.10	30	90, 91, 91 **[Mean = 91]**
Wheat straw	0.10	89	92, 89, 93 **[Mean = 91]**
Wheat straw	0.10	182	103, 100, 97 **[Mean = 100]**
Wheat straw	0.10	363	88, 80, 76 **[Mean = 81]**
Wheat straw	0.10	545	94, 105, 97 **[Mean = 99]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recoveries (%)
Wheat straw	0.10	777	97, 71, 92 **[Mean = 87]**
Wheat straw	0.10	1251	83, 87, 91 **[Mean = 87]**
Metabolite M-01 (AE C653711)			
Wheat straw	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat straw	0.10	0	72, 90, 96, 94, 95 **[Mean = 89]**
Wheat straw	0.10	30	62, 80, 83 **[Mean = 75]**
Wheat straw	0.10	89	82, 85, 88 **[Mean = 85]**
Wheat straw	0.10	182	105, 93, 86 **[Mean = 95]**
Wheat straw	0.10	363	98, 93, 96 **[Mean = 96]**
Wheat straw	0.10	546	91, 97, 94 **[Mean = 94]**
Wheat straw	0.10	782	86, 87, 79 **[Mean = 84]**
Wheat straw	0.10	1251	88, 92, 93 **[Mean = 91]**
Metabolite M-04 (AE C657378)			
Wheat straw	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat straw	0.10	0	67, 67, 77, 80, 84 **[Mean = 75]**
Wheat straw	0.10	30	78, 81, 84 **[Mean = 81]**
Wheat straw	0.10	89	93, 106, 99 **[Mean = 99]**
Wheat straw	0.10	182	91, 88, 96 **[Mean = 92]**
Wheat straw	0.10	363	84, 86, 84 **[Mean = 85]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recoveries (%)
Wheat straw	0.10	553	91, 94, 95 **[Mean = 93]**
Wheat straw	0.10	770	73, 73, 72 **[Mean = 73]**
Wheat grain	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat grain	0.10	0	74, 86, 88, 81, 97 **[Mean = 85]**
Wheat grain	0.10	28	79, 97, 77 **[Mean = 84]**
Wheat grain	0.10	114	107, 94, 93 **[Mean = 98]**
Wheat grain	0.10	168	76, 90, 87 **[Mean = 84]**
Wheat grain	0.10	349	91, 101, 97 **[Mean = 96]**
Wheat grain	0.10	552	79**, 78**, * **[Mean = 79]**
Wheat grain	0.10	754	87, 94, 89 **[Mean = 90]**
Wheat Green Material	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat Green Material	0.10	0	74, 87, 86, 79, 83 **[Mean = 82]**
Wheat Green Material	0.10	30	98, 94, 86 **[Mean = 93]**
Wheat Green Material	0.10	89	72, 66, 90 **[Mean = 76]**
Wheat Green Material	0.10	182	98, 108, 106 **[Mean = 104]**
Wheat Green Material	0.10	363	92, 93, 96 **[Mean = 94]**
Wheat Green Material	0.10	551	95, 93, 90 **[Mean = 93]**
Wheat Green Material	0.10	769	74, 78, 73 **[Mean = 75]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recoveries (%)
Metabolite M-05 (AE 1344122)			
Wheat straw	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat straw	0.10	0	73, 76, 83, 93, 76 **[Mean = 80]**
Wheat straw	0.10	30	95, 79, 91 **[Mean = 88]**
Wheat straw	0.10	84	77, 96, 93 **[Mean = 89]**
Wheat straw	0.10	182	72, 74, 74 **[Mean = 73]**
Wheat straw	0.10	363	77, 77, 82 **[Mean = 79]**
Wheat straw	0.10	553	79, 77, 80 **[Mean = 79]**
Wheat straw	0.10	770	59, 60, 56 **[Mean = 58]**
Wheat grain	0.10	0	61,79, 82,64, 83 **[Mean = 74]**
Wheat grain	0.10	28	95, 100, 100 **[Mean = 98]**
Wheat grain	Control	0	n.a. (residue < 0.01 mg/kg)
Wheat grain	0.10	114	94, 80, 108 **[Mean = 94]**
Wheat grain	0.10	168	61,77,71 **[Mean = 70]**
Wheat grain	0.10	349	80, 90, 89 **[Mean = 86]**
Wheat grain	0.10	552	74, 67, * **[Mean = 71]**
Wheat grain	0.10	754	74, 77, 82 **[Mean = 78]**
Wheat Green Material	Control	0	n.a. (residue < 0.01 mg/kg)

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recoveries (%)
Wheat Green Material	0.10	0	74, 79, 79, 82, 75 **[Mean = 78]**
Wheat Green Material	0.10	30	71,71,69 **[Mean = 70]**
Wheat Green Material	0.10	89	78, 85, 92 **[Mean = 85]**
Wheat Green Material	0.10	182	69, 68, 64 **[Mean = 67]**
Wheat Green Material	0.10	363	82, 80, 81 **[Mean = 81]**
Wheat Green Material	0.10	581	91, 114, 117 **[Mean = 107]**
Wheat Green Material	0.10	769	56, 62, 65 **[Mean = 61]**

*: One recovery sample was identified as outlier
**: Mean of two measurements.

III. CONCLUSION

No degradation during the deep-freezer storage of 25 months could be observed. The recoveries from stored samples were at a similar level as those from concurrent recovery experiments. Therefore, it can be assumed that all residues of fluopicolide and its metabolites M-01, M-04 and M-05 in samples of plant origin (wheat, grain) are stable for at least 25 months under deep-freezer storage conditions. Due to low recoveries after 3 months, M-05 can only be considered stable for up to 3 months in wheat green material – the other analytes are stable for 25 months in wheat green material.

Fluopicolide and its metabolites M-01 were also found to be stable within wheat straw under deep-freezer storage conditions for 41 months. Metabolites M-04 and M-05 were found to remain stable for 25 months in deep-frozen wheat straw.

Assessment and conclusion by applicant:

Residues of fluopicolide, M-01, M-04 and M-05 are stable within wheat grain (high starch matrix). For wheat green material (high water matrix), fluopicolide, M-01, M-04 are stable for a period of up to 25 months. Due to low recoveries after 3 months, M-05 can only be considered stable for up to 3 months wheat green material.

Residues of fluopicolide, M-01 are stable within wheat straw (unique matrix) for a period of up to 41 months.

Residues of M-04 and M-05 are stable within wheat straw (unique matrix) for a period of up to 25 months.

Data Point:	KCA 6.1/05
Report Author:	[redacted]
Report Year:	2004
Report Title:	Residues of AE C638206 and major metabolites in milk and edible cattle tissues following 28 days dosing of technical product to lactating cows; 2002. Final report.
Report No:	02-105
Document No:	M-219457-01-2
Guideline(s) followed in study:	EU (=EEC): 7031/VI/95 rev. 4; USEPA (=EPA): OPPTS 860.1480
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The study investigated the stability of fluopicolide (AE C638206) and its metabolites, M-01 (AEC653711) and M-02 (AEC657188) in livestock products when stored deep-frozen at < -18 °C.

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for fluopicolide, M-01 and M-02. The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg (for milk and muscle) and 0.05 mg/kg (for fat, kidney and liver). The fortified specimens were stored in a freezer at < -18 °C.

Fluopicolide and its metabolites were analysed according to the method AR 303-02. The limit of quantification was 0.01 mg/kg (for milk), 0.02 mg/kg (for muscle) and 0.05 mg/kg (for fat, liver, and kidney). The validity of the method was verified by analysing freshly fortified specimens concurrently with each set of stored specimens – these procedural recoveries were considered to be acceptably to support the results obtained from the stored samples.

Samples were analysed at set intervals. The recoveries show that residues of fluopicolide and its metabolites M-01 and M-02 are stable for at least 2 months in milk, 4 months in fat and muscle and 9 months in liver and kidney.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	• Fluopicolide (FLC) • Metabolite M-01 • Metabolite M-02
	Batch no.:	• R001737 (FLC) • R001724 (M-01), 8808018 (M-01) • RAW244055/1 (M-02)
	Active Ingredient / Purity:	• R001737 (99.3%) • R001724 (97.0%), 8808018 (97.0%) • RAW244055/1 (97.2%)
	Storage:	• Fluopicolide: + 5 ±5 °C • Metabolite M-01: - 20 ±5 °C • Metabolite M-02: - 20 ±5 °C
	Expiry date:	• R001737 (Feb 2005), MQY4627 (Sep 2005) • R001724 (Aug 2003), 8808018 (May 2004), 08018ET (Sep 2007) • RAW244055/1 (Apr 2006)
2.	**Test commodity:**	Bovine products / tissues
	Portion:	Milk, muscle, fat, kidney and liver

B. STUDY DESIGN AND METHODS

Study design:

A storage stability study was conducted to investigate the stability of fluopicolide (AE C638206) and its metabolites M-01 (AEC653711) and M-02 (AEC657188) in livestock tissues and products under storage conditions at < -18 °C for a period of 2 months (for milk), 4 months (for muscle and fat) and 9 months (for liver and kidney).

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for the parent fluopicolide and the metabolites M-01 and M-02. The substrates were bovine milk, muscle, fat, liver and kidney.

The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg (for milk and muscle) and 0.05 mg/kg (for fat, liver, and kidney). The fortified specimens were stored in a freezer at < - 18 °C.

Analytical Part:

At each storage interval, fluopicolide and its metabolites, M-01 and M-02 were determined in the stored control samples and in the stored spiked samples according to the following method:

Method	AR 303-02
Extraction	Extracted with acidified water and acetone – solution was separated from the solid material by mechanical shaking.
Detection	LC/MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in milk) 0.02 mg/kg (for fluopicolide, M-01 and M-02, in muscle) 0.05 mg/kg (for fluopicolide, M-01 and M-02, in fat, liver and kidney)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev. 4.

Freshly fortified specimens with a nominal concentration of 0.1 mg/kg were analysed concurrently with each set of stored specimens. The results of these procedural recoveries are presented in the following table for each of the tested matrices. The majority of the procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte / matrix combination. However, some of the procedural recoveries exceed 110%, though this is still considered to be acceptable, as it maximises the levels of the residues within the tested sample. These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples.

II. RESULTS AND DISCUSSION

The following table summarises the amount of fluopicolide, M-01 and M-02 recovered in the stored samples after the various storage intervals, as well as the procedural recoveries from samples freshly fortified at the respective sampling points.

Table 6.1- 26 Residue stability of fluopicolide and its metabolites (M-01 and M-02) in bovine tissues and milk following storage at -20°C

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)	Fresh concurrent recovery (%)
Fluopicolide					
Milk (Bovine)	Control	0	<0.010	-	-
Milk (Bovine)	0.100	0	0.093	93	92
Milk (Bovine)	Control	0.5 (13 days)	<0.010	-	-
Milk (Bovine)	0.100	0.5 (13 days)	0.095	95	92
Milk (Bovine)	Control	1 (51 days)	0.010	-	-
Milk (Bovine)	0.100	1 (51 days)	0.238	238*	131
Milk (Bovine)	Control	2 (83 days)	<0.010	-	-
Milk (Bovine)	0.100	2 (83 days)	0.094	94	101
Muscle (Bovine)	Control	0	<0.020	-	-
Muscle (Bovine)	0.100	0	0.090	90	86, 92
Muscle (Bovine)	Control	4	<0.020	-	-
Muscle (Bovine)	0.100	4	0.086	86	82

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)	Fresh concurrent recovery (%)
Muscle (Bovine)	0.100	4	0.090	90	
Fat (Bovine)	Control	0	<0.050	-	-
Fat (Bovine)	0.500	0	0.450	90	92
Fat (Bovine)	Control	4	<0.050	-	-
Fat (Bovine)	0.500	4	0.468	93	90
Fat (Bovine)	0.500	4	0.505	101	
Liver (Bovine)	Control	0	<0.050	-	-
Liver (Bovine)	0.500	0	0.533	107	110
Liver (Bovine)	Control	9	<0.050	-	-
Liver (Bovine)	0.500	9	0.498	100	92
Liver (Bovine)	0.500	9	0.403	81	
Kidney (Bovine)	Control	0	<0.050	-	-
Kidney (Bovine)	0.500	0	0.463	93	92
Kidney (Bovine)	Control	9	<0.050	-	-
Kidney (Bovine)	0.500	9	0.498	99	89
Kidney (Bovine)	0.500	9	0.488	98	
Metabolite M-01					
Milk (Bovine)	Control	0	0.010	-	-
Milk (Bovine)	0.100	0	0.108	108	111
Milk (Bovine)	Control	0.5 (13 days)	<0.010	-	-
Milk (Bovine)	0.100	0.5 (13 days)	0.113	113	122
Milk (Bovine)	Control	1 (51 days)	0.010	-	-
Milk (Bovine)	0.100	1 (51 days)	0.118	118	130
Milk (Bovine)	Control	2 (83 days)	<0.010	-	-
Milk (Bovine)	0.100	2 (83 days)	0.115	115	122
Muscle (Bovine)	Control	0	<0.020	-	-
Muscle (Bovine)	0.100	0	0.095	95	91, 107
Muscle (Bovine)	Control	4	<0.020	-	-
Muscle (Bovine)	0.100	4	0.095	95	80
Muscle (Bovine)	0.100	4	0.094	94	
Fat (Bovine)	Control	0	<0.050	-	-
Fat (Bovine)	0.500	0	0.493	98	90
Fat (Bovine)	Control	4	<0.050	-	-
Fat (Bovine)	0.500	4	0.488	98	86
Fat (Bovine)	0.500	4	0.490	98	
Liver (Bovine)	Control	0	<0.05	-	-

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)	Fresh concurrent recovery (%)
Liver (Bovine)	0.500	0	0.493	99	93
Liver (Bovine)	Control	9	<0.050	-	-
Liver (Bovine)	0.500	9	0.473	94	100
Liver (Bovine)	0.500	9	0.470	94	
Kidney (Bovine)	Control	0	<0.050	-	-
Kidney (Bovine)	0.500	0	0.460	92	100
Kidney (Bovine)	Control	9	<0.050	-	-
Kidney (Bovine)	0.500	9	0.478	95	101
Kidney (Bovine)	0.500	9	0.430	86	
Metabolite M-02					
Milk (Bovine)	Control	0	<0.010	-	-
Milk (Bovine)	0.100	0	0.090	90	89
Milk (Bovine)	Control	0.5 (13 days)	<0.010	-	-
Milk (Bovine)	0.100	0.5 (13 days)	0.078	78	85
Milk (Bovine)	Control	1 (51 days)	0.010	-	-
Milk (Bovine)	0.100	1 (51 days)	0.093	93	106
Milk (Bovine)	Control	2 (83 days)	<0.010	-	-
Milk (Bovine)	0.100	2 (83 days)	0.087	87	90
Muscle (Bovine)	Control	0	<0.020	-	-
Muscle (Bovine)	0.100	0	0.106	106	107, 109
Muscle (Bovine)	Control	4	<0.020	-	-
Muscle (Bovine)	0.100	4	0.104	104	91
Muscle (Bovine)	0.100	4	0.098	98	
Fat (Bovine)	Control	0	<0.050	-	-
Fat (Bovine)	0.500	0	0.488	98	93
Fat (Bovine)	Control	4	<0.050	-	-
Fat (Bovine)	0.500	4	0.450	90	90
Fat (Bovine)	0.500	4	0.458	92	
Liver (Bovine)	Control	0	<0.050	-	-
Liver (Bovine)	0.500	0	0.548	110	108
Liver (Bovine)	Control	9	<0.050	-	-
Liver (Bovine)	0.500	9	0.535	107	86
Liver (Bovine)	0.500	9	0.515	103	
Kidney (Bovine)	Control	0	<0.050	-	-
Kidney (Bovine)	0.500	0	0.473	95	103
Kidney (Bovine)	Control	9	<0.050	-	-

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries (%)	Fresh concurrent recovery (%)
Kidney (Bovine)	0.500	9	0.505	101	104
Kidney (Bovine)	0.500	9	0.438	87	

* Results was discounted as the analysis of the subsequent time point did not confirm the result.

III. CONCLUSION

Samples of bovine liver, bovine kidney, bovine muscle, bovine fat and bovine milk were fortified at 0.01 mg/kg with fluopicolide and its metabolites M-01 and M-02 and were stored at low temperatures (< -18 °C) for up to 9 months. Samples were analysed at set intervals. The recoveries show that residues of fluopicolide and its metabolites M-01 and M-02 are stable for at least 2 months in milk, 4 months in fat and muscle and 9 months in liver and kidney.

The study was previously considered to be acceptable during the first EU review process for inclusion of fluopicolide on Annex I. The study complies with the current testing requirements specified within OECD 506. On this basis, the study is considered to remain acceptable and support the reported frozen storage stability periods for each of the tested compounds within the respective livestock matrices.

Assessment and conclusion by applicant:

Residues of fluopicolide, M-01 and M-02 are stable within livestock product for the following periods:
2 months (83 days): Bovine milk
4 months: Bovine muscle and fat
9 months: Bovine liver and kidneys

New data for AIR:

New studies have been completed to cover all 5 storage stability commodity groups indicated in Annex 1 of the OECD test guideline 506 (2007) and honey. The new studies cover the stability of metabolites M-04 and M-05 in sunflower seed (high oil matrix), dry beans seed (high protein matrix) cucumbers (high water matrix), strawberry (high acid matrix), barley grain (high starch matrix) and also the stability of metabolite M-06 in barley grain. The stability of fluopicolide and metabolite M-01 in honey was also demonstrated (to support the residues in honey study summarised within section CA 6.10.1). These studies have not been previously reviewed at the EU level and they have been summarised in this document for the first time.

Data Point:	KCA 6.1/06
Report Author:	[redacted]
Report Year:	2013
Report Title:	Storage stability of residues of AE C638206 and its metabolites (AE C653711 and AE C657188) in sunflower during deep freeze storage for up to 24 months
Report No:	10-07
Document No:	M-439984-02-1
Guideline(s) followed in study:	Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances; US EPA Residue Chemistry Test Guideline OPPTS 860.1380: Storage Stability Data; OECD Test Guideline 506, adopted 16 October 2007
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The study investigated the stability of fluopicolide (AE C638206), M-01 (AEC653711) and M-02 (AE C657188) in sunflower seed under storage conditions at < -18 °C for a period of 24 months and residues were considered to be sufficiently stable over this period.

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for fluopicolide, M-01 and M-02.

The fortification level was at a nominal concentration (fresh weight basis) of 0.2 mg/kg. The fortified

At each storage interval (nominal storage intervals of 0, 8, 12, 19 and 24 months) fluopicolide and M-01 were determined in the stored control samples and in the stored spiked samples according to the analytical method 01209.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	• Fluopicolide (FLC) • Metabolite M-01 • Metabolite M-02
	Batch no.:	• MOY4627 (FLC) • 08018ET (M-01) • RAW244055/1 (M-02), SES 10250-1-1 (M-02)
	Active Ingredient / Purity:	• MOY4627 (99.2%) • 08018ET (96.2%) • RAW244055/1 (97.2%), SES 10250-1-1 (98.5%)
	Storage:	• Fluopicolide: + 5 ±5 °C • Metabolite M-01: - 20 ±5 °C • Metabolite M-02: - 20 ±5 °C
	Expiry date:	• MOY4627 (Jul 2013) • 08018ET (Aug 2015) • RAW244055/1 (Mar 2011), SES 10250-1-1 (Sep 2015)
2.	**Test commodity:**	Sunflower
	Crop part:	Sunflower seed

B. STUDY DESIGN AND METHODS

Study design:

A storage stability study was conducted to investigate the stability of fluopicolide (AE C638206) and its metabolites M-01 (AEC653711) and M-02 (AEC653188) in sunflower seed under storage conditions at < - 18 °C for a period of 24 months.

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for the parent fluopicolide and the metabolites M-01 and M-02.

The fortification level was at a nominal concentration (fresh weight basis) of 0.2 mg/kg. The fortified specimens were stored in a freezer at < - 18 °C.

Analytical Part:

At each storage interval, fluopicolide, M-01 and M-02 were determined in the stored control samples and in the stored spiked samples according to the following method:

Method	01209
Extraction	Extracted with acidified water and acetone – solution was separated from the solid material by centrifugation.
Detection	HPLC/MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in sunflower seed).

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Freshly fortified specimens with a nominal concentration of 0.1 mg/kg were analysed concurrently with each set of stored specimens. The results of these procedural recoveries are presented in the following tables for each of the tested matrices. The majority of the procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte / matrix combination and the %RSD values are <20% (where applicable). Some of the procedural recoveries for fluopicolide at the early time-points (day 0 and day 241) are below the 70 % lower limit (at 63 % and 60 %, respectively). These results are considered to be acceptable, as the results for the later time-points show that the residues remain stable over longer-term storage periods. These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples.

Table 6.1- 27 Procedural recoveries for fluopicolide in sunflower seed

Sample matrix	Period (days)	Fortification level (mg/kg)	Date of extraction	Recovery values (%)	Mean Recovery (%)	% RSD
Sunflower seed	0	0.2	2010-12-10	67, 60, 63	63	5.5
	241		2011-08-08	60, 59	60	
	371		2011-12-16	76, 79	78	-
	580		2012-07-12	71, 71, 71	71	0
	731		2012-12-10	77, 76, 79	77	1.5

Table 6.1- 28 Procedural recoveries for metabolite M-01 in sunflower seed

Sample matrix	Period (days)	Fortification level (mg/kg)	Date of extraction	Recovery values (%)	Mean Recovery (%)	% RSD
Sunflower seed	0	0.2	2010-12-10	91, 92, 93	92	1.0
	241		2011-08-08	118, 119	119	-
	371		2011-12-16	92, 97	95	-
	580		2012-07-12	79, 75, 77	77	2.6
	731		2012-12-10	79, 77, 81	79	2.5

Table 6.1- 29 Procedural recoveries for metabolite M-02 in sunflower seed

Sample matrix	Period (days)	Fortification level (mg/kg)	Date of extraction	Recovery values (%)	Mean Recovery (%)	% RSD
Sunflower seed	0	0.2	2010-12-10	86, 83, 91	87	4.7
	241		2011-08-08	89, 89	89	-
	371		2011-12-16	79, 84	82	-
	580		2012-07-12	96, 95, 97	96	1.0
	731		2012-12-10	87, 92, 89	89	2.8

II. RESULTS AND DISCUSSION

The following table summarises the amount of fluopicolide, M-01 and M-02 recovered in the stored samples after the various storage intervals, as well as the procedural recoveries from samples freshly fortified at the respective sampling points.

Table 6.1- 30 Residues stability of fluopicolide and its metabolites (M-01 and M-02) in sunflower seed following storage at -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Fluopicolide				
Sunflower seed	Control	0	<0.01	-
Sunflower seed	0.2	0	0.136, 0.142, 0.137	69, 71, 69 **[Mean = 70]**
Sunflower seed	0.2	241	0.118, 0.120, 0.108	59, 60, 54 **[Mean = 58]**
Sunflower seed	0.2	371	0.167, 0.144, 0.147	84, 72, 80 **[Mean = 79]**
Sunflower seed	0.2	580	0.144, 0.141, 0.147	72, 71, 74 **[Mean = 72]**
Sunflower seed	0.2	731	0.155, 0.152, 0.160	78, 76, 80 **[Mean = 78]**
Metabolite M-01				
Sunflower seed	Control	0	<0.01	-
Sunflower seed	0.2	0	0.198, 0.197, 0.196	99, 99, 98 **[Mean = 99]**
Sunflower seed	0.2	241	0.211, 0.214, 0.215	106, 107, 108 **[Mean = 107]**
Sunflower seed	0.2	371	0.195, 0.193, 0.192	97, 97, 96 **[Mean = 97]**
Sunflower seed	0.2	580	0.147, 0.149, 0.150	73, 75, 75 **[Mean = 74]**
Sunflower seed	0.2	731	0.148, 0.143, 0.145	74, 72, 73 **[Mean = 73]**
Metabolite M-02				
Sunflower seed	Control	0	<0.01	-
Sunflower seed	0.2	0	0.175, 0.179, 0.185	88, 90, 92 **[Mean = 90]**
Sunflower seed	0.2	241	0.197, 0.188, 0.190	99, 94, 95 **[Mean = 96]**
Sunflower seed	0.2	371	0.183, 0.181, 0.160	92, 91, 80 **[Mean = 88]**
Sunflower seed	0.2	580	0.182, 0.180, 0.181	91, 90, 91 **[Mean = 91]**
Sunflower seed	0.2	731	0.177, 0.177, 0.172	89, 89, 86 **[Mean = 88]**

For fluopicolide, the mean values reported for the stored spiked samples were 70% and 58% respectively, at storage interval 0 and 241 days. Nevertheless, this is considered to be acceptable, as the procedural recovery means were similar at the same time-points:63% and 60%. At storage interval 371, 580 and 731 days the fluopicolide contact within the stored samples were within the acceptable range of 70-110%, this suggests that the lower detected amount in the first two time-points is likely due to analytical issues, rather than degradation of fluopicolide within the sample matrix.

III. CONCLUSION

Sunflower seed samples were fortified at 0.2 mg/kg with fluopicolide and its metabolites M-01, M-02. The fortified samples were stored at low temperatures at -18ºC and analysed at set intervals. The recoveries show that residues of fluopicolide and its metabolites are M-01 and M-02 are stable for up to 24 months in sunflower seeds.

The study was previously considered to be acceptable during the first EU review process for inclusion of fluopicolide on Annex I. The study complies with the current testing requirements specified within OECD 506. On this basis, the study is considered to remain acceptable and support the reported frozen storage stability periods for each of the tested compounds within the respective plant matrices.

Assessment and conclusion by applicant:

Residues of fluopicolide, M-01 and M-02 are stable within sunflower seed (high oil matrix) for a period of up to 24 months.

Data Point:	KCA 6.1/07
Report Author:	[redacted]
Report Year:	2020
Report Title:	Storage stability of fluopicolide metabolites AE C657378 and AE C656948-methyl-sulfoxide (AE 1344122) in/on sunflower, dry bean, cucumber, strawberry and barley and AE C643890 in/on barley during freezer storage for up to 24 months - Interim report
Report No:	EE18-001
Document No:	M-685332-01-1
Guideline(s) followed in study:	OECD Guideline for the Testing of Chemicals. Stability of Pesticide Residues in Stored Commodities 506. 2007-10-16; US EPA OPPTS 860.1380, Storage Stability Data; Coordenação Geral de Acreditação do Inmetro NIT-DICLA 035.
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Supportive only

Executive summary

Samples of sunflower seed (high oil matrix), dry beans seed (high protein matrix), cucumbers (high water matrix), strawberry (high acid matrix), barley grain (high starch matrix) were fortified with fluopicolide (0.1 mg/kg) and M-01 (0.1 mg/kg) and stored deep frozen (≤ -18°C).

The stored samples were analysed using a validated HPLC-MS method at the 0, ~30, ~90, ~180, ~360, and ~540-day time-points, to confirm the residue levels of fluopicolide and M-01. The residue levels remained relatively consistent over the course of the 18-month storage period (recoveries were >70%), indicating that fluopicolide and M-01 remain stable when frozen for this period of time. No residues of fluopicolide or M-01 were found within the control samples. The concurrent recoveries made at each time-point were comparable with the recoveries obtained within the validation data for the analytical method, which supports the reliability of the sample analysis and of the obtained results.

The results presented demonstrate the storage stability of the samples up to the (nominal) 540-day time-point from the interim report. The study will continue to the 730-day (2-year) time-point, which will be presented within the final study report (expected early 2021).

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	• Metabolite M-04 • Metabolite M-05 • Metabolite M-06
	Batch no.:	• 1119-DC/3 (M-04) • YG3228 (M-05) • RDL 305-3-7 (M-06)
	Active Ingredient / Purity:	• 1119-DC/3 (98.1%) • YG3228 (98.8%) • RDL 305-3-7 (94.3%)
	Storage:	• Metabolite M-04: + 5 ±5 °C • Metabolite M-05: + 5 ±5 °C • Metabolite M-06: + 5 ±5 °C
	Expiry date:	• 1119-DC/3 (Mar 2022) • YG3228 (Feb 2026) • RDL 305-3-7 (May 2025)
2.	**Test commodity:**	Barley, strawberry, cucumber, sunflower and dry bean
	Crop part:	Barley (grain), strawberry (fruit), cucumber (fruit), sunflower (seed) and dry bean (seed)

B. STUDY DESIGN AND METHODS

Study design:

A storage stability study was conducted to investigate the stability of M-04 (AE C657378), M-05 (AE 1344122) in barley, strawberry, cucumber, sunflower and dry bean under storage conditions at < - 18 °C for a period of 18 months. The stability of M-06 (AE C643890) was investigated in barley under storage conditions at < - 18 °C for a period of 18 months (nominal 540 days).

Portions of untreated substrate were fortified with the analytes. Separate batches were prepared for the metabolites M-04, M-05 and M-06. The substrates were barley (grain), strawberry (fruit), cucumber (fruit), sunflower (seed) and dry bean (seed).

The fortification level was at a nominal concentration (fresh weight basis) of 0.1 mg/kg. The fortified specimens were stored in a freezer at < - 18 °C. After (nominal) 30, 90, 180, 360 and 540 days, three fortified per analyte and one control samples of each tested plant material were removed from the deep-freezer and analysed using the HPLC-MS/MS method.

Analytical Part:

Residues of M-04 and M-05 were analysed within the samples according to the following method:

Method	00782/M006
Extraction	Mixture of acetone/water, adjusted to pH 2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for M-04 and M-05 in sunflower seeds, dry bean seeds, cucumber, strawberries and barley grain)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to assess the accuracy of the residue analyses, recoveries were determined by analysing freshly fortified samples alongside the stored fortified samples. At all storage intervals except for day 0, two concurrent recoveries were determined at a level of 0.10 mg/kg. No additional concurrent recoveries were determined on day 0, since there were five freshly fortified storage samples. Analysis was performed within 24 hours after extraction. The procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte / matrix combination and the %RSD values are <20% (where applicable). These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples. The results are presented in the table below:

Table 6.1- 31 Summary of concurrent recoveries of metabolite M-04 and M-05 from various plant matrices.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean
Metabolite M-04					
Sunflower seed	0.1	0	1	95	95
Sunflower seed	0.1	30	2	89, 90	90
Sunflower seed	0.1	97	2	96, 94	95
Sunflower seed	0.1	163	2	85, 95	90
Sunflower seed	0.1	183	2	86, 90	88
Sunflower seed	0.1	387	2	102, 101	102
Sunflower seed	0.1	568	2	94, 91	93
Dry bean seed	0.1	0	1	91	91
Dry bean seed	0.1	32	1	90	90
Dry bean seed	0.1	96	1	101	101
Dry bean seed	0.1	182	1	86	86
Dry bean seed	0.1	392	2	78, 84	81
Dry bean seed	0.1	573	1	106	106
Cucumber	0.1	0	1	105	105
Cucumber	0.1	30	1	91	91
Cucumber	0.1	93	2	98, 102	100
Cucumber	0.1	178	2	98, 93	96
Cucumber	0.1	385	2	99, 113	106

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean
Cucumber	0.1	576	2	92, 89	91
Strawberry	0.1	0	1	107	107
Strawberry	0.1	30	2	98, 96	97
Strawberry	0.1	98	1	112	112
Strawberry	0.1	182	2	82, 75	79
Strawberry	0.1	386	2	90, 88	89
Strawberry	0.1	567	2	93, 90	92
Barley grain	0.1	0	2	97, 88	93
Barley grain	0.1	31	2	97, 96	97
Barley grain	0.1	91	2	84, 85	85
Barley grain	0.1	183	2	85, 84	85
Barley grain	0.1	391	2	89, 70	80
Barley grain	0.1	573	2	97, 100	99
Metabolite M-05					
Sunflower seed	0.1	0	1	88	88
Sunflower seed	0.1	30	2	83, 75	79
Sunflower seed	0.1	97	2	80, 85	83
Sunflower seed	0.1	183	2	85, 86	86
Sunflower seed	0.1	387	2	79, 88	84
Sunflower seed	0.1	568	2	81, 84	83
Dry bean seed	0.1	0	1	81	81
Dry bean seed	0.1	32	1	84	84
Dry bean seed	0.1	96	1	87	87
Dry bean seed	0.1	182	1	81	81
Dry bean seed	0.1	392	2	75, 77	76
Dry bean seed	0.1	573	2	82, 82	82
Cucumber	0.1	0	1	96	96
Cucumber	0.1	30	1	88	88
Cucumber	0.1	93	2	96, 95	96
Cucumber	0.1	178	2	89, 83	86
Cucumber	0.1	385	2	97, 94	96
Cucumber	0.1	567	2	87, 85	86
Strawberry	0.1	0	1	104	104
Strawberry	0.1	30	2	84, 83	84
Strawberry	0.1	98	2	100, 101	101
Strawberry	0.1	182	2	88, 80	84

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean
Strawberry	0.1	386	2	77, 76	77
Strawberry	0.1	567	2	88, 86	87
Barley grain	0.1	0	2	82, 92	87
Barley grain	0.1	31	2	93, 92	93
Barley grain	0.1	91	2	83, 85	84
Barley grain	0.1	183	2	83, 83	83
Barley grain	0.1	360	1	77	77
Barley grain	0.1	540	2	88, 93	91
Metabolite M-06					
Barley grain	0.1	0	2	88, 94	91
Barley grain	0.1	31	2	93, 88	91
Barley grain	0.1	63	2	95, 99	97
Barley grain	0.1	91	2	89, 86	88
Barley grain	0.1	183	2	95, 95	95
Barley grain	0.1	391	2	96, 88	92
Barley grain	0.1	573	2	99, 105	102

II. RESULTS AND DISCUSSION

The following table summarises the amount of M-04, M-05 and M-06 recovered in the stored samples after the various storage intervals, as well as the procedural recoveries from samples freshly fortified at the respective sampling points.

Table 6.1-32 Stability of M-04, M-05 and M-06 residues in various matrices following storage at -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (%)
Metabolite M-04			
Sunflower seed		0 (control)	Not detected above LOQ
Sunflower seed	0.1	0	93, 93, 94, 81, 87 **[Mean = 90%]**
Sunflower seed	0.1	30	88, 88, 83 **[Mean = 86%]**
Sunflower seed	0.1	97	78, 74, 75 **[Mean = 76%]**
Sunflower seed	0.1	163	83, 87, 95 **[Mean = 88%]**
Sunflower seed	0.1	183	88, 98, 104 **[Mean = 97%]**
Sunflower seed	0.1	387	107, 107 **[Mean = 107%]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (%)
Sunflower seed	0.1	568	92, 93, 91 **[Mean = 92%]**
Dry bean seed	-	0 (control)	Not detected above LOQ
Dry bean seed	0.1	0	93, 82, 100, 96 **[Mean = 93%]**
Dry bean seed	0.1	32	93, 90, 86 **[Mean = 90%]**
Dry bean seed	0.1	96	93, 92, 95 **[Mean = 93%]**
Dry bean seed	0.1	182	88, 90 **[Mean = 89%]**
Dry bean seed	0.1	392	96, 100, 98 **[Mean = 98%]**
Dry bean seed	0.1	573	89, 105 **[Mean = 97%]**
Cucumber fruit	-	0 (control)	Not detected above LOQ
Cucumber fruit	0.1	0	95, 102, 95, 94, 87 **[Mean = 95%]**
Cucumber fruit	0.1	30	96, 96, 99 **[Mean = 97%]**
Cucumber fruit	0.1	93	102, 101 **[Mean = 102%]**
Cucumber fruit	0.1	178	98, 95, 95 **[Mean = 96%]**
Cucumber fruit	0.1	385	99, 92, 91 **[Mean = 95%]**
Cucumber fruit	0.1	576	100, 98, 105 **[Mean = 101%]**
Strawberry fruit	-	0 (control)	Not detected above LOQ
Strawberry fruit	0.1	0	98, 96, 99, 97, 97 **[Mean = 97%]**
Strawberry fruit	0.1	30	91, 91, 80 **[Mean = 87%]**
Strawberry fruit	0.1	98	110, 105, 113 **[Mean = 109%]**
Strawberry fruit	0.1	182	91, 88, 94 **[Mean = 91%]**
Strawberry fruit	0.1	386	91, 85, 91 **[Mean = 89%]**
Strawberry fruit	0.1	567	83, 87 **[Mean = 85%]**
Barley grain	-	0 (control)	Not detected above LOQ
Barley grain	0.1	0	104, 97, 101, 93, 88 **[Mean = 97%]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (%)
Barley grain	0.1	31	92, 85, 82 **[Mean = 86%]**
Barley grain	0.1	91	92, 89, 92 **[Mean = 91%]**
Barley grain	0.1	183	86, 87, 86 **[Mean = 86%]**
Barley grain	0.1	391	100, 92, 90 **[Mean = 94%]**
Barley grain	0.1	573	96, 102, 105 **[Mean = 101%]**
Metabolite M-05			
Sunflower seed	-	0 (control)	Not detected above LOQ
Sunflower seed	0.1	0	93, 96, 96, 96, 98 **[Mean = 96%]**
Sunflower seed	0.1	30	88, 83, 88 **[Mean = 86%]**
Sunflower seed	0.1	97	84, 83, 87 **[Mean = 85%]**
Sunflower seed	0.1	183	92, 92, 93 **[Mean = 92%]**
Sunflower seed	0.1	391	99, 101, 90 **[Mean = 97%]**
Sunflower seed	0.1	568	88, 99, 102 **[Mean = 96%]**
Dry bean seed	-	0 (control)	Not detected above LOQ
Dry bean seed	0.1	0	93, 92, 91, 97 **[Mean = 93%]**
Dry bean seed	0.1	32	93, 90, 90 **[Mean = 91%]**
Dry bean seed	0.1	96	95, 95, 95 **[Mean = 95%]**
Dry bean seed	0.1	182	92, 87, 85 **[Mean = 88%]**
Dry bean seed	0.1	392	105, 102, 96 **[Mean = 101%]**
Dry bean seed	0.1	573	95, 90, 76 **[Mean = 87%]**
Cucumber fruit	-	0 (control)	Not detected above LOQ
Cucumber fruit	0.1	0	91, 105, 100, 98 **[Mean = 99%]**
Cucumber fruit	0.1	30	97, 93, 107 **[Mean = 99%]**
Cucumber fruit	0.1	93	99, 99, 102 **[Mean = 100%]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (%)
Cucumber fruit	0.1	178	97, 95, 96 **[Mean = 96%]**
Cucumber fruit	0.1	385	108, 110, 109 **[Mean = 109%]**
Cucumber fruit	0.1	576	97, 99, 96 **[Mean = 97%]**
Strawberry fruit	-	0 (control)	Not detected above LOQ
Strawberry fruit	0.1	0	110, 104, 95, 104, 88 **[Mean = 100%]**
Strawberry fruit	0.1	30	106, 102, 102 **[Mean = 103%]**
Strawberry fruit	0.1	98	109, 101, 100 **[Mean = 103%]**
Strawberry fruit	0.1	182	96, 94, 86 **[Mean = 92%]**
Strawberry fruit	0.1	386	105, 106, 73 **[Mean = 95%]**
Strawberry fruit	0.1	567	87, 93, 90 **[Mean = 90%]**
Barley grain	-	0 (control)	Not detected above LOQ
Barley grain	0.1	0	84, 85, 88, 85, 84 **[Mean = 85%]**
Barley grain	0.1	31	94, 83, 87 **[Mean = 88%]**
Barley grain	0.1	91	102, 102, 108 **[Mean = 104%]**
Barley grain	0.1	183	96, 88, 88 **[Mean = 91%]**
Barley grain	0.1	391	86, 81, 85 **[Mean = 84%]**
Barley grain	0.1	573	100, 73, 96 **[Mean = 90%]**
Metabolite M-06			
Barley grain	-	0 (control)	Not detected above LOQ
Barley grain	0.1	0	80, 80, 99, 95, 93 **[Mean = 89%]**
Barley grain	0.1	31	84, 73, 70 **[Mean = 76%]**
Barley grain	0.1	63	93, 88, 86 **[Mean = 89%]**
Barley grain	0.1	91	90, 82, 84 **[Mean = 85%]**
Barley grain	0.1	183	95, 84, 81 **[Mean = 87%]**

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (%)
Barley grain	0.1	391	88, 92, 83 **[Mean = 88%]**
Barley grain	0.1	573	104, 98, 82 **[Mean = 95%]**

III. CONCLUSION

Representative plant commodities (sunflower seed, dry bean seed, cucumber, strawberry, and barley grain) were fortified at 0.1 mg/kg with M-04 and M-05 (and M-06 for barley grain, only). The metabolites M-04 and M-05 were fortified in wheat matrices only. The fortified samples were stored at low temperatures at -18ºC and analysed at set intervals. The recoveries show that residues of M-04, M-05 and M-06 were stable for up to 18 months in the tested commodities.

The study was previously considered to be acceptable during the first EU review process for inclusion of fluopicolide on Annex I. The study complies with the current testing requirements specified within OECD 506. On this basis, the study is considered to remain acceptable and support the reported frozen storage stability periods for each of the tested compounds within the respective plant matrices.

Assessment and conclusion by applicant:

Residues of fluopicolide, M-04 and M-05 are stable within sunflower seed (high oil matrix), dry bean seed (high protein matrix), barley grain (high starch matrix), strawberries (high acid matrix) and cucumber (high water matrix) for a period of up to 18 months (at < -18 ºC). Metabolite M-06 was also demonstrated to be stable within barley grain (high starch matrix for a period of up to 18 months (at < -18 ºC).

This is an interim report, the full storage period covering 24 months in the respective commodities will be provided when the study is finalized.

Data Point:	KCA 6.1/08
Report Author:	[redacted]
Report Year:	2020
Report Title:	Report amendment no. 1 to final report - Residue analytical method 01592 and short term storage stability of fluopicolide (AE C638206) and its metabolite BAM (AE C653711) in/on honey by HPLC-MS/MS
Report No:	S19-00989
Document No:	M-680827-02-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC Guidance document on residue analytical methods, SANCO/825/00/rev. 8.1, European Commission, Directorate General Health and Consumer Protection 16/11/2010 European Commission Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414, SANCO/3029/99 rev. 4, 11/07/00 OECD 506, 2007: OECD Guideline for the Testing of Chemicals – Stability of Pesticide Residues in Stored Commodities SANTE/11956/2016 rev.9
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

Samples of honey were fortified (0.1 mg/kg = 10xLOQ) with either fluopicolide or M-01 and stored deep-frozen (at ≤ -18°C) for a period of 6 months. The samples were analysed after nominal storage intervals of 0, 30, 87, and 183 days, using method 01592 (an HPLC-MS/MS method, which was validated within the same report).

The mean recovery rates were 109% for fluopicolide in honey and 99% for metabolite M-01 in honey.

Altogether, the study results demonstrate that the residues of the analytes are stable in honey for at least 6 months under deep-freezer storage conditions (≤-18°C).

The stability of fluopicolide and metabolite M-01 stock solutions in acetonitrile and in mixed secondary standard solutions in acetonitrile was tested over a period of 141 days after storage of the standard solutions at 1–10 °C under dark conditions. The analytes were stable in the stock and secondary standard solutions when stored at 1–10 °C under dark conditions. The stability of the analytes in the final extracts was checked for the sample material honey. Residues of all analytes were stable over a time period of 8 days after storage of the final extracts at 1–10 °C under dark conditions.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	• Fluopicolide (FLC) • Metabolite M-01
	Batch no.:	• MOY4627 (FLC) • 08018ET (M-01)
	Active Ingredient / Purity:	• MOY4627 (99.2%) • 08018ET (96.2%)
	Storage:	• Fluopicolide: ≤ + 10 °C (dark, dry) • Metabolite M-01: ≤ + 10 °C (dark, dry)
	Expiry date:	• MOY4627 (Jul 2026) • 08018ET (Aug 2020)
2.	**Test commodity:**	Honey

B. STUDY DESIGN AND METHODS

Study design:

Aliquots of homogenised matrix material were transferred into a plastic tube with screw cap and fortified with the test items. For storage samples the analytes were fortified separately, while concurrent recovery samples were prepared by fortifying all analytes jointly as a mix. The storage samples were fortified with either 0.1 mg/kg fluopicolide or 0.1 mg/kg M-01, corresponding to the 10xLOQ level for each of the analytes.

At time zero, five spiked samples per analyte and two control samples were analysed on day 0 (zero-time analysis).

After 1 month (30 days), 3 months (87 days) and 6 months (183 days) of storage (deep-frozen at ≤ -18°C), three fortified samples per analyte and one control sample were removed from the deep-freezer and allowed to reach room temperature. Subsequently, two blank samples of honey were fortified with a mix of the analytes to determine the concurrent recoveries (fortification levels were at the same magnitude as the spiked storage samples). These samples were extracted and analysed concurrently with the remaining (unfortified) control samples and the spiked storage samples.

The stability of residues of all analytes in the final extract was determined after approximately one week for honey at the 0.10 mg/kg level (stored at 1 °C to 10 °C under dark conditions).

The stability of the standard solutions was also checked. The stock solutions and mixed secondary standard solutions prepared in the respective solvents (acetonitrile) were stored at 1 °C to 10 °C for 141 days in the dark, which was sufficient to cover the length of time they were used in this study (i.e. 97 days). After this time freshly prepared dilutions of the stored solutions were compared to freshly prepared dilutions of freshly prepared solutions by triplicate injection. One mass transition per analyte was evaluated.

Analytical Part:

Residues of fluopicolide and M-01 were analysed within the samples according to the following method:

Method	01592
Extraction	Mixture of acetone/water (1/1, v/v).
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide and M-01 in honey)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to assess the accuracy of the residue analyses, recoveries were determined by analysing freshly fortified samples alongside the stored fortified samples. At all storage intervals except for day 0, two concurrent recoveries were determined at a level of 0.10 mg/kg. No additional concurrent recoveries were determined on day 0, since there were five freshly fortified storage samples. Analysis was performed within 24 hours after extraction. The procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte / matrix combination. These procedural results demonstrate acceptable method performance and support the analytical results obtained for the fortified deep-frozen samples. The results are presented in the table below:

Table 6.1- 33 Summary of concurrent recoveries of fluopicolide and M-01 from honey.

Matrix	Spike level (mg/kg)	Storage interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean
Fluopicolide					
Honey	0.1	30	2	100, 105	103
		87	2	109, 110	110
		183	2	107, 109	108
Metabolite M-01 (BAM)					
Honey	0.1	30	2	106, 113	110
		87	2	107, 111	109
		183	2	98, 99	99

The above results are closely aligned with the validation data generated as part of the method validation phase, which indicates that the results obtained as part of the storage stability study are reliable for each of the tested time-points.

II. RESULTS AND DISCUSSION

The following table shows the levels obtained for fluopicolide and M-01 (initially fortified at 0.1 mg/kg, respectively) when stored within honey under deep frozen conditions for a period of up to 6 months. The initial honey samples were analysed and confirmed to have no residues of fluopicolide or M-01 above the limit of detection.

Table 6.1- 34 Residue stability of fluopicolide and M-01 in honey following storage at ≤ -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Fluopicolide				
Honey	0.1	0	112; 110; 111; 110; 109	110
Honey	0.1	30	102; 104; 101	102
Honey	0.1	87	104; 107; 108	106
Honey	0.1	183	109; 110; 109	109
Metabolite M-01 (BAM)				
Honey	0.1	0	100; 102; 101; 101; 104	102
Honey	0.1	30	116; 104; 100	107
Honey	0.1	87	102; 104; 101	102
Honey	0.1	183	105; 98; 95	99

III. CONCLUSION

All method validation data are in compliance with the guideline requirements for pre-registration methods SANCO/3029/99 rev. 4 and for post registration monitoring and control methods SANCO/825/00, rev. 8.1.

After a deep-freezer storage (≤-18°C) period of about 6 months, the mean recovery rates from the stored samples were 109% for fluopicolide in honey and 99% for AE C653711 in honey. Furthermore, the mean concurrent recoveries of all investigated days of storage determined from freshly fortified samples were in a range of 103-110% for fluopicolide in honey and in a range of 99-110% for M-01 in honey.

All analytes can be considered stable in the investigated matrices under deep-freezer storage conditions (≤-18°C) for at least 6 months.

Assessment and conclusion by applicant:

Fluopicolide and the metabolite M-01 are stable in honey matrices under deep-freezer storage conditions (≤-18°C) for at least 6 months.

Data Point:	KCA 6.1/09
Report Author:	[redacted]
Report Year:	2020
Report Title:	Storage stability of AE B102859 in/on plant matrices for 24 months
Report No:	P642160508
Document No:	M-681941-01-1
Guideline(s) followed in study:	Guideline OCSPP 860.1380: Storage Stability Data OECD (2007). Guidance for the Testing of Chemicals. Stability of Pesticide Residues in Stored Commodities. 506
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

Samples of sunflower seed, dry bean seed, grapes, lettuce, and barley grain were fortified (0.1 mg/kg = 10xLOQ) with M-09 and stored deep-frozen (at ≤ -18°C) for a period of up to 24 months. The samples were analysed after nominal storage intervals of 0, 30, 90, 180, 540, and 720 days, using method 01209/M001 (an HPLC-MS/MS method).

Altogether, the study results demonstrate that the residues of M-09 are stable in sunflower seed, dry bean seed, grapes, lettuce, and barley grain, for at least 24 months under deep-freezer storage conditions (≤-18°C).

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** Metabolite M-09
   Batch no.: U03470
   Active Ingredient / Purity: 99.9%
   Storage: Not stated
   Expiry date: November 2020
2. **Test commodity:** Sunflower seed, dry bean seed, grapes, lettuce, and barley grain

B. STUDY DESIGN AND METHODS

Study design:

Aliquots of homogenised matrix material were transferred into a plastic tube with screw cap and fortified with the test items. For storage samples the analytes were fortified separately, while concurrent recovery samples were prepared by fortifying all analytes jointly as a mix. The storage samples were fortified with 0.1 mg/kg M-09

At time zero, five spiked samples per analyte and two control samples were analysed on day 0 (zero-time analysis).

After 1 month (28 days), 3 months (96 days), 6 months (176 days), 18 months (545 days), and 24 months (722 days) of storage (deep-frozen at ≤ -18°C), 3 - 5 fortified samples per analyte and one control sample were removed from the deep-freezer and allowed to reach room temperature. Subsequently, two blank samples of honey were fortified with a mix of the analytes to determine the concurrent recoveries (fortification levels were at the same magnitude as the spiked storage samples). These samples were extracted and analysed concurrently with the remaining (unfortified) control samples and the spiked storage samples.

Analytical Part:

Residues of M-09 were analysed within the samples according to the following method:

Method	01209/M001
Extraction	Extracted with acidified water and acetone – solution was separated from the solid material by centrifugation.
Detection	HPLC/MS/MS
LOQ	0.01 mg/kg (for M-09 in sunflower seed, dry bean seed, grapes, lettuce, and barley grain).

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

Freshly fortified specimens with a nominal concentration of 0.1 mg/kg were analysed concurrently with each set of stored specimens. The results of these procedural recoveries are presented in the following tables for each of the tested matrices. The procedural recoveries meet the acceptability criteria; the mean recoveries are within the range 70 - 110% for each analyte /matrix combination and the %RSD values are <20% (where applicable).

Table 6.1- 35 Summary of concurrent recoveries of fluopicolide and M-01 from honey.

Sample	Date of extraction (yyyy-mm-dd)	Storage interval (days)		Concurrent recoveries (%)	
		Nominal	Actual	Fortification level = 0.01 mg/kg	Fortification level = 0.1 mg/kg
Sunflower seed	2017-03-23	0	0	84, 86 [Mean = 85]	88, 94 [Mean = 91]
	2017-04-20	30	28	-	88, 96 [Mean = 92]
	2017-06-27	90	96	-	90, 93 [Mean = 92]
	2017-09-15	180	176	-	75, 81 [Mean = 78]
	2018-09-19	540	545	-	96, 99 [Mean = 98]
	2019-03-15	720	722	-	73, 83 [Mean =78]
Dry bean seed	2017-03-23	0	0	93, 101 [Mean =97]	92, 93 [Mean = 93]
	2017-04-20	30	28	-	89, 95 [Mean = 92]
	2017-06-27	90	96	-	94, 103 [Mean = 99]
	2017-09-15	180	176	-	89, 91 [Mean = 90]
	2018-09-19	540	545	-	98, 98 [Mean = 98]
	2019-03-15	720	722	-	85, 91 [Mean = 88]
Grapes	2017-03-22	0	0	86, 95 [Mean = 91]	94, 98 [Mean = 96]
	2017-04-19	30	28	-	100, 99 [Mean = 100]
	2017-06-26	90	96	-	98, 96 [Mean = 97]
	2017-09-14	180	176	-	86, 108 [Mean = 97]
	2018-09-18	540	545	-	100, 100 [Mean = 100]
	2019-03-14	720	722	-	95, 92 [Mean = 94]

Sample	Date of extraction (yyyy-mm-dd)	Storage interval (days)		Concurrent recoveries (%)	
		Nominal	Actual	Fortification level = 0.01 mg/kg	Fortification level = 0.1 mg/kg
Lettuce	2017-03-22	0	0	90, 95 [Mean = 93]	93, 104 [Mean = 99]
	2017-04-19	30	28	-	98, 100 [Mean = 99]
	2017-06-26	90	96	-	93, 105 [Mean = 99]
	2017-09-14	180	176	-	92, 80 [Mean = 86]
	2018-09-18	540	545	-	98, 98 [Mean = 98]
	2019-03-14	720	722	-	102, 97 [Mean = 100]
Barley grain	2017-03-23	0	0	93, 92 [Mean = 93]	90, 92 [Mean = 91]
	2017-04-20	30	28		89, 86 [Mean = 88]
	2017-06-27	90	96	-	96, 99 [Mean = 98]
	2017-09-15	180	176	-	97, 93 [Mean = 95]
	2018-09-19	540	545		97, 100 [Mean = 99]
	2019-03-15	720	722	-	81, 83 [Mean = 82]

The above results are closely aligned with the validation data generated as part of the method validation phase, which indicates that the results obtained as part of the storage stability study are reliable for each of the tested time-points.

II. RESULTS AND DISCUSSION

The following table shows the levels obtained for M-09 (initially fortified at 0.1 mg/kg, respectively) when stored within honey under deep frozen conditions for periods of up to 24 months. The initial samples were analysed and confirmed to have no residues of M-09 above the limit of detection.

Table 6.1- 36 Residue stability of M-09 in various plant matrices following storage at ≤ -18°C

Commodity	Storage period (days)	Residue level in stored samples		
		Recovery (mg/kg)	Recovery (%)	Average (%)
Sunflower seed	0	0.099 0.094 0.100 0.095 0.087	99 94 100 95 87	95
	28	0.093 0.083 0.084	93 83 84	87
	96	0.081 0.077 0.087	81 77 87	82
	176	0.073 0.081 0.082	73 81 82	79
	545	0.085 0.083 0.083	85 83 83	84
	722	0.079 0.071 0.073	79 71 73	74
Dry bean seed	0	0.095 0.093 0.094 0.091 0.091	95 93 94 91 91	93
	28	0.083 0.091 0.095	83 91 95	90
	96	0.099 0.097 0.104	99 97 104	100
	176	0.094 0.096 0.094	94 96 94	95
	545	0.095 0.097 0.094	95 97 94	95
	722	0.071 0.081 0.083	71 81 83	78

Commodity	Storage period (days)	Residue level in stored samples		
		Recovery (mg/kg)	Recovery (%)	Average (%)
Grapes	0	0.100 0.099 0.099 0.101 0.102	100 99 99 101 102	100
	28	0.100 0.103 0.096	100 103 96	100
	96	0.099 0.097 0.096	99 97 96	97
	176	0.090 0.104 0.083	90 104 83	92
	545	0.098 0.098 0.099	98 98 99	98
	722	0.091 0.092 0.103	91 92 103	95
Lettuce	0	0.095 0.098 0.099 0.101 0.105	95 98 99 101 105	100
	28	0.102 0.100 0.098	102 100 98	100
	96	0.099 0.094 0.092	99 94 92	96
	176	0.085 0.094 0.092	85 94 92	90
	545	0.096 0.095 0.098	96 95 98	96
	722	0.095 0.089 0.094	95 89 94	93

Commodity	Storage period (days)	Residue level in stored samples		
		Recovery (mg/kg)	Recovery (%)	Average (%)
Barley grain	0	0.093 0.095 0.089 0.093 0.084	93 95 89 93 84	91
	28	0.088 0.093 0.089	88 93 89	90
	96	0.086 0.086 0.088	86 86 88	87
	176	0.080 0.076 0.080	80 76 80	79
	545	0.078 0.075 0.074	78 75 74	76
	722	0.090 0.091 0.091	90 91 91	91

III. CONCLUSION

All method validation data are in compliance with the guideline requirements for pre-registration methods SANCO/3029/99 rev. 4 and for post registration monitoring and control methods SANCO/825/00, rev. 8.1.

After a deep-freezer storage (≤-18°C) period of about 24 months, the mean recovery rates from the stored samples were >70% for M-09 in the various plan matrices (sunflower seed, dry bean seed, grapes, lettuce, and barley grain). Furthermore, the mean concurrent recoveries of all investigated days of storage determined from freshly fortified samples were in a range of 70-110%.

M-09 can be considered stable in the investigated matrices under deep-freezer storage conditions (≤-18°C) for at least 24 months.

Assessment and conclusion by applicant:

Fluopicolide and the metabolite M-01 are stable in sunflower seed, dry bean seed, grapes, lettuce, and barley grain, under deep-freezer storage conditions (≤-18°C) for at least 24 months.

Storage stability of residues in plant sample extracts

The storage stability of pesticide residues in sample extracts is generally checked during the development of the necessary analytical residue methods. Since the validity of such methods depends on factors such as reproducibility and the possibility for interruption during the work-up process, it has to be concluded that the stability during a possible storage of samples in extracts is always guaranteed. Additionally, when conducting residue analysis on regular samples, the whole analytical procedure is routinely monitored by performing concurrent recovery experiments with each sample set.

The following studies are currently in progress and will be submitted at the indicated timepoints:

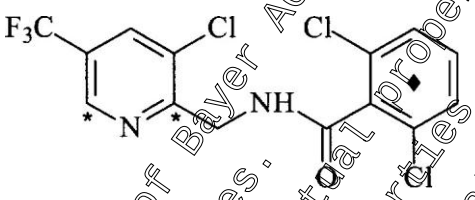
Table 6.1- 37: Further studies to be submitted

Dossier node	Draft title	Study ID	Planned submission
KCA 6.1	Storage Stability of Fluopicolide (AE C638206) and its metabolites BAM (AE C653711) and PCA (AE C657188) in/on Sunflower and Dry bean during freezer storage for up to 24 months	EE18-002	Interim: November 2020 Final: 2nd Quarter 2021
KCA 6.1	Storage Stability of Fluopicolide metabolites AE C653378 and AE C656948-methyl-sulfoxide (AE 1344122) in/on Sunflower, Dry bean, Cucumber, Strawberry and Barley and AE C643890 in/on Barley during freezer storage for up to 24 months	EE18-001	Interim: August 2020 Final: 2nd Quarter 2021

CA 6.2 Metabolism, distribution and expression of residues

The metabolism of fluopicolide in plant and animal matrices was investigated using [^{14}C]-pyridinyl- and [^{14}C]-phenyl- labelled fluopicolide. The structure of fluopicolide and position of the radiolabels are given in Figure 6.2-1 below.

Figure 6.2-1: [^{14}C] label positions of fluopicolide



♦ → = Position of radiolabel in [U-^{14}C-pheny]-Fluopicolide
* → = Position of radiolabel in [2,6-^{14}C-pyridinyl]-Fluopicolide

CA 6.2.1 Metabolism, distribution and expression of residues in plants

Studies on the metabolism and distribution of fluopicolide applied as a foliar spray on potatoes, grapes and lettuce (covering three different crop groups: root crops, fruit crops and leafy crops) were submitted and reviewed for the first inclusion of fluopicolide into Annex I of Council Directive 91/414/EEC. These studies were deemed to be acceptable and the plant residue definition for risk assessment and monitoring were set as follows (SANCO/10164/09):

Plant residue definition for monitoring:	Fluopicolide
Plant residue definition for risk assessment:	1. Fluopicolide
	2. 2,6-dichlorobenzamide (metabolite M-01, BAM)

The review of fluopicolide MRLs under article 12(1) of Regulation (EC) No 396/2005 did not include the consideration of additional plant metabolism studies, however a new metabolism study for seed oilseed rape has been provided within this dossier. This new study is submitted here to support the representative use on oilseed rape, applied as a seed treatment.

The plant metabolism studies available for fluopicolide are listed in the following table. In this renewal dossier, updated summaries are provided for the following listed studies.

Table 6.2.1- 1 A summary of the available fluopicolide crop metabolism studies at renewal.

Report reference	Author, Year	Crop Category	Crop	Application	Fluopicolide label	Evaluated in the original inclusion	New data to support the renewal
M-241268-02-1	[redacted] 2004	Fruit crop	Grapes	Foliar	[U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-Fluopicolide	✓	
M-241267-03-1	[redacted] 2004	Root and tuber crop	Potato	Foliar	[U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-Fluopicolide	✓	
M-241269-02-1	[redacted] 2004	Leafy crop	Lettuce	Foliar Soil drench	[U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-Fluopicolide	✓	
M-358357-01-1	[redacted], 2009	Oilseed crop	Oilseed rape	Seed treatment	[U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-Fluopicolide		✓

The following applications were made for the foliar treated crops in the respective studies for each of the radiolabels (U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-fluopicolide):

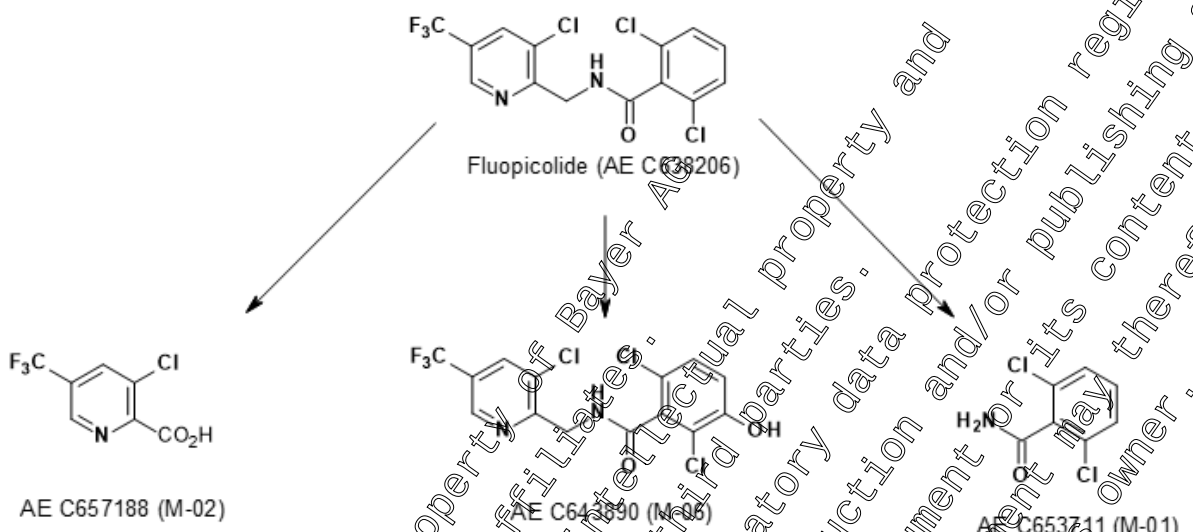
- Grapes were treated with three foliar application at rates of 0.12–0.17 kg a.i./ha and in additional trials at approximately 10-times the notified rate.
- Potatoes were treated two times at a rate of 0.2 kg a.i./ha.
- Lettuce was treated with two foliar applications at a rate of 0.2 kg a.i./ha.

In all three foliar studies, radioactive residues were mainly found in the surface wash and in extracts of the treated samples. Levels of bound residues were low. Metabolism of fluopicolide was shown to be moderate. In directly treated plant parts mainly fluopicolide was found besides low concentrations of the metabolites M-01, M-02 and M-06 (all below 2% of TRR). Higher levels of metabolites were found in lettuce after soil drench application and in potato tubers (maximal 25% of M-01, 12% of M-02 and 2% of M-06).

The following metabolic pathway was proposed:

- Hydrolysis of the urea bond of fluopicolide to form metabolites M-01 and M-02.
- Hydroxylation in position 3 of the phenyl ring to form metabolite M-06.

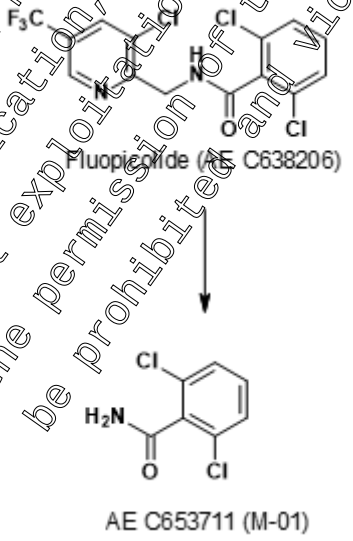
The common metabolic pathway for plants treated with foliar and soil drench applications of fluopicolide, is as follows:



These studies are therefore considered to support the proposed representative foliar uses on potatoes and lettuce, and the soil treatment use for cucumbers.

In a new study, oilseed rape was seed treated at a rate of approximately 200g a.i./ha (20 g a.i./kg seed) for each of the radiolabels [U-^{14}C-phenyl]- and [2,6-^{14}C-pyridyl]-fluopicolide). The only observed metabolic reaction was the cleavage of fluopicolide to M-01. Label specific metabolites of the 2,6-^{14}C-pyridyl label were not detected in the raw agricultural commodities. Therefore, it was assumed, that M-01 was most probably formed in the soil.

The metabolic pathway for oilseed rape which has been seed treated with fluopicolide, is as follows:



Data already evaluated during the first EU review process for inclusion on Annex I.

Grapes

Data Point:	KCA 6.2.1/02
Report Author:	[redacted]
Report Year:	2004
Report Title:	Metabolism of [U-14C-phenyl]- and [2,6-14C pyridinyl]-AE C638206 in vines (Amended report replacing report CU99E503, Document B004329)
Report No:	B004860
Document No:	M-241268-02-1
Guideline(s) followed in study:	EU (=EEC): Directive 96/68/EC; USEPA (=EPA): OPPTS 860.1300
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

This study was conducted to determine the extent and nature of the metabolic breakdown of [U-^{14}C-phenyl]- and [2,6-^{14}C pyridinyl]-AE C638206 (^{14}C-labelled fluopicolide) in grape vines treated under a typical field application pattern.

Grapevines (var. Sunbelt and Niagara) were grown under greenhouse conditions in pots. The grapevines were divided into seven groups before treatment. Five groups were designated for treatment and two groups were maintained as control vines. One group was treated with [U-^{14}C-phenyl]-AE C638206 at the 1X rate, one group was treated with [2,6-^{14}C-pyridinyl]-AE C638206 at the 1X rate, two groups were treated with [U-^{14}C-phenyll-AE C638206 at the 10X rate, and one group was treated with [2,6-^{14}C pyridinyl-AE C638206 at the 10X rate. Each treatment group was treated three times. The first treatment was between BBCH growth stages 55 and 57, the second treatment was between BBCH growth stages 71 and 73, and the third treatment was 21 to 28 days prior to normal harvest. The nominal application rate for the 1X rate was 167 g ai/ha at the first application and 116.5 g ai/ha at each subsequent application for a total seasonal application rate of 400 g ai/ha. Immature grapevine samples were analysed on Day Zero (immediately post-treatment) and Day 27 and 28 (immediately prior to the second treatment), as an aid to identification of residues at final harvest. The raw agricultural commodity, grapes, was analysed in duplicate at maturity (Day 111 and Day 112). Grapevine samples were collected at harvest as a potential aid to metabolite identification and are not a raw agricultural commodity of grapes.

The residue in the grape and foliage samples was recovered by an acetonitrile wash and an acetonitrile extraction. Metabolites in the extractable residue were identified and quantified by TLC against a standard mix. Filter bound residues were determined by combustion analysis.

Good agreement was obtained throughout the results from the duplicate samples of grape and foliage samples. The vast majority of residue at all timepoints was solvent extractable.

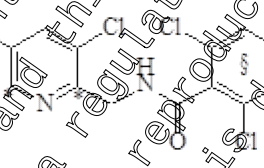
Chromatography results of the individual extracts derived from the duplicate samples showed excellent correlation. Analysis of the extractable residues showed a qualitatively similar metabolic profile in all grape vine tissues. The principle residues were identified as fluopicolide (AE C638206). Minor metabolites M-01 (AE C653711) and M-06 (AE C643890) were identified in phenyl-label treated grapes. One minor metabolite, M-02 (AE C657188), was identified in the pyridinyl-label treated grapes.

Radioactive residues in grapes treated with [^{14}C]-AE C638206 were principally extractable with acetonitrile. Greater than 89% of the total radioactive residue was identified in the samples at final harvest. The majority of the residue in the raw agricultural commodity consists of fluopicolide (AE C638206), with minor amounts of M-01 (AE C653711), M-02 (AE C657188), and M-06 (AE C643890). No other single metabolite comprised more than 1% of the total residue in any matrix. The metabolic profile of fluopicolide (AE C638206) in grapes was found to be similar to that reported in other plant systems.

I Materials and Methods

A. Materials

1. Test Material:

Chemical structure	 Label positions: § = [U-^{14}C-phenyl]-Fluopicolide * = [2,6-^{14}C-pyridyl]-Fluopicolide
Preferred IUPAC name	2,6-dichloro-N-[(3-chloro-5-(trifluoromethyl)-2pyridyl)methyl]benzamide
Radiolabelled test material	[U-^{14}C-phenyl]-Fluopicolide [2,6-^{14}C-pyridyl]-Fluopicolide
Lot No.	[U-^{14}C-phenyl]-Fluopicolide = 902AE-1 [2,6-^{14}C-pyridyl]-Fluopicolide = 903AE-1
Specific radioactivity	[U-^{14}C-phenyl]-Fluopicolide = 159 µCi/mg [2,6-^{14}C-pyridyl]-Fluopicolide = 144 µCi/mg
Radiochemical purity	[U-^{14}C-phenyl]-Fluopicolide = 99.6% by HPLC [2,6-^{14}C-pyridyl]-Fluopicolide = 99.5% by HPLC
Preparation of application solution	The test substance was applied as a solution in water.

2. Soil: The soil characteristics were not described in the study report.

3. Plant: Grapevines (var. Sunbelt and Niagara)

B. Study Design

1. Experimental conditions:

The experiment simulated agricultural practice of multiple foliar spray applications of fluopicolide to grapes during the growing period.

Grapevines (var. Sunbelt and Niagara) grown in pots were moved from an outdoor patio into the greenhouse between March 31 and April 6, 1999. Vines were treated at 110 or 112 days (Day Zero) before final harvest (BBCH 55-57), at 84 days before final harvest (BBCH 71-73), and at 21 days before final harvest. Plant samples for Day Zero analyses were harvested immediately following the first treatment after the application dried. Intermediate harvests were performed on May 12 and May 13, 1999, prior to the second treatment. Final harvest samples were harvested on August 4-5, 1999. The schedules of plant husbandry events and treatments, were recorded.

Grapevines were treated one time at a nominal rate of 167 g ai/ha with each label and twice at a nominal rate of 116.5 g ai/ha to give a total treatment rate of 400 g ai/ha for the 1X rate. Grapevines were treated one time at a rate of 1.67 kg ai/ha with each label and twice at a rate of 1.17 kg ai/ha to give a total treatment rate of 4.0 kg ai/ha for the rate. Plants were treated with phenyl labelled AE C638206 on Days 0, 28, and 91 (21-day PHI) with an appropriate amount of the respective formulation. Plants were treated with pyridinyl labelled fluopicolide (AE C638206) on Days 1, 27, and 90 (21 -day PHI) with an appropriate amount of the respective formulation. The material was applied as evenly as possible over the target leaf area using a disposable plastic, hand sprayer. The residue in the sprayer was sprayed onto the target area after the addition of a small quantity of tap water. To contain the spray during application, the floor and other parts of the plants were protected with a plastic covered plastic tray.

The actual application rates achieved are summarised in the following table.

Table 6.2.1- 2 AE C638206 Formulation Details

Application Number	Application	Radiolabel	Final specific activity (µCi/mg)	Application rate (g as/ha)
1X rate				
1	Foliar	U-^{14}C-phenyl	20.0	167
2	Foliar	U-^{14}C-phenyl	20.0	116
3	Foliar	U-^{14}C-phenyl	19.97	116
			Total rate	**399**
1	Foliar	2,6-^{14}C-pyridyl	22.2	169
2	Foliar	2,6-^{14}C-pyridyl	22.04	116
3	Foliar	2,6-^{14}C-pyridyl	22.02	116
			Total rate	**401**
10X rate				
1	Foliar	U-^{14}C-phenyl	20.0	1684
2	Foliar	U-^{14}C-phenyl	20.0	1169
3	Foliar	U-^{14}C-phenyl	19.97	1175
			Total rate	**4028**
1	Foliar	2,6-^{14}C-pyridyl	22.2	1691
2	Foliar	2,6-^{14}C-pyridyl	22.04	1116
3	Foliar	2,6-^{14}C-pyridyl	22.02	1181
			Total rate	**3988**

2. Sampling:
Immature grapevine samples were analysed on Day 0 (immediately post-treatment) and Day 27 and 28 (immediately prior to the second treatment), as an aid to identification of residues at final harvest. The raw agricultural commodity, grapes, was analysed in duplicate at maturity (Day 111 and Day 112). Grapevine foliage samples were collected at harvest as a potential aid to metabolite identification and are not a raw agricultural commodity of grapes.

C. Analytical Procedures
1. Extraction and fractionation:

All samples were immediately subjected to an acetonitrile wash on the day of sampling. Final harvest leaf and grape samples were then ground in a disk mill with dry ice after surface washing. Ground samples were returned to the freezer to allow the dry ice to sublime and for storage at 15 °C until analysis. Total radioactive residues in plant samples were determined by combustion of aliquots of the ground samples followed by liquid scintillation counting (LSC).

Day 0 and immature harvest samples were further extracted two times by maceration using an Ultra-Turrax mill with acetonitrile. Final harvest leaf and grape samples were extracted three times with acetonitrile. The final harvest grape extracts were placed into a separating funnel to separate the acetonitrile from an oily layer that formed during extraction. Where necessary acetonitrile washes and extracts were concentrated by rotary evaporation prior to analysis. Recoveries throughout the sample processing were generally good.

The radioactive content of extracts and concentrated extracts was determined by direct LSC and that of post-extraction residues by combustion followed by LSC.

Total radioactive residues in final harvest plant samples were determined by summing the radioactivity present in the surface wash and the radioactivity present in the ground samples determined by combustion of aliquots. The total residue in the Day 0 and immature harvest plant samples was determined by summing the surface wash, extractable residue and non-extractable residue in the initial extraction.

Each extract was sampled for LSC. Extracted fiber samples were analysed to determine the non-extractable residue by combustion.

2. Identification and characterisation:
Metabolites in the extractable extracts of final harvest samples containing significant residues were identified and quantified by comparison with authentic standards by thin layer chromatography (normal or reverse phase). The extractability and metabolic profiles were similar between the duplicate samples for each label tested. Reverse phase or normal phase TLC, depending on the radiolabel used provided confirmation of the metabolite identification.

3. Storage stability:
All extracts were stored at -15 °C or less prior to analysis. Analysis for the entire study was completed within 3 months of the final harvest.

II Results and Discussion

Good agreement was obtained throughout the results from the duplicate samples of grape and foliage samples. The vast majority of residue at all timepoints was solvent extractable. Mean results of residue levels and the extraction profiles at each timepoint are presented in the following tables.

Table 6.2.1- 3 Total Radioactive Residues and Extractability at Each Harvest (mean of duplicate values)

a) Phenyl

Timepoint	Rate	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0 Foliage(BBCH 55-57)	1X	32.294	97.2	31.384	2.7	0.854	0.2	0.056
	10X	338.816	99.1	336.176	0.7	2.079	0.3	0.562
Immature Foliage (Day 28, BBCH 71-73)	1X	23.636	72.5	17.464	23.8	5.339	3.8	0.833
	10X	269.456	92.0	247.502	6.8	18.689	1.3	3.266
Final Harvest (Day 112) Fruit	1X	1.265	62.5	0.786	33.2	0.424	4.3	0.055
	10X	9.955	78.9	7.864	18.8	1.856	2.4	0.235
Final Harvest (Day 112) Foliage	1X	15.498	49.5	7.722	43.0	6.575	7.6	1.201
	10X	154.455	70.1	108.342	na	na	29.9[1]	46.113[1]

b) Pyridyl

Timepoint	Rate	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0 Foliage(BBCH 55-57)	1X	32.609	97.9	31.936	1.8	0.571	0.4	0.103
	10X	382.420	96.9	370.238	3.1	11.871	0.1	0.311
Immature Foliage (Day 27, BBCH 71-73)	1X	19.225	77.4	14.891	18.1	3.473	4.5	0.861
	10X	270.160	93.3	252.128	5.7	15.272	1.1	2.760
Final Harvest (Day 111) Fruit	1X	1.040	46.1	0.480	48.0	0.499	6.0	0.063
	10X	10.942	73.4	8.059	23.1	2.503	3.5	0.380
Final Harvest (Day 111) Foliage	1X	23.878	51.0	12.162	42.3	10.080	6.8	1.636
	10X	181.054	74.8	134.299	na	na	25.2[1]	46.755[1]

[1] = Residue remaining after surface wash na = not analysed

No appreciable differences in total residues were observed between the phenyl-label treated vines and the pyridyl-label treated vines. The total residue in both treatment labels at each harvest and in each sample type (i.e. vine foliage and grapes) were very similar. In immature grape foliage, residues declined slightly between the initial treatment and just prior to the second treatment from *ca*. 32 mg/kg at Day 0 to *ca*. 21 mg/kg at Day 27-28 for the 1X rate. At final harvest, the mean residue in grapes (*ca*. 1 mg/kg) treated at the 1X rate was considerably lower than in the foliage (*ca*. 20 mg/kg).

The majority of residue in foliage was readily removed by surface washing with > 96% of the TRR removed at Day 0, 72.5 to 93.3% at Day 27-28 and 49.5 to 74.8% in mature foliage at Day 111-112. Subsequent acetonitrile extraction of the washed foliage removed virtually all the remaining residue, with <7% of the TRR remaining as non-extractable residue.

For the phenyl and pyridyl-label treated vines, total residues in grapes at final harvest were low in comparison to the foliage residues (1.265 and 1.040 mg/kg parent equivalents, respectively at the 1X rate, 9.955 and 10.942 mg/kg parent equivalents, respectively at the 10X rate). Acetonitrile surface washes removed a significant amount of the total residues (46.1 to 78.9% TRR). Subsequent acetonitrile extraction removed virtually all the remaining residue (18.8 to 48.0% TRR), with <6% of the TRR remaining as non-extractable residue.

Chromatography results of the individual extracts derived from the duplicate samples showed excellent correlation. The metabolic profiles of identified residues from the final harvest grapes are shown in the following tables. Values are quoted for combined surface wash and acetonitrile extracts in mg/kg parent equivalents and % of total radioactive residue (% TRR).

Table 6.2.1- 4 Identification of AE C638206 Metabolites in Grapes as % of Total Radioactive Residue (mean of duplicate values)

a) Phenyl label

Application Rate	Total Extracted		FLC (AE C638206)		M-01 (AE C653711)		M-06 (AE C643890)		% Total Identified
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
1X Rate	95.7	1.21	91.2	1.152	2.0	0.026	0.2	0.002	93.4
10X Rate	97.7	9.72	95.2	9.482	1.3	0.133	0.1	0.005	96.6

b) Pyridyl label

Application Rate	Total Extracted		FLC (AE C638206)		M-02 (AE C657188)		M-06 (AE C643890)		% Total Identified
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
1X Rate	94.1	0.979	87.4	0.910	2.3	0.024	nd	nd	89.7
10X Rate	96.5	10.562	93.3	10.227	0.7	0.065	nd	nd	94.0

mg/kg values are quoted as parent equivalents
nd = not detected

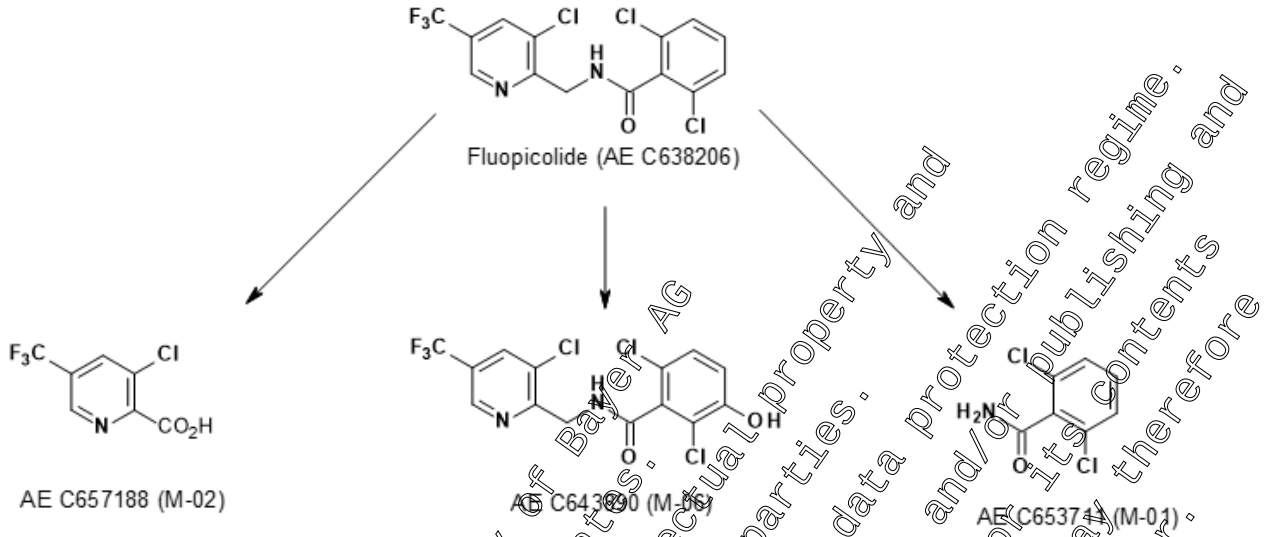
Analysis of the extractable residues showed a qualitatively similar metabolic profile in all grape vine tissues. The principle residues were identified as fluopicolide (AE C638206). The metabolites M-01 (AE C653711), 2%, 0.026 mg/kg at the 1X rate, and M-06 (AE C643890), 0.2%, 0.002 mg/kg at the 1X rate, were identified in minor amounts in phenyl-label treated grapes. One minor metabolite, AE C657188 (2.3%, 0.024 mg/kg at the 1X rate), was identified in the pyridyl label treated grapes.

Grapevine foliage samples were collected at harvest as a potential aid to metabolite identification and are not a raw agricultural commodity of grapes. Analysis of immature foliage identified the majority of the residues as M-02 (AE C638206).

III. Conclusions

Radioactive residues in grapevines treated with [^{14}C]-AE C638206 were principally extractable with acetonitrile, with only small quantities remaining unextracted (maximum in grapes at 1X rate 6% TRR, 0.055 mg/kg) at final harvest. Greater than 80% of the total radioactive residue was identified in the samples at final harvest. The majority of the residue in the raw agricultural commodity consists of fluopicolide (AE C638206), with minor amounts of M-01 (AE C653711), M-02 (AE C657188), and M-06 (AE C643890). No other single metabolite comprised more than 1% of the total residue in any matrix.

The metabolic profile of fluopicolide (AE C638206) in grapes was found to be similar to that reported in other plant systems.



Assessment and conclusion by applicant:

The study is acceptable and demonstrates the metabolic fate of fluopicolide within fruit commodities.

Potato

Data Point:	KCA 6.2.1/03
Report Author:	[redacted]
Report Year:	2005
Report Title:	Metabolism of [U-14C-phenyl]- and [2,6-14C pyridinyl]-AE C638206 in potatoes (amended report replacing report 502CUA, document B004859)
Report No:	B004913
Document No:	M-241267-03-1
Guideline(s) followed in study:	EU (=EEC): Directive 96/68/EC; USEPA (=EPA): OPPTS 860.1300
Deviations from current test guideline:	No deviations from the test guideline were noted with the study report.
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

This study was conducted to determine the extent and nature of the metabolic breakdown of [U- ^{14}C-phenyl]- and [2,6-^{14}C pyridinyl]-AE 0638206 in potatoes treated under a typical field application pattern.

Potatoes (var. Red Pontiac) were grown under field conditions in steel crop tanks. The potatoes were planted in 6 tanks before treatment. Five tanks were designated for treatment and one tank was maintained as an untreated control.

[U- ^{14}C -phenyl]-AE C638206 at the 1X rate, one tank was treated with [2,6- 140 pyridinyl]AE 0638206 at the 1X rate, one tank was treated with [U- ^{14}C-phenyl]-AE 0638206 at the 10X rate, and two tanks were treated with [2,6-^{14}C pyridinyl]-AE C638206 at the 10X rate. Each treatment tank was treated two times. The first treatment was between BBCH growth stages 31 and 33, and the second treatment was 20 days prior to normal harvest. The nominal application rate for the 1X rate was 200 g ai/ha at each application for a total seasonal application rate of 400 g ai/ha. The nominal application rate for the 10x rate was 2.0 kg ai/ha at each application for a total seasonal application rate of 4.00 kg ai/ha. Immature potato leaf samples were analysed on Day Zero (immediately post-treatment) and Day 41 (immature harvest), as an aid to identification of residues at final harvest. The raw agricultural commodity, potatoes, was analysed in duplicate at maturity (Day 69 and Day 70). Aerial plant part samples were collected at harvest as a potential aid to metabolite identification and are not a raw agricultural commodity of potatoes.

The residues in the potato foliage and tuber samples were recovered by an acetonitrile wash and an acetonitrile extraction. Metabolites in the extractable residue were identified and quantified by TLC or HPLC against a standard mix. Fiber bound residues were determined by combustion analysis.

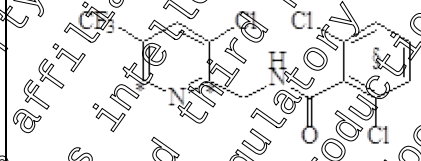
Good agreement was obtained throughout the results from the duplicate samples of potato foliage and tubers. Chromatography results of the individual extracts derived from the duplicate samples at each timepoint showed excellent correlation. Analysis of the extractable residues showed a qualitatively similar metabolic profile in all potato foliage and tuber tissues. The principle residues in potato tubers were identified as fluopicolide (AE C238206) and metabolites M-01 (AE C653711) and M-06 (AE 0643890) in phenyl-label treated potatoes and, AE 0238206 and metabolites M-02 (AE C657188) and M-06 (AE 0643890) in the pyridinyl label treated potatoes. The same metabolic profile was seen in the non-RAC potato foliage.

Radioactive residues in potatoes treated with [^{14}C]-AE 0638206 were principally removed by an acetonitrile surface wash and extractable with acetonitrile (84.4-89.4% TRR). Non-extractable residues (10.7-15.6% TRR) were released by acid hydrolysis to afford hydrolysates and hydrolyzed fiber residues of 5.9-8.7% TRR (0.004-0.007 ppm) and 4.96.9% TRR (0.003-0.006 ppm), respectively. Greater than 78% of the total radioactive residue was identified in the samples at final harvest. The majority of the residue in the potato tubers consisted of the parent compound, fluopicolide (AE 0638206), with significant amounts of M-01 (AE 0653711) and M-02 (AE 0657188) and minor amounts of M-06 (AE 0643890). No other single metabolite comprised more than 2% of the total residue in any matrix. The metabolic profile of fluopicolide (AE 0638206) in potatoes was found to be similar to that reported in other plant systems.

I Materials and Methods

A. Materials

1. Test Material:

Chemical structure	 Label positions: § = [U-^{14}C-phenyl]-Fluopicolide * = [2,6-^{14}C-pyridyl]-Fluopicolide
Preferred IUPAC name	2,6-dichloro-N-[(3-chloro-5-(trifluoromethyl)-2pyridyl)methyl]benzamide
Radiolabelled test material	[U-^{14}C-phenyl]-Fluopicolide [2,6-^{14}C-pyridyl]-Fluopicolide
Lot No.	[U-^{14}C-phenyl]-Fluopicolide = 902AE-1 [2,6-^{14}C-pyridyl]-Fluopicolide = 903AE-1
Specific radioactivity	[U-^{14}C-phenyl]-Fluopicolide = 159 µCi/mg [2,6-^{14}C-pyridyl]-Fluopicolide = 144 µCi/mg
Radiochemical purity	[U-^{14}C-phenyl]-Fluopicolide = 99.6% by HPLC [2,6-^{14}C-pyridyl]-Fluopicolide = 99.5% by HPLC
Preparation of application solution	The test substance was applied as a solution in water.

2. Soil: The soil characteristics were not described in the study report.

3. Plant: Potatoes (variety Red Pontiac)

B. Study Design

1. Experimental conditions:

The experiment simulated agricultural practice of multiple foliar spray applications of fluopicolide to potatoes during the growing

Potatoes (variety Red Pontiac) were planted in Tanks A, B and C in Field Cage 3 and tank D in the control field cage on March 19, 1999 and in Tanks A and B in Field-Cage 9 on March 22. Potatoes were treated at 69 days (Day Zero) before final harvest and at 20 days before final harvest. Plant samples for Day Zero analyses were harvested immediately following the first treatment after the application dried. immature harvests were performed on June 8, 1999. Final harvest samples were harvested on July 6-7, 1999. The schedules of plant husbandry events and treatments were recorded.

Potatoes were treated two times at a nominal rate of 200 g ai/ha with each label to give a total treatment rate of 400 g ai/ha for the IX rate. Potatoes plants were treated two times at a rate of 2.0 kg ai/ha with each label to give a total treatment rate of 4.0 kg ai/ha for the rate. All treatments were applied at the same growth stages. Plants were treated with phenyl labelled fluopicolide (AE 0638206) on Days 1 and 50 (20-day PHI) with an appropriate amount of the respective formulation. Plants were treated with pyridinyl labelled fluopicolide (AE 0638206) on Days 0 and 49 (20-day PHI) with an appropriate amount of the respective formulation. The actual application rates achieved are summarised in the following table.

Table 6.2.1- 5 AE C638206 Formulation Details

Treatment Number	Treatment Rate	Radiolabel	Final specific activity (µCi/mg)	Application rate (g as/ha)
1	1X	U-^{14}C-phenyl	40.00	203.8
2	1X	U-^{14}C-phenyl	39.92	203.0
			Total rate	**406.8**
1	10X	U-^{14}C-phenyl	40.00	2008.9
2	10X	U-^{14}C-phenyl	39.92	2028.9
			Total rate	**4037.8**
1	1X	2,6-^{14}C-pyridyl	40.00	202.9
2	1X	2,6-^{14}C-pyridyl	40.02	200.2
			Total rate	**403.1**
1	10X	2,6-^{14}C-pyridyl	40.00	1909.2
2	10X	2,6-^{14}C-pyridyl	39.92	2025.0
			Total rate	**3934.2**

2. Sampling:

Immature potato leaf samples were analysed on Day 0 (immediately post-treatment) and Day 41 (immature harvest), as an aid to identification of residues at final harvest. The raw agricultural commodity, potatoes, was analysed in duplicate at maturity (Day 69 and Day 70). Foliage samples were collected at harvest as a potential aid to metabolite identification and are not a raw agricultural commodity of potatoes.

C. Analytical Procedures

1. Extraction and fractionation:

All samples were surface washed twice with acetonitrile. Immature harvest and final harvest samples were then ground in a disk mill with dry ice after surface washing. Ground samples were returned to the freezer to allow the dry ice to sublime and for storage at 15 ºC until analysis. Total radioactive residues in plant samples were determined by combustion of aliquots of the ground samples followed by liquid scintillation counting (LSC). Day 0 samples were not ground prior to further extraction.

Day 0 samples were further extracted twice by maceration using an Ultra-Turrax mill with acetonitrile. Immature harvest and final harvest samples were extracted four times with acetonitrile. Where necessary acetonitrile washes and extracts were concentrated by rotary evaporation prior to analysis. The acetonitrile extracts of the final harvest potato tubers at the 1X treatment rate were subjected to a Bakerbond SPE C-18 column clean-up procedure and eluted with water followed by acetonitrile. The water fractions and the acetonitrile fractions were concentrated with a rotary evaporation prior to analysis. Recoveries throughout the sample processing were generally good.

The extracted fibre of the 1X treated potato tubers was subjected to acid hydrolysis with 1N HCl overnight at 50 ºC.

The radioactive content of extracts and concentrated extracts was determined by direct LSC and that of post-extraction residues by combustion followed by LSC.

Total radioactive residues in immature and final harvest plant samples were determined by summing the radioactivity present in the surface wash and the radioactivity present in the ground samples determined by combustion of aliquots. The total residue in the Day 0 plant samples was determined by summing the surface wash, extractable residue and non-extractable residue in the initial extraction.

2. Identification and characterisation:

Metabolites in the extractable extracts of final harvest potato samples containing significant residues were identified and quantified by comparison with authentic standards by thin layer chromatography (normal or reverse phase). The extractability and metabolic profiles were similar between the duplicate samples for each label tested. Reverse phase or normal phase TLC, depending on the radiolabel used provided confirmation of the metabolite identification.

3. Storage stability:

All extracts were stored at -15 °C or less prior to analysis. Analysis for the entire study was completed within 3 months of the final harvest.

II Results and Discussion

Good agreement was obtained throughout the results from the duplicate samples of potato foliage and tubers. The vast majority of residue at all timepoints was solvent extractable. Mean results of residue levels and the extraction profiles at each timepoint are presented in Table 6.1-8.

Potato foliage is not a raw agricultural commodity, but samples were collected at harvest as a potential aid to metabolite identification. In immature potato foliage, residues declined significantly between the initial treatment and the immature harvest just prior to the second treatment from ca. 51 mg/kg at Day 0 to ca. 9 mg/kg at Day 41 for the 1X rate. At final harvest, the mean residue in tubers (ca. 0.07 mg/kg) treated at the 1X rate was considerably lower than in the foliage (ca. 11 mg/kg).

The majority of residue in foliage was readily removed by surface washing with > 98% of the TRR removed at Day 0, 65.2 to 78.7% at Day 41 and 59.2 to 79.5 % in mature foliage at Day 50. The radioactivity remaining in the washed residue (determined by combustion) was 21.3 to 34.9% at Day 41 and 20.5 to 40.8% in mature foliage at Day 50. Subsequent acetonitrile extraction of the washed foliage removed virtually all the remaining residue, with <5% of the TRR remaining as non-extractable residue.

For the phenyl and pyridyl-label treated potatoes, total residues in potato tubers at final harvest were low (0.081 and 0.053 mg/kg parent equivalents, respectively at the 1X rate, 0.502 and 0.771 mg/kg parent equivalents, respectively at the 10X rate). Acetonitrile surface washes removed a small amount of the total residues (10.7 to 16.7% TRR), leaving 83.4 to 89.4% TRR in the washed tubers. Subsequent acetonitrile extraction removed an additional 71.9 to 79.4% of the TRR with 8.9 to 15.6% remaining as non-extractable residues. Extracted potatoes from the 1X treatment were subjected to acid hydrolysis to release additional non-extractable residues. Tubers from the 10X rate were not extracted further. Non-extractable residues represented 0.013 and 0.006 mg/kg parent equivalents at the 1X treatment rate in the phenyl- and pyridyl-label treated crop. Acid hydrolysis of the extracted fibre removed an additional 8.7% and 5.9% of the TRR (0.013 and 0.006 mg/kg) respectively, leaving 6.9% and 4.9% (0.006 and 0.003 mg/kg) in the fibre.

Table 6.2.1- 6 Total Radioactive Residues and Extractability at Each Harvest (mean of replicate values)

a) Phenyl

Timepoint	Rate	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Washed Residue[1]		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0 Foliage (BBCH 31-33)	1X	47.205	98.0	46.266	na	na	1.9	0.897	0.1	0.042
	10X	418.286	98.7	413.753	na	na	1.3	5.265	0.1	0.269
Immature Foliage (Day 41)	1X	10.166	75.5	7.672	24.6	2.494	20.2	2.046	4.4	0.448
	10X	38.930	76.1	29.844	24.0	9.087	21.6	8.177	2.5	0.911
Final Harvest (Day 50) Tubers	1X	0.081	12.6	0.010	87.4	0.071	71.9	0.058	15.6	0.013
	10X	0.502	10.7	0.052	89.4	0.451	79.4	0.402	10.1	0.049
Final Harvest (Day 50) Foliage	1X	12.251	59.2	7.250	40.8	5.002	37.1	4.537	3.8	0.465
	10X	201.621	70.9	149.255	29.2	52.366	na	na	na	na

b) Pyridyl

Timepoint	Rate	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Washed Residue[1]		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0 Foliage (BBCH 31-33)	1X	54.289	98.8	53.650	na	na	1.1	0.591	0.1	0.048
	10X	472.088	99.4	468.922	na	na	0.6	3.336	<0.1	0.130
Immature Foliage (Day 41)	1X	7.622	65.2	4.976	34.9	2.646	30.2	2.288	4.7	0.358
	10X	121.669	78.7	98.071	21.3	23.592	19.1	21.203	2.2	2.389
Final Harvest (Day 50) Tubers	1X	0.053	11.0	0.006	89.1	0.047	78.4	0.041	10.7	0.006
	10X	0.771	16.7	0.131	83.4	0.641	74.5	0.572	8.9	0.069
Final Harvest (Day 50) Foliage	1X	9.631	62.2	5.982	37.9	3.649	33.9	3.272	3.9	0.377
	10X	221.729	79.5	176.258	20.5	45.471	na	na	na	na

[1] Residue remaining after surface wash, further extracted to determined extractable and non extractable residues
na = not applicable

Chromatography results of the individual extracts derived from the duplicate samples at each timepoint showed excellent correlation. The metabolic profiles of identified residues from potato tubers and foliage, which is not a RAC, are shown in Table 6.1-9 and 6.1-10. Values are quoted for combined surface wash and acetonitrile extracts in mg/kg parent equivalents and % of total radioactive residue (% TRR).

Table 6.2.1- 7 Identification of AE C638206 Metabolites in Potato Tubers (mean of duplicate values)

a) Phenyl label

Timepoint	Rate	Total Extracted		FLC (AE C638206)		M-01 (AE C653711)		M-06 (AE C643890)		% Total Identified
		% TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Mature Tubers	1X	84.5	0.068	51.1	0.041	25.4	0.021	2.4	0.003	78.8
	10X	90.1	0.454	65.5	0.327	22.2	0.116	nd	nd	87.7

b) Pyridyl label

Timepoint	Rate	Total Extracted		FLC (AE C638206)		M-02 (AE C657188)		M-06 (AE C643890)		% Total Identified
		%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Mature Tubers	1X	89.4	0.047	70.2	0.037	12.0	0.007	1.7	0.001	83.9
	10X	91.2	0.703	57.0	0.442	26.1	0.195	nd	nd	83.0

mg/kg values are quoted as parent equivalents
nd = not detected

Table 6.2.1- 8 Identification of AE C638206 Metabolites in Foliage (not a RAC) as % of Total Radioactive Residue (mean of replicate values)

a) Phenyl label

Timepoint	Rate	Total Extracted		FLC (AE C638206)		M-01 (AE C653711)		M-06 (AE C643890)		% Total Identified
		%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Day 0 Foliage	1X	99.9	47.163	97.0	45.968	nd	nd	nd	nd	97.0
	10X	100	418.018	97.7	408.625	nd	nd	nd	nd	97.7
Day 41 Foliage	1X	95.7	9.718	88.8	9.027	nd	nd	nd	nd	88.8
	10X	97.7	38.021	90.6	35.364	nd	nd	nd	nd	90.6
Mature Foliage	1X	96.5	11.787	91.0	11.140	1.9	0.229	0.6	0.071	93.4

b) Pyridyl label

Timepoint	Rate	Total Extracted		FLC (AE C638206)		M-02 (AE C657188)		M-06 (AE C643890)		% Total Identified
		%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Day 0 Foliage	1X	99.9	54.241	97.7	53.087	nd	nd	nd	nd	97.7
	10X	100	472.258	98.3	463.931	nd	nd	nd	nd	98.3
Day 41 Foliage	1X	95.4	17.264	89.0	16.078	nd	nd	nd	nd	89.0
	10X	97.8	119.274	94.6	116.074	nd	nd	nd	nd	94.6
Mature Foliage	1X	96.1	9.254	89.8	8.639	0.8	0.075	0.7	0.069	91.3

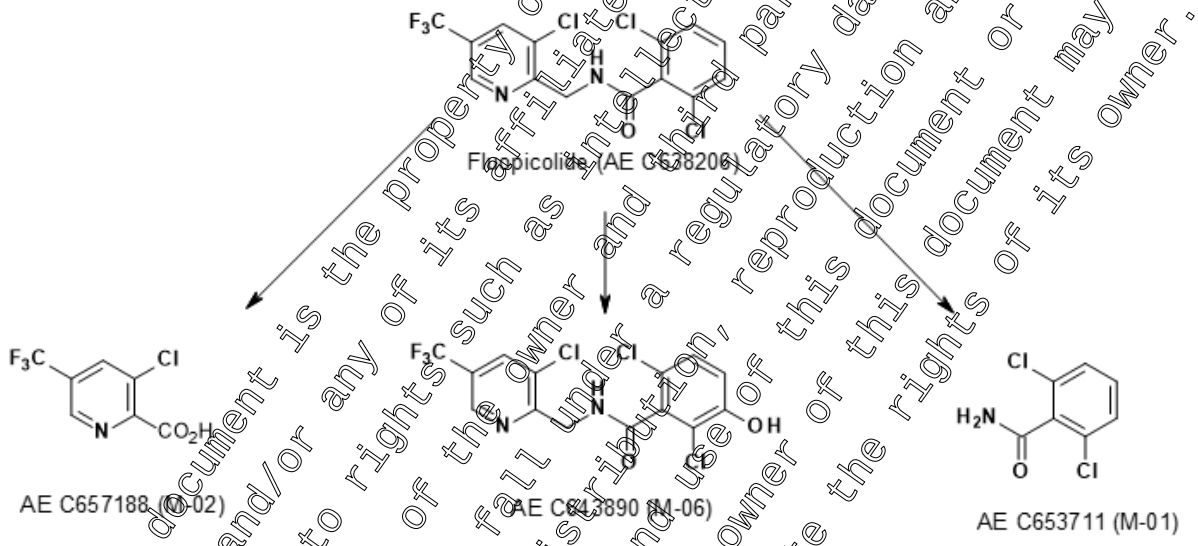
mg/kg values are quoted as parent equivalents
nd = not detected

Analysis of the extractable residues showed a qualitatively similar metabolic profile in all potato foliage and tuber tissues. The principle residues in potato tubers were identified as fluopicolide (AE C638206) and the metabolite M-01 (AE C653711) in phenyl-label treated potatoes and, fluopicolide (AE C638206) and the metabolite M-02 (AE C657188) in the pyridinyl-label treated potatoes. Minor amounts of the metabolite M-06 (AE C643890) was identified in both phenyl- and pyridinyl-label treated potatoes. The same metabolic profile was seen in potato foliage.

III. Conclusions

Radioactive residues in potatoes treated with [^{14}C]-AE C638206 were principally removed by an acetonitrile surface wash and extractable with acetonitrile (84.4 to 89.4% TRR). Non-extractable residues (10.7 to 15.6% TRR, 0.006 to 0.013 mg/kg) were released by acid hydrolysis resulting in hydrolysates and hydrolysed fibre residues of 5.9 to 8.7% TRR (0.003-0.007 ppm) and 4.9 to 6.9% TRR (0.003-0.006 ppm), respectively. Greater than 78% of the total radioactive residue was identified in the samples at final harvest. The majority of the residue in the potato tubers consisted of the parent compound, fluopicolide (AE C638206), with significant amounts of M-01 (AE C653711) and M-02 (AE C657188) and minor amounts of M-06 (AE C643890). No other single metabolite comprised more than 2% of the total residue in any matrix.

The metabolic profile of fluopicolide in potatoes was found to be similar to that reported in other plant systems:



Assessment and conclusion by applicant:

The study is acceptable and demonstrates the metabolic fate of fluopicolide within root/tuber commodities.

The total 1X rate applied was 0.4 kg a.s./ha and the total 10X rate was 4 kg a.s./ha. Based on the representative use for potatoes (with a maximum seasonal application rate of 0.4 kg a.s./ha for fluopicolide), the corresponding N-rates for the total rate applied within the metabolism study are 1 N and 10 N for the 1X and 10X rates, respectively.

Lettuce

Data Point:	KCA 6.2.1/01
Report Author:	[redacted]
Report Year:	2004
Report Title:	Metabolism of [U-14C-phenyl]- and [2,6-14C pyridinyl]-AE C638206 in Lettuce (Amended report replacing report 505CU, Document B004330)
Report No:	B004861
Document No:	M-241269-02-1
Guideline(s) followed in study:	EU (=EEC): Directive 96/68/EC; USEPA (=EPA): OPPTS 860.1300
Deviations from current test guideline:	No deviations from the test guideline were noted with the study report.
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

This study was conducted to determine the extent and nature of the metabolic breakdown of [U-^{14}C-phenyll- and [2,6-^{14}C pyridinyl]-AE C638206 in lettuce treated under a typical field application pattern.

Lettuce (var. Black Seeded Simpson) was grown under confined conditions in 3 plots. One plot was designated for the [2,6-^{14}C pyridinyl]-AE C638206 foliar application, one plot was divided into two halves with one half being designated for the [U-^{14}C-phenyl]- AE C638206 foliar application and other half being designated for the [U-^{14}C-phenyl]- AE C638206 soil application and one plot remained untreated.

Lettuce was treated two times via foliar application with formulated radiolabelled test substance. The rate for each treatment was 200 g ai/ha so that the total treatment (400 g ai/ha) reflected the maximum seasonal application. The first treatment was 41 days post planting and the second treatment was 21 days later (14 days prior to final harvest). Lettuce from the final harvests of the [U-^{14}C-phenyl]-AE C638206 and [2,6- ^{14}C pyridinyl]-AE C638206 treated plots was utilized to determine the metabolic profile at maturity.

Additionally, the furrows between a group of lettuce plants was treated once with formulated [U-^{14}C-phenyl]-AE C638206. The rate for the treatment was 200 g ai/ha, which is equal to the maximum proposed soil drench rate. The furrows were treated 41 days post-planting, while the immature lettuces were not treated directly by the drench. Lettuce leaves from the final harvests of the [U-^{14}C-phenyll-AE C638206 treated soil plots were utilized to determine the metabolic profile at maturity.

The residue in the Lettuce was recovered by an acetonitrile wash and an acetonitrile extraction. Metabolites in the extractable residue were identified and quantitated by TLC against a standard mix. Fibre bound residues were quantitated by combustion analysis.

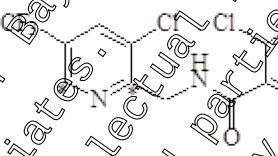
Good agreement was obtained throughout the results from the duplicate samples of lettuce samples. The vast majority of residue (>95% of TRR) at all timepoints was solvent extractable. Chromatography results of the individual extracts derived from the duplicate samples at each timepoint showed excellent correlation. The metabolic profiles of identified residues from all the lettuce samples are shown in Table B. Analysis of the extractable residues showed a qualitatively similar metabolic profile in all lettuce leaf tissues. The principle residues were identified as fluopicolide (AE C638206). Minor metabolites M-01 (AE C653711) and M-06 (AEC643890) were identified in phenyl-label treated lettuce. One additional minor metabolite, M-02 (AE C657188), was identified in the pyridinyl-label treated lettuce. (M-06 was also identified in the pyridinyl-label treated lettuce.)

Radioactive residues in lettuce leaves treated with [^{14}C]-AE C638206 were principally extractable with acetonitrile. Greater than 91% of the total radioactive residue was identified in the samples at final harvest. The majority of the residue in the raw agricultural commodity consists of fluopicolide (AE C6438206), with minor amounts of M-01 (AE C653711), M-02 (AE C657188), and M-06 (AE C643890). No other single metabolite comprised more than 1% of the total residue in any matrix. The metabolic profile of fluopicolide in lettuce was found to be similar to that reported in other plant systems.

I Materials and Methods

A. Materials

1. Test Material:

Chemical structure	 Label positions: § = [U-^{14}C-phenyl]-Fluopicolide * = [2,6-^{14}C-pyridyl]-Fluopicolide
Preferred IUPAC name	2,6-dichloro-N-[(3-chloro-5-(trifluoromethyl)-2pyridyl)methyl]benzamide
Radiolabelled test material	[U-^{14}C-phenyl]-Fluopicolide [2,6-^{14}C-pyridyl]-Fluopicolide
Lot No.	[U-^{14}C-phenyl]-Fluopicolide = 902AE-1 [2,6-^{14}C-pyridyl]-Fluopicolide = 903AE-1
Specific radioactivity	[U-^{14}C-phenyl]-Fluopicolide = 159 µCi/mg [2,6-^{14}C-pyridyl]-Fluopicolide = 144 µCi/mg
Radiochemical purity	[U-^{14}C-phenyl]-Fluopicolide = 99.6% by HPLC [2,6-^{14}C-pyridyl]-Fluopicolide = 99.5% by HPLC
Preparation of application solution	The test substance was applied as a solution in water.

2. Soil: The soil characteristics were not described in the study report.

3. Plant: Lettuce (var. Black Seeded Simpson)

B. Study Design

1. Experimental conditions:

The experiment simulated agricultural practice of multiple foliar spray applications of fluopicolide to lettuces during the growing period or a soil drench application made between the furrows of the growing plants.

Lettuce (var. Black Seeded Simpson) was sown in three separate stainless-steel tank inserts (83.8 cm wide by 152.4 cm long by 30.5 cm deep) in seven rows, 19 cm apart on October 13, 1999. Each sown plot was located in a separate field cage. Once the lettuce had sprouted the middle row of one of the plots was removed and replaced with a stainless-steel partition. One side of this plot was used for the [U-^{14}C-phenyl]-AE C638206 foliar application and the other half was used for the [U-^{14}C-phenyl]-AE C638206 soil drench application. The lettuce plants were treated at 41 days (November 23, 1999). One plot was treated with [2,6-^{14}C pyridinyl]-AE C638206 (foliar application) and the partitioned plot was treated with [U-14C-phenyl-AE C638206 (half of the plot was treated by a foliar application and the other half by a soil application). The third planted plot remained untreated. Plant samples for Day Zero analyses of the foliar applications were harvested immediately following the first treatment after the application dried. An intermediate harvest was performed on December 14, 1999, 21 days after the initial treatment and just prior to the second foliar application. Final harvest samples were taken on December 28, 1999. The schedule of the plant husbandry events and treatments, were recorded in the study report.

Lettuce was treated two times at a nominal rate of 200 g ai/ha with each label to give a total treatment rate of 400 g ai/ha for the foliar treated plots. All foliar treatments were applied at the same growth stages. The first treatment was 41 days post planting and the second treatment was 21 days later (14 days prior to final harvest). In addition, a single soil drench application of the phenyl label at a rate of 200 g a.i./ha was applied at the same time as the first foliar applications.

Table 6.2.1- 9 AE C638206 Formulation Details

Application Number	Application	Radiolabel	Final specific activity (µCi/mg)	Application rate (g as/ha)
1	Foliar	U-^{14}C-phenyl	39.7	202.81
2	Foliar	U-^{14}C-phenyl	39.4	202.50
			Total rate	**405.31**
1	Soil Drench	U-^{14}C-phenyl	39.7	202.81
			Total rate	**202.81**
1	Foliar	2,6^{14}C-pyridyl	40.2	202.03
2	Foliar	2,6^{14}C-pyridyl	40.1	202.03
			Total rate	**404.06**

2. Sampling:

Immature lettuce samples were taken from each foliar application plot on Day 0 (immediately after treatment) and from all foliar application and soil drench plots on Day 21 (immediately prior to the second foliar treatment), as an aid to identification of residues at final harvest. Lettuce was harvest at maturity on Day 35 from all plots.

Soil samples were collected at Day 0, Day 21 and Day 35 (final harvest) from the soil drench plot but were not analysed.

All samples from the foliar treatments were immediately subjected to an acetonitrile wash on the day of sampling. Immature and final harvest lettuce samples were then ground in a disk mill with dry ice after surface washing. Ground samples were returned to the freezer to allow the dry ice to sublime and for storage at -15 ºC until analysis. Total radioactive residues in plant samples were determined by combustion of aliquots of the ground samples followed by liquid scintillation counting (LSC). Day 0 samples were not ground prior to further extraction.

Samples from the soil drench treatment were not surface washed. Immature and final harvest lettuce samples were ground in a disk mill with dry ice as for foliar treatment samples. Total radioactive residues in plant samples were determined by combustion of aliquots of the ground samples followed by liquid scintillation counting (LSC). Day 0 plant samples were not taken for the soil drench treatment.

Samples were further extracted three or four times by maceration using an Ultra-Turrax mill with acetonitrile. Where necessary acetonitrile washes and extracts were concentrated by rotary evaporation prior to analysis. Recoveries throughout the sample processing were generally good.

The radioactive content of extracts and concentrated extracts was determined by direct LSC and that of post-extraction residues by combustion followed by LSC.

Total radioactive residues in immature and final harvest plant samples were determined by summing the radioactivity present in the surface wash, if conducted, and the radioactivity present in the ground samples determined by combustion of aliquots. The total residue in the Day 0 plant samples was determined by summing the surface wash, extractable residue and non-extractable residue in the initial extraction.

C. Analytical Procedures

1. Extraction and fractionation:

For the Day Zero harvest of the foliar treatments, weighed samples were extracted by maceration using an Ultra-Turrax with approximately 100 mL of acetonitrile (three times) followed by filtration through a Buchner funnel. Filtrates from extractions were combined and concentrated. These samples were not extracted further.

For the immature harvest (Day 21) and final harvest of the foliar treatments, weighed samples were extracted by maceration using an Ultra-Turrax with approximately 50mL of acetonitrile (one time) and with approximately 100 mL of acetonitrile (two times) followed by filtration through a Buchner funnel. Filtrates from extractions were combined and concentrated. These samples were not extracted further.

For the final harvest of the soil treatments, samples were ground in dry ice and then extracted three times with acetonitrile followed by filtration through a Buchner funnel. Filtrates from extractions were combined and concentrated. These samples were not extracted further.

Each extract was sampled for LSC. Extracted fiber samples were analysed to determine the non-extractable residue by combustion.

2. Identification and characterisation:

Metabolites in the extractable extracts of final harvest lettuce leaf samples containing significant residues were identified and quantified by comparison with authentic standards by thin layer chromatography (normal or reverse phase). The extractability and metabolic profiles were similar between the duplicate samples for each label tested. Reverse phase or normal phase TLC, depending on the radiolabel used provided confirmation of the metabolite identification.

3. Storage stability:

Samples were extracted and analysed by TLC within 10 days of harvest. Chromatography by TLC up to 6 months after the initial analyses showed that the chromatographic profile remained unchanged. All extracts were stored at -15 ºC or less prior to analysis. Analysis for the entire study was completed within 3 months of the final harvest.

II Results and Discussion

Good agreement was obtained throughout the results from the duplicate samples of lettuce samples. The vast majority of residue (>95% of TRR) at all timepoints was solvent extractable. Mean results of residue levels and the extraction profiles at each timepoint are presented in the Table 6.1.1-2.

Table 6.2.1- 10 Total Radioactive Residues and Extractability at Each Harvest (mean of duplicate values)

a) Phenyl

Timepoint	Treatment	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0	Foliar	10.837	95.4	10.332	4.6	0.494	0.1	0.012
Immature Harvest (Day 21)	Foliar	1.327	61.0	0.809	37.6	0.498	1.5	0.020
	Soil Drench	0.076	na	na	97.2	0.073	2.9	0.002
Final Harvest (Day 35)	Foliar	13.385	84.6	11.33	14.8	1.964	0.7	0.089
	Soil Drench	0.175	na	na	95.9	0.169	4.1	0.007

b) Pyridyl

Timepoint	Treatment	Total Radioactive Residue (mg/kg)	Surface Wash Residue		Extractable Residue		Non-Extractable Residue	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Day 0	Foliar	13.359	96.6	12.907	3.4	0.442	0.1	0.010
Immature Harvest (Day 21)	Foliar	1.307	66.6	0.869	32.5	0.425	1.0	0.013
Final Harvest (Day 35)	Foliar	14.503	84.0	12.179	15.1	2.184	1.0	0.140

na = not applicable

In immature lettuce samples, residues declined significantly between the initial foliar treatment and the immature harvest just prior to the second foliar treatment from *ca.* 12 mg/kg at Day 0 to *ca.* 1 mg/kg at Day 21. At final harvest, the residue in lettuce leaves from the foliar treatment areas was *ca.* 13 mg/kg.

Total residues were significantly lower in lettuce treated with phenyl-label soil drench than in lettuce treated by phenyl-label foliar application. In immature lettuce leaves (Day 21), the TRR for the foliar applied treated lettuce was 1.327 ppm compared to 0.076 ppm for the soil drench treated lettuce. At final harvest, the mean residue in foliar treated lettuce was 13.385 ppm while the mean residue in the soil drench lettuce was 0.175 ppm.

The majority of residue in lettuce treated by foliar application was readily removed by surface washing with > 95% of the TRR removed at Day 0, *ca.* 64% at Day 21 prior to the second application and *ca.* 84% in mature lettuce at Day 35. Subsequent acetonitrile extraction of the washed samples removed virtually all the remaining residue, with <2% of the TRR remaining as non-extractable residue.

Acetonitrile extraction of the lettuce treated by soil drench removed virtually all the crop residue with >95% extracted and <5% of the TRR remaining as non-extractable residue.

Chromatography results of the individual extracts derived from the duplicate samples at each timepoint showed excellent correlation. The metabolic profiles of identified residues from all the lettuce samples are shown in Table 6.1.1-3. Values are quoted for combined surface wash and acetonitrile extracts in mg/kg parent equivalents and % of total radioactive residue (% TRR).

Table 6.2.1- 11 Identification of AE C638206 Metabolites in Lettuce (mean of replicate values)

a) Phenyl label

Timepoint	Application	Total Extracted		FLC AE C638206		M-01 AE C653711		M-06 AE C643890		% Total Identified
		%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Day 0	Foliar	99.9	10.826	97.5	10.568	0.1	0.009	nd	nd	97.6
Immature Harvest (Day 21)	Foliar	98.6	1.307	92.5	1.227	3.9	0.052	1.0	0.013	97.3
	Soil Drench	97.2	0.073	74.5	0.057	16.5	0.013	nd	nd	91.0
Final Harvest (Day 35)	Foliar	99.4	13.294	95.9	12.845	0.9	0.112	nd	nd	96.8
	Soil Drench	95.9	0.169	71.7	0.128	19.8	0.034	2.8	0.005	91.5

b) Pyridyl label

Timepoint	Application	Total Extracted		FLC AE C638206		M-02 AE C657188		M-06 AE C643890		% Total Identified
		%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	
Day 0	Foliar	99.9	13.349	96.1	12.816	nd	nd	nd	nd	96.1
Immature Harvest (Day 21)	Foliar	99.1	1.294	94.7	1.237	1.5	0.019	1.4	0.018	97.6
Final Harvest (Day 35)	Foliar	99.1	14.363	96.4	13.979	0.6	0.078	nd	nd	97.0

mg/kg values are quoted as parent equivalents
nd = not detected

Analysis of the extractable residues showed a qualitatively similar metabolic profile in all lettuce leaf tissues. Virtually all of the radioactive residues were identified (91.5 to 97.0% TRR at maturity).

Following foliar applications, the major residue was identified as AE C638206 accounting for >95% of the TRR at final harvest in both phenyl- and pyridyl-label treated lettuce. The metabolite AE C653711 was identified in minor amounts (0.9% TRR, 0.112 mg/kg) in mature lettuce treated by phenyl-label foliar application and the metabolite AE C657188 was identified in minor amounts (0.6% TRR, 0.078 mg/kg) in mature lettuce treated by pyridyl-label foliar application. Minor amounts of the metabolite AE C643890 was identified in foliar treated lettuce at 1.0 and 1.4% TRR in phenyl- and pyrdinyl-label treated lettuce at immature harvest but the metabolite was not detected at final harvest.

Following phenyl-label soil drench application the major residue was also identified as fluopicolide (AE C638206) at 71.7% of the TRR at final harvest in lettuce. The metabolite M-01 (AE C653711) was identified 19.8% of the TRR which represented a concentration of 0.034 mg/kg parent equivalents. Minor amounts of the metabolite M-06 (AE C643890) was identified at 2.8% TRR (0.005 mg/kg) at final harvest. It was concluded that the parent compound fluopicolide (AE C638206) was metabolised in soil to form M-01 (AE C653711), which was then taken up by the lettuce plant. Hence in the foliar applied treated lettuce the parent compound, fluopicolide (AE C638206) and M-01 (AE C653711) represented 95.9% and 0.9% of the TRR, respectively while in the soil drench treated lettuce, parent formed 71.1% of TRR and M-01 (AE C653711) formed 19.8% of the TRR.

III. Conclusions

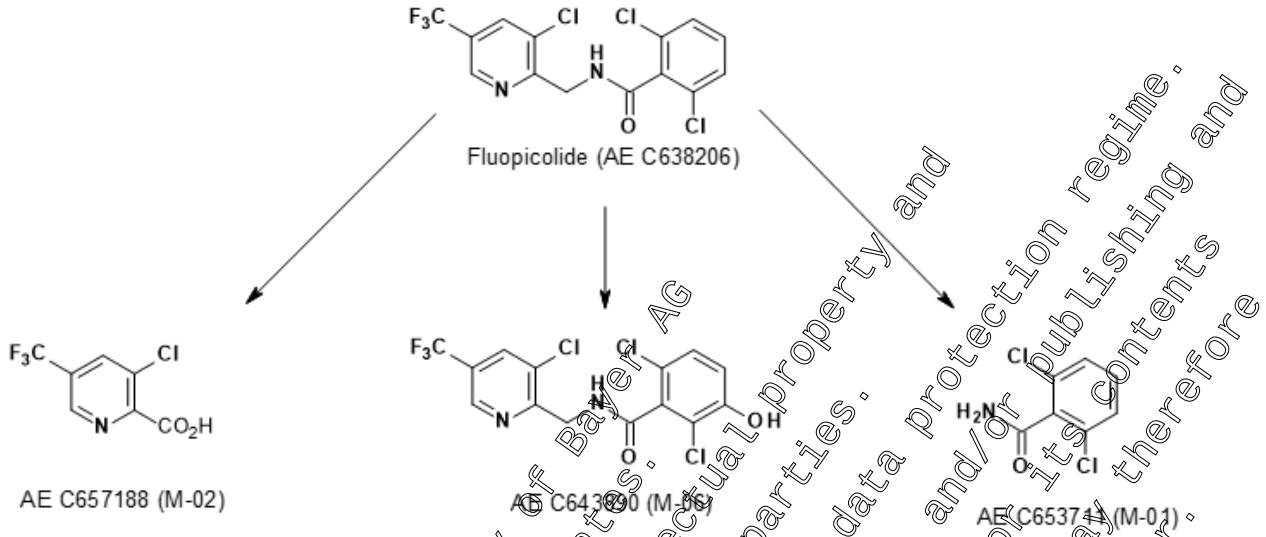
No appreciable differences in total residues were observed between the phenyl-label treated lettuce and the pyridinyl-label treated lettuce when the treatment was applied as a foliar application. The total residues in both treatment labels at each harvest were very similar for the foliar applied treatments.

In immature lettuce leaves, residues declined significantly between the initial treatment and just prior to the second treatment with initial mean residue levels of 10.837-13.359 ppm at Day Zero declining to 1.307-1.327 ppm at Day 21 (pre-second treatment). At final harvest, the mean residue in lettuce leaves was 13.385-14.503 ppm for the foliar applications.

Significant differences in total residues were observed between the phenyl-label foliar application and the soil drench. In immature lettuce leaves (Day 21), the T RR for the foliar applied treated lettuce was 1.327 ppm as compared to 0.076 ppm for the soil drench applied treated lettuce. At final harvest, the mean residue in foliar treated lettuce was 13.385 ppm while the mean residue in the soil drench treated lettuce was 0.175 ppm. Further, in the foliar applied treated lettuce the parent compound, fluopicolide (AE C638206) was found at 95.9% of the T

RR while in the soil drench treated lettuce, the parent compound was found at 71 of TRR. The major metabolite M-01 (AE C653711) was found in the soil drench treated lettuce at 19.8% of TRR while in the foliar applied treated lettuce, M-01 (AE C653711) was found at 0.9% of TRR. The metabolite, M-06 (AE C643890), was found at 2.8% of T RR in the soil drench treated lettuce and was not found in the foliar applied treated lettuce. No other single metabolite comprised more than 1% of the total residue in any matrix.

The metabolic profile of fluopicolide in lettuce was found to be similar to that reported in other plant systems:



Assessment and conclusion by applicant:

The study is acceptable and demonstrates the metabolic fate of fluopicolide within leafy commodities.

The total rate applied was 0.4 kg a.s./ha for the foliar application and 0.2 kg a.s./ha for the soil drench application. Based on the representative use for lettuce (with a maximum seasonal application rate of 0.2 kg a.s./ha for fluopicolide), the corresponding N-rate for the total rate applied within the metabolism study is 2 N (for the foliar application).

The soil drench application is relevant for cucumbers; this is acceptable according to the advice in OECD 501, as common metabolic pathways are observed for the lettuce soil drench application and the three foliar applications (on grapes, potatoes, and lettuce). The GAP for cucumbers indicates a maximum seasonal application rate of 0.3 kg a.s./ha for fluopicolide), the corresponding N-rate relative to the total rate applied within the metabolism study is 0.7 N.

Oilseed rape

New data for AIR:

Data Point:	KCA 6.2.1/04
Report Author:	[redacted]
Report Year:	2009
Report Title:	Metabolism of [phenyl-UL-14C] and [pyridyl-2,6-14C]fluopicolide in oilseed rape after seed treatment
Report No:	MEF-09/516
Document No:	M-358357-01-1
Guideline(s) followed in study:	OECD 501; US EPA OPPTS 860.1300; EU 91/414/EEC amended by 96/68/EC; Canadian PMRA Ref.: DACO 6.3; Japanese MAFF Notification No. 12 - Nousan 8147, Appendix 2-4-1
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

The metabolism of the fungicide ^{14}C-fluopicolide was investigated in oilseed rape after seed treatment with a 10x overdose. The test items were [phenyl-UL-^{14}C]Fluopicolide and [pyridyl-2,6-^{14}C]Fluopicolide, both formulated as a FS 540 formulation. The application rates amounted to 117.6 g a.i./ha (19.6 g a.i./kg seeds) for the phenyl-UL-^{14}C label and 111.6 g a.i./ha (18.6 g a.i./kg seeds) for the pyridyl-2,6-^{14}C-label. The plant cultivation was performed under artificial temperature and light conditions in the greenhouse. Forage was harvested at growth stage BBCH 17-19 (7 to 9 leaves or more unfolded) and seeds at BBCH 89 (maturity, fully ripe: nearly all pods ripe, seeds dark and hard). Before conventional extraction, the rape seeds samples were degreased with n-heptane. The samples were analysed for total radioactive residue content (TRR) and extracted with acetonitrile/water. Extracts were concentrated and analysed by HPLC, LSC and HPLC-MS with aid of co-chromatographed reference items.

The TRRs in forage amounted to 0.107 mg/kg (phenyl-UL-^{14}C label) and 0.108 mg/kg (pyridyl-2,6-^{14}C label). The TRRs in seeds were 0.057 mg/kg (phenyl-UL-^{14}C label) and 0.059 mg/kg (pyridyl-2,6-^{14}C label).

Negligible amounts of the residue (≤ 0.002 mg/kg) were detected in the n-heptane extracts, which were not further investigated. For both labels approx. 98% of the TRR for forage and approx. 94% of the TRR for seeds were extractable. Residues in solids (PES) amounted to ≤ 6.1% of the TRR (≤ 0.004 mg/kg).

Parent compound was found in amounts of 83.0% (0.089 mg/kg) of the TRR (phenyl-UL-^{14}C label) and 88.6% (0.095 mg/kg) of the TRR (pyridyl-2,6-^{14}C label) in forage. In seeds 40.1% (0.023 mg/kg) of the TRR (phenyl-UL-^{14}C label) and 77.5% (0.046 mg/kg) of the TRR (pyridyl-2,6-^{14}C label) were identified as parent compound.

The major metabolite 2,6-dichlorobenzamide (M-01, BAM) was identified in RACs of the phenyl-UL-^{14}C label, only. Label specific metabolites of the pyridyl-2,6-^{14}C label were not detected. Most probably 2,6-dichlorobenzamide was formed in the soil and amounted to 0.012 mg/kg (11.5% of the TRR) in forage and 0.021 mg/kg (37.3% of TRR) in seeds.

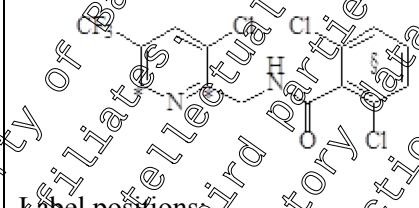
All other metabolites were not identified, due to the very low amount (each ≤ 4.1% of the TRR and ≤ 0.002 mg/kg) in the RACs.

On the basis of the nature and amount of metabolites found in the extracts of forage and seeds, the metabolic pathway of [phenyl-UL-^{14}C]-Fluopicolide and [pyridyl-2,6-^{14}C]-Fluopicolide in seed-treated rape was proposed. The metabolic reaction involved was the cleavage of fluopicolide leading to 2,6-dichlorobenzamide (M-01, BAM).

I Materials and Methods

A. Materials

1. Test Material:

Chemical structure	 Label positions: § = [U-^{14}C-phenyl]-Fluopicolide *= [2,6-^{14}C-pyridyl]-Fluopicolide
Preferred IUPAC name	2,6-dichloro-N-[(3-chloro-5-(trifluoromethyl)-2-pyridyl)methyl]benzamide
Radiolabelled test material	[U-^{14}C-phenyl]-Fluopicolide [2,6-^{14}C-pyridyl]-Fluopicolide
Lot No.	[U-^{14}C-phenyl]-Fluopicolide = KATH 6199 [2,6-^{14}C-pyridyl]-Fluopicolide = KATH 6200
Specific radioactivity	[U-^{14}C-phenyl]-Fluopicolide = 5.50 MBq/mg [2,6-^{14}C-pyridyl]-Fluopicolide = 6.77 MBq/mg
Radiochemical purity	[U-^{14}C-phenyl]-Fluopicolide = >99% by HPLC [2,6-^{14}C-pyridyl]-Fluopicolide = >99% by HPLC
Preparation of application solution	The test substance was applied as a solution in water.

2. Soil: The soil characteristics were not described in the study report.

3. Plant: Oilseed rape (var. Black Seeded Simpson)

B. Study Design

1. Experimental conditions:

Test plant and test site: The plant cultivation was performed under artificial temperature and light conditions in the greenhouse. Plants were irrigated as needed. Six flowerpots were used for each radiolabel. Each flowerpot had a surface area of approx. 0.1 m² (diameter: 36 cm) and was filled with sandy loam soil. Twelve rape seeds of the species Ability were sown in each pot.

Seed treatment: The test items were formulated as FS 540 formulations containing 80 g fluopicolide, 60 g fluoxastrobin and 400 g clothianidin per litre. For each application suspension an amount of the test item corresponding to a 10 x overdose was mixed with a 1 x amount of the FS 540 blank formulation and homogenised. The FS 540 blank formulation contained 60 g/L non-radiolabelled fluoxastrobin and 400 g/L non-radiolabelled clothianidin. The homogenised mixture was diluted with small portions of water to a final concentration of approx. 4 mg test item/mL by stirring. A volume of 25 µL of the application suspension was pipetted on each seed in the soil (planting hole). Then the seed was covered with soil. This procedure simulated the seed treatment and sowing of agricultural practise.

Sampling and sample work-up:

Forage: Three plants of each flowerpot were harvested by cutting off the plants shortly above the soil (growth stage: BBCH code 17-19, 7 to 9 leaves or more unfolded). The forage sample was homogenised with liquid nitrogen using a Polytron (Kinematica AG, Littau/Luzern, Switzerland). An aliquot of the homogenised sample was used for extraction. Residual sample material was stored in aliquots at ≤18°C.

Seeds: The part of each oilseed rape plant, where the pods were growing, was covered with a plastic bag. At maturity (growth stage: BBCH code 89, fully ripe: nearly all pods ripe, seeds dark and hard) the plants were harvested. Seeds were separated from the pods. An aliquot of the seeds sample was used for extraction and the remaining rest was stored in aliquots at ≤18°C.

The pods were homogenised with liquid nitrogen using a Polytron (Kinematica AG, Littau/Luzern, Switzerland). The homogenised pod sample was stored at ≤18°C and was not further investigated.

C. Analytical Procedures

1. Extraction and fractionation:

Before conventional extraction, an aliquot of each rape seeds sample was extracted once with n-heptane, to remove the oil matrix in the sample. An aliquot of each homogenised rape forage sample and the rape seeds sample after extraction with n-heptane were conventionally extracted three times with acetonitrile/water (8/2; v/v) and once with acetonitrile using a Polytron homogeniser. Due to the high matrix in the extracts, the combined extract of each sample was purified by Solid Phase Extraction (SPE) and concentrated to a volume, suitable for HPLC chromatography (profiling).

TRR-values were calculated from the sum of the radioactivity in the extracts (including n-heptane extract) and the corresponding solids.

Solids 1, that is plant residues remaining after conventional extraction of rape seeds were exhaustively extracted (microwave assistance) with different mixtures of acetonitrile/water with and without formic acid. The exhaustive extracts without formic acid were combined, purified by SPE and concentrated to a volume, suitable for HPLC chromatography (profiling).

2. Identification and characterisation:

Parent Compound and metabolites in the combined extracts were quantified by HPLC. The identification of the parent compound was performed in an isolated HPLC fraction of the combined extract of forage by LC-MS/MS. The identification of the metabolite 2,6-dichlorobenzamide was performed in an isolated HPLC-fraction of the combined extract of forage (phenyl-UL-^{14}C label) by LCMS/ MS. Additionally, the assignment of 2,6-dichlorobenzamide was performed with the radiolabelled reference item by comparison of the HPLC retention times.

Comparisons of the metabolite patterns in the extracts were used for the assignment of metabolites in rape seeds (phenyl-UL-^{14}C label) and in the RACs of the pyridyl-2,6-^{14}C label.

The ^{14}C-radioactivity of liquid samples was determined by liquid scintillation counting (LSC).

The limit of quantitations (LOQ) in HPLC of each RAC extracts are presented below:

Table 6.2.1- 12 Overview of the estimated LOQs for the HPLC-analysis of the conventional extracts

RACs	Lowest detectable amount (= LOQ)	
	phenyl-UL-^{14}C label	pyridyl-2,6-^{14}C label
Forage	<0.001 mg/kg	<0.001 mg/kg
Seeds	0.001 mg/kg	<0.001 mg/kg

3. Storage stability:

All samples were stored at temperatures ≤ -18 °C before extraction and analysis. All RACs were extracted within 15 days after sampling. Therefore it was concluded that the results of this study were not negatively influenced by storage effects. The limit of storage stability was not demonstrated in the course of this study.

II Results and Discussion

Following seed treatment of ^{14}C-labelled fluopicolide (phenyl-UL-^{14}C and pyridyl-2,6-^{14}C fluopicolide labels) at a use rate of 117.6 g a.i./ha for the phenyl-UL-^{14}C label and 111.6 g a.i./ha for the pyridyl-2,6-^{14}C-label, the measured total radioactive residues (TRR) for the raw agricultural commodities. The TRR values in different plant parts resulted from numerical addition of the radioactivity in extracts and the respective solid extracted matrices, the amount of respective sample and the specific radioactivity of the radiolabelled test item.

Table 6.2.1- 13 Total Radioactive Residues (TRRs) in rape (phenyl-UL-^{14}C label and pyridyl-2,6-^{14}C label) following seed treatment.

Matrix	Timing and Applic. No.	PHI (days)	TRR (ppm)	
			Phenyl-UL-^{14}C label	Pyridyl-2,6-^{14}C label
Forage	At growth stage BBCH 17-19	43	0.107	0.108
Seeds	At growth stage BBCH 89	160	0.057	0.059

The majority of the radioactivity in forage and seeds was conventionally extracted with acetonitrile/water (8/2; v/v) and acetonitrile. Negligible amounts of residue (≤ 0.002 mg/kg) were detected in the n-heptane extracts of rape seeds. They were not further investigated, due to the high load of the oil matrix. The remaining residues in the solids of seeds were exhaustively (microwave assistance at 120°C) extracted using different mixtures of acetonitrile/water with and without formic acid.

For both labels approx. 98% of the TRR for forage and approx. 94% of the TRR for seeds were extractable.

All conventional and exhaustive extracts were investigated by HPLC with ^{14}C-detection. The following table presents the resulting composition of residues in rape matrices.

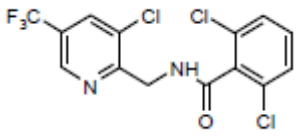
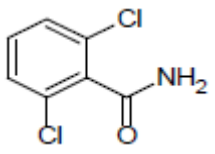
Table 6.2.1- 14 Distribution of residues in different parts of rape (phenyl-UL-^{14}C label and pyridyl-2.6-^{14}C label) following seed treatment.

Solvent Fraction	Rape Forage		Rape Seeds	
	%TRR	ppm	%TRR	ppm
Distribution of the Metabolites in Rape (phenyl-UL-^{14}C label) at approx. 120 g a.i./ha (10 x overdose experiment)				
Conventional extraction:	**98.3**	**0.106**	**58.5**	**0.034**
Fluopicolide	83.0	0.089	21.0	0.012
2.6-dichlorobenzamide	11.5	0.012	26.1	0.015
- unidentified compounds:	3.8	0.004	7.5	0.004
number of unidentified compounds	5		3	
amount of the largest compound	1.0	0.001	4.0	0.002
- characterised by extraction with n-heptane			3.9	0.002
Exhaustive extraction:	**---**	**---**	**35.5**	**0.020**
Fluopicolide			19.1	0.011
2.6-dichlorobenzamide			11.2	0.006
- unidentified compounds:			1.6	0.001
number of unidentified compounds			1	
amount of the largest compound			1.6	0.001
- characterised by extraction with acetonitrile/water (1/1) + 2.5 mL formic acid			3.5	0.002
Total extractable	**98.3**	**0.106**	**94.0**	**0.054**
Total identified	**94.5**	**0.102**	**77.4**	**0.044**
Total characterised	**3.8**	**0.004**	**16.5**	**0.009**
Total bound residues (PES)*	**1.7**	**0.002**	**6.1**	**0.003**
Accountability**	**100.0**	**0.107**	**100.0**	**0.057**
Distribution of the Metabolites in Rape (pyridyl-2.6-^{14}C label) at approx. 120 g a.i./ha (10 x overdose experiment)				

Solvent Fraction	Rape Forage		Rape Seeds	
	%TRR	ppm	%TRR	ppm
Conventional extraction:	**97.8**	**0.105**	**57.7**	**0.034**
Fluopicolide	88.6	0.095	46.3	0.027
- unidentified compounds:	9.2	0.010	7.8	0.005
number of unidentified compounds	11		8	
amount of the largest compound	3.0	0.003	4.1	0.002
- characterised by extraction with n-heptane			3.7	0.002
Exhaustive extraction:	---	---	**36.2**	**0.021**
Fluopicolide			31.2	0.019
- unidentified compounds:			0.2	0.001
number of unidentified compounds			1	
amount of the largest compound			0.2	0.001
- characterised by extraction with acetonitrile/water (1/1) + 2.5 mL formic acid			4.8	0.003
Total extractable	**97.8**	**0.105**	**93.9**	**0.055**
Total identified	**88.6**	**0.095**	**77.5**	**0.046**
Total characterised	**9.2**	**0.010**	**16.5**	**0.010**
Total bound residues (PES)*	**2.2**	**0.002**	**6.1**	**0.004**
Accountability**	**100.0**	**0.108**	**100.0**	**0.059**

* Residues remaining after exhaustive extractions.
** Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) * 100.

Table 6.2.1- 15 Identification of compounds from metabolism study

Common name/code	Chemical name	Chemical structure
Fluopicolide	2,6-dichloro-N-[2-chloro-3-(trifluoromethyl)-2-pyridylmethyl]benzamide	
Metabolite M01, BAM	2,6-dichlorobenzamide	

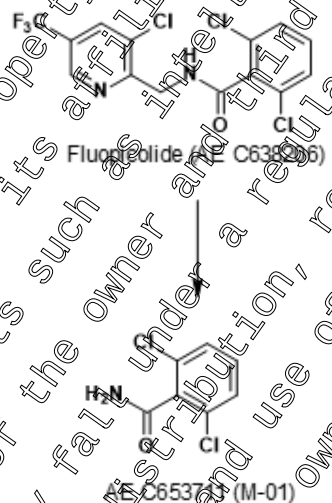
III. Conclusions

The metabolism of fluopicolide in oilseed rape was investigated following seed treatment with an 10 x overdose application rate of 117.6 g a.i./ha (19.6 g a.i./kg seeds) for the phenyl-UL-^{14}C label and 111.6 g a.i./ha (18.6 g a.i./ kg seeds) for the pyridyl-2,6-^{14}C-label. Low residues were detected, in spite of an 10 x overdose treatment. Nearly the complete residues in forage were conventionally extractable. Residues in seeds were sufficiently extracted by conventional extraction and a subsequent exhaustive extraction with microwave assistance. In all RACs the major residue was the parent compound. The only prominent metabolite was 2.6-dichlorobenzamide (M-01, BAM). All other metabolites were detected in low amounts (≤ 4.1% of TRR and ≤ 0.002 mg/kg).

The only observed metabolic reaction is the cleavage of fluopicolide to 2,6-dichlorobenzamide.

Label specific metabolites of the pyridyl-2,6-^{14}C label were not detected in the RACs. Therefore, it was assumed, that 2,6-dichlorobenzamide was most probably formed in the soil.

The metabolic pathway for oilseed rape which has been seed treated with fluopicolide, is as follows:



Assessment and conclusion by applicant:

The study is acceptable and demonstrates the metabolic fate of fluopicolide within pulses/oilseed commodities.

The rate to seeds was 18.6 - 19.6 g a.i./kg seeds. Based on the representative use for oilseed rape (applied at a rate of 2 g a.i./kg seeds), the corresponding N-rate for the metabolism study is approximately 9- 10 N.

CA 6.2.2 Poultry

The calculations show that the dietary burden for poultry (broiler, layer, and turkey) exceeds the trigger value of 0.004 mg kg bw/day for both fluopicolide and M-01 (CA 6.4.1). Therefore, a metabolism studies covering these compounds are required. The fluopicolide hen metabolism study was previously reviewed at the EU level.

Following repeated oral administration of [^{14}C]-AE C638206 with a dose equivalent to 1 or 10 ppm in the diet for 14 days to the laying hen with either the phenyl or the pyridyl radiolabel the overall recoveries of radioactivity were quantitative and ranged from between a mean of 83% to a mean of 96%.

Table 6.2.2- 1 Overall Recovery of radioactivity from laying hens following 14 daily oral administrations of [^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm

Data expressed as percentage of administered dose.

Sample	Phenyl radiolabel				Pyridyl radiolabel			
	1 ppm diet		10 ppm diet		1 ppm diet		10 ppm diet	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Excreta	81.92	7.15	94.59	2.925	92.63	2.51	92.00	3.16
Egg White	0.04	0.03	0.04	0.02	0.04	0.01	0.02	0.01
Egg Yolk	0.04	0.04	0.05	0.03	0.09	0.01	0.06	0.01
Cage wash	0.46	0.38	0.43	0.14	2.82	1.15	2.34	0.46
Final cage wash	0.28	0.23	0.21	0.06	n.a.*	n.a.	n.a	n.a.
Tissues	0.24	0.07	0.23	0.06	0.09	0.02	0.06	0.01
Total	82.97	7.145	95.56	2.91	95.69	1.63	94.49	2.99

n.a. = not applicable as value was included in cage wash result

The majority of the administered radioactivity was recovered in the excreta (82-95%) leaving only low levels of radioactivity in the tissues and eggs. The levels of radioactivity recovered in the tissues of the phenyl radiolabel groups were consistently higher (approximately three-fold) than those recovered for the pyridyl radiolabel groups. This suggests that the fate of the pyridyl radiolabel differed to some extent to that of the phenyl radiolabel which, in turn, implies that a proportion of the administered AE C638206 had been metabolised allowing the separation of the phenyl and pyridyl rings.

At the 1 ppm dose level the mean radioactive residues found in the egg whites varied between 0.001 to 0.011 µg equiv./g with a tendency towards higher concentrations, albeit very low, for the phenyl radiolabel group. At the 10 ppm dose level this tendency was more pronounced with the concentration of radioactivity in the egg whites from the phenyl group being, on average, three times higher than those from the pyridyl dose group. In both groups the concentrations remained low, varying between 0.001 to 0.066 µg equiv./g.

At the 1 ppm dose level the mean radioactive residues found in the egg yolks varied between 0.001 to 0.023 µg equiv./g again with a tendency towards higher concentrations, albeit very low, for the phenyl radiolabel group. At the 10 ppm dose level this tendency was more pronounced with the concentration of radioactivity in the egg yolks from the phenyl group being, on average, twice those from the pyridyl dose group. In both groups the concentrations remained low, varying between 0.003 to 0.198 µg equiv./g. The following table summarizes the egg data.

Table 6.2.2- 2 Concentrations of radioactivity in the egg yolks and whites of laying hens following 14 daily oral administrations of [^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Values are expressed in terms of µg equivalents per gram sample.

Sample	Timepoint	Phenyl radiolabel		Pyridyl radiolabel	
		1 ppm	10 ppm	1 ppm	10 ppm
Egg Yolk	24 h	BLQ	BLQ	0.002	0.003
	48 h	0.001	0.009	0.001	0.008
	72 h	0.005	0.034	0.003	0.022
	96 h	0.007	0.064	0.009	0.043
	120 h	0.010	0.024	0.008	0.058
	144 h	0.014	0.099	0.008	0.066
	168 h	0.012	0.156	0.010	0.077
	192 h	0.014	0.156	0.011	0.083
	216 h	0.015	0.159	0.011	0.079
	240 h	0.019	0.154	0.011	0.077
	264 h	0.023	0.178	0.011	0.089
	288 h	0.019	0.198	0.014	0.085
	312 h	0.020	0.134	0.013	0.087
	335 h	0.020	0.180	0.013	0.084
Egg White	24 h	BLQ	0.001	0.001	0.003
	48 h	0.004	0.022	0.001	0.009
	72 h	0.004	0.034	0.002	0.011
	96 h	0.005	0.027	0.002	0.013
	120 h	0.005	0.005	0.002	0.010
	144 h	0.007	0.034	0.002	0.013
	168 h	0.011	0.030	0.001	0.010
	192 h	0.003	0.049	0.002	0.012
	216 h	0.003	0.047	0.002	0.011
	240 h	0.004	0.037	0.001	0.011
	264 h	0.005	0.034	0.001	0.011
	288 h	0.007	0.066	0.003	0.009
	312 h	0.006	0.054	0.002	0.013
	335 h	0.004	0.043	0.002	0.013

The tissue concentrations for both radiolabels are presented in the following table.

Table 6.2.2- 3 Concentrations of radioactivity in the tissues of laying hens following 14 daily oral administrations of [^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Data expressed in terms of µg [^{14}C]-AE C638206 equivalents/g tissue.

Sample	Phenyl Radiolabel				Pyridyl Radiolabel			
	1 ppm diet		10 ppm diet		1 ppm diet		10 ppm diet	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Liver	0.126	0.057	0.976	0.416	0.041	0.008	0.275	0.049
Skin with fat	0.008	0.003	0.069	0.011	0.003	0.001	0.022	0.011
Muscle	0.004	0.001	0.039	0.006	0.002	0.000	0.011	0.003
Fat	0.006	0.001	0.061	0.023	0.003	0.001	0.026	0.014
Blood	0.018	0.006	0.192	0.059	0.020	0.004	0.125	0.021
Plasma	0.003	0.001	0.042	0.015	0.002	0.001	0.016	0.005

The highest tissue concentrations were consistently observed in the liver at both dose levels and using both radiolabels. As already discussed for the eggs and the total tissue recovery data, the radioactivity concentrations in the tissues from the dose group that received the phenyl radiolabel were higher than those from the dose group that received the pyridyl radiolabel. At the 10 ppm dose level the concentrations in the edible tissues (excluding blood and plasma) were approximately three times higher in the phenyl dose group compared to the pyridyl dose group. The blood and plasma concentrations did not consistently show the same degree of difference between the radiolabels as the edible tissues.

There was no evidence of any accumulation of radioactivity in eggs or edible tissues.

The identified metabolites of AE C638206 in the hen are proposed to be formed by hydroxylation of the chlorophenyl ring in the meta and para positions to give metabolites AE 0712556 and AE C643890, respectively. Each of these metabolites is conjugated with sulphate or hydroxylated in a second position to give a proposed dihydroxy intermediate, which is further metabolised to a sulphate conjugate. Additionally a methyl sulphone conjugate of AE C638206 and AE C653711 have been observed in the liver.

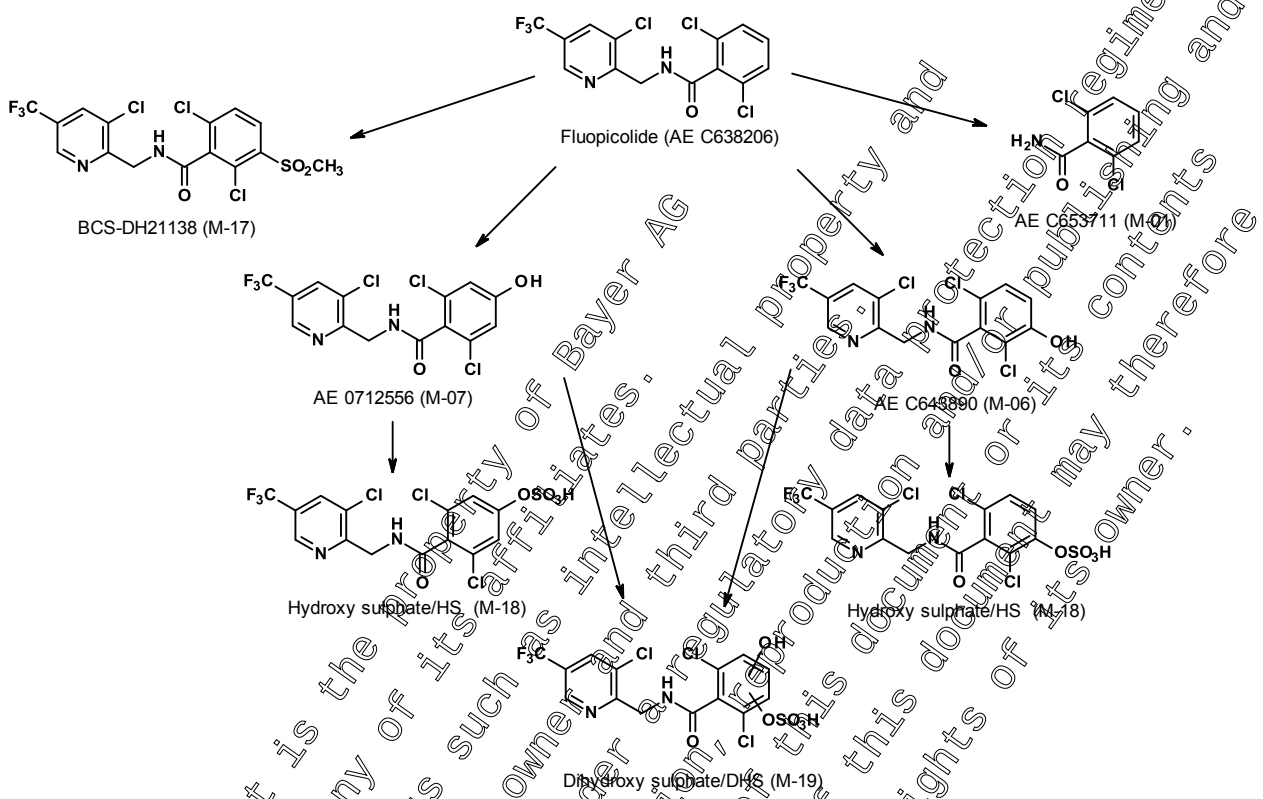
In addition to the identified metabolites complementary work was performed on the unidentified polar fractions in the liver and kidney. In the phenyl radiolabel study cell fractionation demonstrated that bulk of the metabolite residues (78.2%) were found in three cellular fractions. Water soluble low molecular weight proteins, amino acids and peptides contained 23.3% of TRR; sulphurated glucosaminoglycans contained 29.1% of TRR and a further 25.8% of TRR was found in the high molecular weight proteins. There was no significant association of the radioactive residues of AE C638206 and RNA or DNA. The pyridyl radiolabel study took an alternative approach and demonstrated that the bulk of the radioactivity was associated with amino acids and peptides by use of a VYDAC HPLC column which could resolve such components. These results suggest that the residues of AE C638206 were in association with proteins in the hen liver.

The tissue distribution and egg radioactivity concentrations both indicated that higher levels were achieved with the phenyl radiolabel. The tissue recoveries demonstrated a much lower proportion of the radioactivity being left in the tissues of the pyridyl radiolabel groups compared to the phenyl radiolabel groups at the end of the study. The presence of a methyl sulphone conjugate of AE C638206 and the presence of AE C653711 in the phenyl radiolabel study both, together with the proposed metabolic pathway for AE C638206 in the rat (see section 3, 5.1 of Annex II), provide a possible explanation for the observed differences in tissue and egg levels. The presence of AE C653711 shows that a proportion of the parent molecule had been cleaved, probably by oxidative N-dealkylation, to form both AE C653711 (BAM) containing the phenyl portion of the parent molecule and AE C657188 (PCA) which contained the pyridyl portion of the parent. When administered to the rat [^{14}C]-PCA was seen to be

eliminated *via* the urine unchanged. BAM, on the other hand, underwent significant biotransformation which included conjugation with glutathione that was subsequently metabolised through to a mercapturic acid conjugate, a cysteine conjugate and a thiomethyl metabolite. The rat also produced such metabolites (and many more) after administration of [^{14}C]-AE C638206. It was noteworthy that the majority of the biotransformations occurred on the phenyl ring of AE C638206 as opposed to the pyridyl ring. The investigations into the polar metabolites in the liver and kidney in both studies demonstrated that they were associated with amino acids, peptides and proteins. Such associations are known to occur when amino acid conjugates and thiomethyl groups are formed. Thus, assuming that the majority if not all, of these metabolites were formed on the phenyl ring (either as parent or after cleavage) then it would be expected that higher tissue levels would be observed with the phenyl radiolabel compared to the pyridyl radiolabel as more of the radioactivity would be in association with liver and kidney peptides/proteins. On the other hand in the pyridyl radiolabel experiment the radiolabelled portion of the molecule that was cleaved would be expected to be eliminated in the urine as PCA resulting in relatively lower tissue radioactivity concentrations.

The proposed metabolic pathway for [^{14}C]-AE C638206 in the hen following repeated administration is presented in Figure 6.2.2-1.

Figure 6.2.2-1: The Proposed Metabolic Pathway for [^{14}C]-AE C638206 in the Laying Hen



Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.2.2/01
Report Author:	[redacted]
Report Year:	2009
Report Title:	(14C)-AE C638206: Absorption, distribution, metabolism and excretion following repeated oral administration to the laying hen
Report No:	2014/004-D1145
Document No:	M-233977-03-1
Guideline(s) followed in study:	US EPA Sub-division O, Series 171-4b and OPPTS 860.1300; EU 96/68/EC Annex I, Section 6.2
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The objectives of this study were to determine the routes and rates of excretion of [phenyl-U-^{14}C]-AE C638206 and/or its radiolabelled metabolites following a 14 day repeat dose regimen in the laying hen at two dose levels (1 & 10 ppm diet). To provide information on the levels [phenyl-U-^{14}C]-AE C638206 and/or its radiolabelled metabolites in excreta, eggs and selected tissues following repeat administrations of [phenyl-U-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm of daily food consumption. To investigate the number, quantity and identity of radiolabelled metabolites present in tissues, eggs, and excreta. To provide an indication, from the levels of radioactivity in excreta, eggs and selected tissues, of the material balance.

Material and Methods:

Species, strain: Hen, Hisex bovine

Source: [redacted]

Number and sex: 10 laying females

Age/body weight: 19-22 weeks/1 to 2 kg on arrival.

Acclimatisation: The hens were acclimatised for 21 days. During acclimatisation, the hens were placed in individual metabolism cages suitable for the separate collection of excreta and eggs and acclimatised in the cages for 7 days. During the acclimatisation period in the cages, food consumption and egg production were measured. The appearance and behaviour of the animals were observed twice daily (*am* and *pm*). Prior to dosing, the hens were subject to a veterinary inspection to ensure they were fit for experimentation.

Animal identification: Individual leg tags.

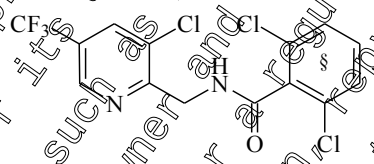
Environmental conditions: Rooms maintained at 10-25 °C, relative humidity of 38 to 86% and a minimum of 10 air changes/hr. Fluorescent lighting provided a 16 hour light (07:00 to 23:00) and 8 hour dark.

Food and water: Hens were offered a total of 150 g of a mixture of a commercially available ground concentrate (507 P.H.L. Mash, Farmway Ltd, Darlington, UK) and grit (Supa, Fringill Farm Supplies Ltd, UK) per day. The ratio of concentrate to grit was established during acclimatisation and maintained throughout the study. Food consumption was recorded daily. Mains water was available *ad libitum*. Alcontrol Laboratories (Bradford, England) undertook periodic analysis of the drinking water for heavy metals and chlorinated hydrocarbons. The results of these analyses are maintained in a central file at Covance.

Test Material:

Non-radiolabelled: Batch: R001732
Purity = 99.3%.

Radiolabelled: [phenyl-U-^{14}C]-AE C638206.
Batch: DCR11/3.
Specific activity: 5.81 MBq/mg (157 µCi/mg).
Radiopurity: 99.4%.



§ = position of radiolabel.

Treatment:

Capsules containing appropriate amounts of admixed [phenyl-U-^{14}C]-AE C638206 and non-radiolabelled AE C638206 were administered orally once daily for 14 consecutive days.

Group designation	Number of animals	Nominal dose level	
		Equivalent dietary concentration (ppm diet)*	Radioactive dose (MBq/day)
A	5	1	0.87
B	5	10	5

*These doses are based on an assumed consumption of 0.15 kg dry matter/day.

Sampling:

Following the administration of [phenyl-U-^{14}C]-AE C638206 the hens were returned to individual metabolism cages. Eggs were collected afternoon and morning following dose administration, and excreta was collected at 24-h intervals until necropsy. At each collection of excreta, cage debris were removed and pooled by animal over the study period. At approximately 23 h to 24 h after the last dose administration, the hens were removed from the metabolism cages and killed by cervical dislocation. A terminal sample of blood was collected and a portion was centrifuged to prepare plasma. The metabolism cages were rinsed with water then methanol to provide final cage washes. The muscle, fat (peritoneal and perirenal), liver (whole organ) and skin (including subcutaneous fat) were taken or sampled.

Eggs were separated into white and yolk and pooled, by animal over 24 h periods. The excreta was homogenised with water where appropriate. Tissues were homogenised in the presence of dry ice prior to storage.

Radioassay:

All radioassays were performed in at least duplicate.

Radioactivity was measured for 5 min or for 2 sigma % using Packard Tri-Carb liquid scintillation counters (Perkin Elmer Life Sciences Ltd, Pangbourne, Berkshire) with the facilities for computing quench-corrected disintegrations per minute (dpm).

Efficiency correlation curves were prepared for organic, aqueous, and combusted sample types and were routinely checked by the use of (^{14}C)-toluene quenched standards (obtained from Packard Biosciences). The spectrometer was recalibrated if a deviation of greater than 3% was observed when counting quality control standards.

The limit of quantification for the analysis of each sample type was applied to uncorrected sample counts and was defined as twice the background disintegration rate obtained from the measurement of blank samples.

Chromatography:

Excreta, eggs and tissues were extracted by various methods including solvent extraction, protease hydrolysis and acid hydrolysis and the extracts were analysed by two HPLC systems for metabolite quantification. Both systems were reverse-phase gradient elution methods using a Columbus X-Terra C18 (250 x 4.6 mm, 5 µm) column. Identification work was performed with LC-MS and comparison with authentic standards.

Results

Group A received a dose corresponding to 1.17 ppm diet, and Group B a dose corresponding to 10.7 ppm diet. Over the 14 days of the study there was a quantitative recovery of radioactivity for both dose Group A and B (*ca* 83% and 96% respectively).

Radioactivity was detected in eggs at all time points with the exception of day one samples where radioactivity was detected in only one egg white sample. At the low dose level, the concentration of radioactivity reached a steady-state level by 7-12 days after the first dose administration in both egg white (maximum, 0.011 ppm; 0.011 µg equivalents/g) and yolk (0.023 ppm). At the high dose level, the steady state conditions were achieved by day 12 in egg white (0.066 ppm) and yolk (0.198 ppm). The data for the eggs are presented in Table 6.2.1-2.

Table 6.2.2- 4 Overall Recovery of radioactivity from laying hens following 14 daily oral administrations of [phenyl-U-^{14}C] - AE C638206 at the nominal dose levels of 1 and 10 ppm

Tissue	Per cent of administered dose			
	1 ppm diet		10 ppm diet	
	Mean	SD	Mean	SD
Excreta	81.92	7.154	94.59	2.925
Egg White	0.038	0.026	0.038	0.017
Egg Yolk	0.042	0.036	0.052	0.029
Cage wash	0.458	0.378	0.434	0.144
Final cage wash	0.278	0.231	0.210	0.057
Tissues	0.235	0.074	0.234	0.056
Total	82.97	7.145	95.56	2.91

Table 6.2.2- 5 Concentrations of radioactivity in the egg yolks and whites of laying hens following 14 daily oral administrations of [phenyl-U-^{14}C] - AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Values are expressed in terms of µg equivalents per gram sample.

Time	Group A (1 ppm diet)				Group B (10 ppm diet)			
	Egg Yolk		Egg White		Egg Yolk		Egg White	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Day 1	BLQ	NA	BLQ	NA	BLQ	NA	0.001	NA
Day 2	0.001	0.001	0.004	0.003	0.009	NA	0.022	NA
Day 3	0.005	NA	0.004	NA	0.034	0.012	0.034	0.001
Day 4	0.007	NA	0.005	NA	0.064	NA	0.027	NA
Day 5	0.010	NA	0.005	NA	0.024	NA	0.005	NA
Day 6	0.014	NA	0.007	NA	0.099	0.045	0.054	0.008
Day 7	0.012	0.006	0.011	0.006	0.156	0.035	0.030	0.009
Day 8	0.014	NA	0.003	NA	0.196	NA	0.049	NA
Day 9	0.015	NA	0.003	NA	0.159	NA	0.047	NA
Day 10	0.019	NA	0.004	NA	0.154	NA	0.035	NA
Day 11	0.023	NA	0.005	NA	0.178	0.032	0.034	0.013
Day 12	0.019	NA	0.007	NA	0.198	NA	0.066	NA
Day 13	0.020	NA	0.006	NA	0.134	NA	0.054	NA
Day 14	0.020	NA*	0.004	NA	0.180	0.022	0.043	0.009

BLQ – Below limit of quantification
NA – Not applicable (arising when less than three eggs produced in a day)

The concentrations of radioactivity in the tissues are shown in Table 6.2.1.-3. Radioactivity was detected in all tissues ca 24 h after the last dose administration with the highest concentration being detected in the liver at both dose levels. The levels of radioactivity in the skin, fat and muscle were all below the level of systemic exposure (blood) at both dose levels.

Table 6.2.2- 6 Concentrations of radioactivity in the tissues of laying hens following 14 daily oral administrations of [phenyl-U-^{14}C] - AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Tissues	Concentration of radioactive residues (ppm)			
	Dose Group A (1 ppm diet)		Dose Group B (10 ppm diet)	
	Mean	SD	Mean	SD
Plasma	0.003	0.001	0.042	0.015
Blood	0.018	0.006	0.192	0.059
Fat	0.006	0.001	0.061	0.023
Liver	0.126	0.057	0.976	0.416
Skin	0.008	0.003	0.069	0.011
Muscle	0.004	0.001	0.039	0.006

The major metabolite detected in the excreta 24 h after the first dose was AE C643890, which accounted for 56% of the excreted radioactivity. There was a small amount (4.2%) of unchanged AE C638206 also present.

Table 6.2.2- 7 Proportion of Radioactivity Identified/characterised following 14 daily oral administrations of [phenyl-U-^{14}C] - AE C638206 at the nominal dose level of 10 ppm in diet

Tissue	Residue level (ppb)	% Extracted	% Total ^{14}C-residue identified/characterised						
			AE C638206	AE C643890	AE C653711	Metabolite 1	Unknown	Polar	Non-extracted
0-24 h Excreta	n.a.	77.6	4.2	56	n.d.	n.d.	2.8	n.d.	22.4
Egg white	43	98	2.5	n.d.	n.d.	51	n.d.	n.d.	2
Egg yolk	154	82	11	n.d.	n.d.	n.d.	13	45	23
Liver	976	78	n.d.	5.4	37	n.d.	22	n.d.	22
Skin	69	69	n.d.	15	n.d.	10	n.d.	34	31
Fat	61	76	6	n.d.	n.d.	38	n.d.	19	24
Muscle	39	56	n.d.	n.d.	n.d.	n.d.	n.d.	56	44

n.d. = not detected.
n.a. = not applicable.

In the tissues, AE C638206 was identified as a major component in the egg white, egg yolk and fat. Metabolite 1 (a methyl sulphone conjugate of AE C638206) was the major metabolite in egg white and fat, and AE C643890 was the major identified metabolite in the skin.

Table 6.2.2- 8 Concentration of TRR Identified/Characterised following 14 daily oral administrations of [phenyl-U-^{14}C] - AE C638206 at a nominal dose level of 10 ppm in diet

Tissue	Residue level (ppb)	Extracted (ppb)	Total ^{14}C-residue identified/characterised (ppb)						
			AE C638206	AE C643890	AE C653711	Metabolite 1	Unknown	Polar	Non-extracted
Egg white	43	42	1	n.d.	n.d.	22	n.d.	n.d.	1
Egg yolk	154	126	17	n.d.	n.d.	n.d.	20	69	35
Liver	976	762	n.d.	53	361	n.d.	212	n.d.	214
Skin	69	47	n.d.	10	n.d.	7	n.d.	23	22
Fat	61	46	4	n.d.	n.d.	23	n.d.	12	15
Muscle	39	22	n.d.	n.d.	n.d.	n.d.	n.d.	22	17

All the data presented in the above table were produced from experimental measurements and have not been normalised.
n.d. = not detected.

The residues in the liver proved difficult to extract with organic solvents. The liver was extracted with organic solvents, acid hydrolysed and treated with a mixture of β-D-glucuronidase and aryl sulphatase. In the majority of cases the final extract contained mainly polar metabolites eluting close to the solvent front by HPLC. The most successful extraction followed protease digestion and resulted in 68.6% TRR being available for HPLC analysis. The results of this analysis are summarised in Table 6.2.1-5 above.

The main metabolite present in the liver was identified as AE C653711, which accounted for 37% of the TRR (361 ppb). As the liver contained non-extractable residues, it was fractionated into the main cellular components in order to determine the distribution of the metabolites in the cellular fractions. The bulk of the metabolite residues (78.2%) were found in three cellular fractions. Water soluble low molecular weight proteins, amino acids and peptides contained 23.3% of TRR; sulphurated glucosaminoglycans contained 29.1% of TRR and a further 25.8% of TRR was found in the high molecular weight proteins. These results suggest that the metabolites (since no parent was seen) of AE C638206 were probably bound to proteins in the hen liver. There was no significant association of the radioactive residues of AE C638206 and RNA or DNA.

Conclusion

Following the daily oral dosing of hens with a dose equivalent to 1 or 10 ppm AE C638206 in the diet for 14 days, the mean recovery of radioactivity was 83 and 96% of the administered dose respectively. Overall a mean of 82% of the administered radioactivity was eliminated in the excreta from the 1 ppm group and a mean of 95% of the administered radioactivity was eliminated for the 10 ppm dose group. The residue levels were generally 10 times higher at the high dose with the exception of the liver and egg white (7.7 and 7 times respectively). At the high dose (Group B), the highest concentration of residues was found in the liver (0.976 µg equivalents/g) and egg yolk (up to 0.198 µg equivalents/g). The remaining edible tissues contained residues below 0.07 µg equivalents/g. The level of residues in the eggs reached steady-state concentration by day 7-12 after the first dose. The main identified metabolites in the tissues were unchanged AE C638206, AE C643890, Metabolite 1 (a methyl sulphone conjugate of AE C638206) and AE C653711, which was the major metabolite in the liver.

Assessment and conclusion by applicant:

The study is acceptable

Data Point:	KCA 6.2.2/02
Report Author:	[redacted]
Report Year:	2009
Report Title:	The distribution and metabolism of (14C)-AE C638206 in the laying hen
Report No:	21552
Document No:	M-233361-02-1
Guideline(s) followed in study:	US EPA, Subdivision O, Series 171-4, OPPTS 860.1300, EU 91/414/EEC as amended by 96/58/EC Annex 1, Section 6.2
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The objectives of this study were to determine the routes and rates of excretion of [pyridyl-2,6-^{14}C]-AE C638206 and/or its radiolabelled metabolites following a 14 day repeat dose regimen in the laying hen at two dose levels (1 & 10 ppm diet). To provide information on the levels [pyridyl-2,6-^{14}C]-AE C638206 and/or its radiolabelled metabolites in excreta, eggs and selected tissues following repeat administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm of daily food consumption. To investigate the number, quantity and identity of radiolabelled metabolites present in tissues, eggs, and excreta. To provide an indication, from the levels of radioactivity in excreta, eggs and selected tissues, of the material balance.

Material and Methods

Species, strain: Hen.

Source: [redacted]

Number and sex: 16 laying females.

Age/body weight: 25 weeks/1.51 to 2.21 kg on arrival.

Acclimatisation: During the acclimatisation period (13 days) the hens were subjected to veterinary examination to ensure that they were in good health and suitable for inclusion in the study. Egg laying was documented during the acclimatisation period and the 10 hens with the most consistent laying pattern were chosen for inclusion in the study. During the acclimatisation and study period the hens were individually housed in stainless steel metabolism cages specifically designed for the collection of excreta.

Animal identification: Individual leg tags.

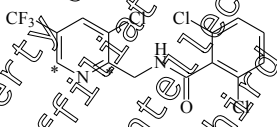
Environmental conditions: Room temperature and relative humidity were recorded daily, with ranges of 18-23°C and 33-75%, respectively. Throughout the acclimatisation and study period, the hens were maintained on a 16 h light/ 8 h dark cycle.

Food and water: The birds were offered a commercially available layer feed (Layers Pellets, Dodson & Horrell Limited) in individual feeders *ad libitum*. Food consumption was monitored and recorded daily throughout the acclimatisation and study period. Domestic mains quality water was also available *ad libitum*.

Test Material:

Non-radiolabelled: Batch: R001737,
Purity = 99.3%.

Radiolabelled: [pyridyl-2,6-^{14}C]-AE C638206.
Batch: GAR2034/4.
Specific activity: 6.77 MBq/mg (183 µCi/mg).
Radiopurity: >99%.



* = position of radiolabel in 2 and 6 positions of pyridine ring.

Treatment:

Dose capsules for each hen were administered once daily between 0900 – 1000 h for 14 consecutive days. The capsules were either placed manually in the crop of the hens and the throat stroked to induce swallowing or administered into the crop using a plastic gavage. The food consumption data indicated that each hen ate an average of 154 g per day and the target daily dose of [^{14}C]-AE C638206 was, therefore 0.154 mg (1 ppm) and 1.54 mg (10 ppm). The low dose group (hens 1-5F) were dosed with the low dose level capsules and the high dose group (hens 6-10F) received the high dose capsules.

Sampling:

Excreta was collected at 24 h intervals following administration of the first daily dose up until the time of killing. The cages were washed with water at the time of each 24 h excreta collection and the cage wash retained for analysis. Eggs were collected predose and then twice daily throughout the study period. The eggs were separated into egg white and egg yolk prior to analysis. Approximately 23 h after administration of the final dose, a blood sample was removed from the wing vein and the hens then immediately sacrificed by i.v. pentabarbitone injection. The carcasses were washed with water and plucked and the following tissues were removed: Whole Blood, Thigh Muscle, Plasma, Breast Muscle, Skin (with fat), Abdominal Fat Pad and Liver. Any whole eggs still in the oviduct at sacrifice were collected and treated as described previously. All other partially formed eggs present in the carcass were pooled for each bird prior to analysis.

Radioassay:

Each vial containing scintillant was analysed for 5 min, together with representative standard and blank samples, on a liquid scintillation analyser (Packard 1600TR Liquid Scintillation Analyser) with automatic quench correction using an external standard method. Scintillation vials were allowed to heat and light stabilise prior to analysis. Blanks were subtracted from the counts to give net dpm. per sample.

A limit of quantification of 30 dpm. above background has been instituted in these laboratories. If results arose from data less than 30 dpm. above background, the fact is noted in the results section of the report.

Chromatography:

Excreta, eggs and tissues were extracted by various methods including solvent extraction, protease hydrolysis and acid hydrolysis and the extracts were subjected to one or two HPLC systems for metabolite quantification. The first being a reverse-phase gradient elution using an X-Terra C18 (250 x 4.6 mm, 5 µm) column and the second using a VYDAC Protein and Peptide C18 (250 x 4.6 mm, 5 µm) column. Identification work was performed with LC-MS and comparison with authentic standards.

Findings:

The major route of elimination of radioactivity was *via* excreta with a mean of 92.63% and 92.00% of the administered dose being excreted 335 h after administration of the first dose to birds in the low and high dose groups, respectively. Cage wash accounted for a mean of 2.32% and 2.34%, respectively. Mean recovery of radioactivity in egg white, egg yolk and retained tissues were very low for both groups.

The mean overall recovery of radioactivity from the birds in the low and high dose groups was 95.69% and 94.49% of the total administered dose, respectively.

Table 6.2.2- 9 Overall Recovery of radioactivity from laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm in the diet

Sample	Recovery of Total Radioactivity (% of Administered Dose)			
	Target dose level: 1 ppm in diet		Target dose level: 10 ppm in diet	
	Mean	SD	Mean	SD
Excreta	92.63	2.51	92.00	3.16
Cage Wash	2.32	1.15	2.34	0.46
Egg White	0.04	0.01	0.02	0.01
Egg Yolk	0.09	0.01	0.06	0.01
Pre-Lay Eggs	0.03	0.01	0.01	0.00
Tissues	0.09	0.02	0.06	0.01
Total	95.69	1.63	94.49	2.99

The pattern of distribution of radioactivity into egg whites and egg yolks was similar between the dose groups. Concentrations of radioactivity were higher in the egg yolk than in the egg white. The peak concentration of total radioactivity in egg yolk was observed at 288 h post first dose (mean value of 0.014 µg equiv.g^{-1}) for the low dose level and at 264 h post first dose (mean value of 0.089 µg equiv.g^{-1}) for the high dose level. Mean concentrations of 0.001 to 0.003 µg equiv.g^{-1} were observed in the low dose level egg white samples throughout the collection period. For the high dose level, mean concentrations for the egg white samples remained between 0.003 and 0.013 µg equiv.g^{-1} throughout the collection period. Comparison of residue levels in the egg whites and egg yolks at the high and low dose level showed that the levels did not quite increase in direct proportion with the 10 fold increase in dose level with a mean seven-fold increase in the levels for the 10 ppm group for both sample types.

The highest mean concentration of radioactivity in tissues from the low and the high dose groups were recorded in the liver (0.041 µg equiv.g^{-1} and 0.275 µg equiv.g^{-1}, respectively). Concentrations of radioactivity in the abdominal fat, skin with fat, breast muscle and thigh muscle ranged from 0.002 to 0.003 µg equiv.g^{-1} at the low dose level and 0.010 to 0.026 µg equiv.g^{-1} at the high dose level. The overall distribution of total radioactivity within the tissues was broadly similar for both dose levels. Comparison of residue levels in tissues at the high and low dose level showed a reasonable correlation based on a 10 fold increase in dose level.

Radioactivity was extracted from pooled samples of excreta, liver, abdominal fat, skin with fat, breast muscle, thigh muscle, egg yolk (96 h and 312 h) and egg white (96 h and 312 h) at the high dose level and from excreta, liver and egg yolk (312 h) at the low dose level with solvent and, where appropriate, additional enzymatic (liver and egg yolk) and hydrolytic methods (liver).

Extraction efficiencies for the high dose samples were >93.5% of the total radioactive residue for the excreta, egg yolk, and egg white. The extraction efficiency for the liver and fat were slightly lower at 80.0% and 88.6% TRR respectively. The skin with fat extraction efficiency was 62.8% TRR. Only low extraction efficiencies for breast (17.7% TRR) and thigh (23.6% TRR) muscle were achieved due to the very low initial residue levels (0.010 and 0.011 µg equiv.g^{-1}, respectively).

Table 6.2.2- 10 Concentrations of radioactivity in the egg yolks and whites of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Values are expressed in terms of µg equivalents per gram sample.

Sample	Time point	Nominal 1 ppm in diet		Nominal 10 ppm in diet	
		Mean	SD	Mean	SD
Egg Yolk	PreDose	N.A.	N.A.	N.A.	N.A.
	24 h	°0.002	°0.001	°0.003	°0.002
	48 h	0.001	0.001	0.008	0.002
	72 h	0.003	0.001	0.022	0.004
	96 h	0.009	0.002	0.043	0.009
	120 h	0.008	0.001	0.058	0.011
	144 h	0.008	0.002	0.066	0.013
	168 h	0.010	0.002	0.077	0.013
	192 h	0.011	0.002	0.085	0.015
	216 h	0.011	0.002	0.079	0.015
	240 h	0.011	0.002	0.077	0.016
	264 h	0.011	0.002	0.089	0.008
	288 h	0.014	0.003	0.085	0.013
	312 h	0.013	0.002	0.087	0.011
	335 h	0.013	0.002	0.084	0.011
Egg White	PreDose	N.A.	N.A.	N.A.	N.A.
	24 h	0.001	0.001	°0.003	°0.002
	48 h	0.001	0.000	0.009	0.004
	72 h	0.002	0.001	0.011	0.004
	96 h	0.002	0.001	0.013	0.007
	120 h	0.002	0.000	0.010	0.003
	144 h	0.002	0.001	0.013	0.006
	168 h	0.001	0.000	0.010	0.004
	192 h	0.002	0.001	0.012	0.003
	216 h	0.002	0.001	0.011	0.002
	240 h	0.001	0.000	0.011	0.005
	264 h	0.001	0.000	0.011	0.003
	288 h	0.003	0.001	0.009	0.004
	312 h	0.002	0.001	0.013	0.001
	335 h	0.002	0.001	0.013	0.005

N.A. = Not applicable

° = Mean includes results calculated from data less than 30 dpm above background

Table 6.2.2- 11 Concentrations of radioactivity in the tissues of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm in diet

Sample	Mean Tissue Concentration of Radioactivity (µg.equiv.g^{-1})			
	Tissues taken 335 h post dose 1			
	Target dose level: 1 ppm in diet		Target dose level: 10 ppm in diet	
	Mean	SD	Mean	SD
Abdominal Fat Pad	0.003	0.001	0.026	0.014
Liver	0.041	0.008	0.275	0.049
Thigh Muscle	0.002	0.000	0.011	0.002
Breast Muscle	°0.002	0.000	0.010	0.003
Skin with Fat	0.003	0.001	0.022	0.011
Pre-Lay Eggs	0.010	0.006	0.079	0.013
Plasma	0.002	0.001	0.016	0.005
Whole Blood	0.020	0.004	0.125	0.021

° = Mean includes results calculated from data less than 30 dpm. above background

Radio-HPLC profiles of excreta extracts from hens 6-10F (high dose) and 1-5F (low dose) collected 48 h and 335 h after dose administration were consistent and contained two major components which were identified as AE C638206 and AE C643890 by co-chromatography and by LC-MS. Parent AE C638206 represented 1.64 to 4.39% of dose (25.2 to 65.3% TRR). The metabolite AE C643890 represented 0.83 to 2.29% of dose (12.3 to 33.9% TRR). A component (retention time *ca* 50 min), which was assigned as a sulphate conjugate of dihydroxy parent by LC-MS analysis of solvent extracts of high dose excreta, was present in each of the excreta sample extracts and represented up to 1.44% of dose (22.2% TRR). Sulphate conjugates of hydroxylated parent were also detected at retention times of *ca* 49 min (hydroxy sulphate) and 52 min (dihydroxy sulphate) and represented between 0.05 to 0.48% of dose (0.8 to 7.1% TRR). Up to 5 additional, minor, components were present at retention times ranging from approximately 42 min to 56 min and levels up to 0.20% of dose (3.0% TRR).

The solvent extract from the high dose group (hens 6-10F) liver was found to contain 11 components. Only hydroxy parent AE 0712556 represented greater than 10 app., reaching a level of 0.016 ppm (5.9% TRR). Two minor metabolites in this sample were assigned as sulphate conjugates of hydroxylated parent. Initially, the enzyme hydrolysate from this sample was found to contain 5 components. Two of these were at levels of 0.001 and 0.002 ppm. The other 3 represented 0.021 ppm (7.6% TRR) to 0.053 ppm (19.3% TRR) and were present as poorly resolved tailing peaks. Using a second HPLC method specific for the separation of peptides, the enzyme hydrolysate was subsequently shown to contain 11 components, accounting for levels of 0.003 to 0.022 ppm (1.0 to 7.8% TRR). The 6M HCl hydrolysate was found to contain 9 components at levels of 0.001 to 0.006 ppm (0.1 to 2.1% TRR).

Only the enzyme hydrolysate from the low dose group (hens 1-5F) liver contained sufficiently high residue levels for HPLC analysis. Four components were detected, accounting for levels of 0.002 to 0.008 ppm (5.5 to 18.9% TRR). Four components were detected in abdominal fat from the high dose group with the major being AE 0712556 (47.3% TRR, 0.012 ppm). AE C638206 was identified as one of the 3 minor components. The same 4 components were detected in skin with fat from the high dose group. The major one was again AE 0712556 (29.9% TRR, 0.007 ppm) with AE C638206 being identified as one of the 3 minor components. Residue levels in the abdominal fat and skin with fat from the low dose group were too low for analysis.

The major component in the 96 h egg yolk from the high dose group (hens 6-10F) was assigned as a sulphate conjugate of dihydroxy parent (retention time *ca* 51 min) and accounted for 0.015 ppm (34.0% TRR). The metabolite AE 0712556 was detected and accounted for 0.004 ppm (9.6% TRR). Parent AE C638206 was also detected at a level of 0.005 ppm (10.5% TRR). Four minor unidentified components were detected at levels up to 0.002 ppm (3.9% TRR). One of these peaks was assigned as a sulphate conjugate of hydroxy parent and accounted for 0.002 ppm (3.9% TRR).

The major component in the 312 h egg yolk from the high dose group (hens 6-10F) was the metabolite AE 0712556 which accounted for 0.014 ppm (15.9% TRR). The major component was assigned as a sulphate conjugate of dihydroxy parent and was present at a level of 0.013 ppm (15.3% TRR). Parent AE C638206 was detected at a level of 0.003 ppm (3.3% TRR). A further minor component was present at a level of 0.006 ppm (7.1% TRR) and was assigned as a sulphate conjugate of hydroxy parent.

Neither of the enzyme hydrolysates from either egg yolk sample contained sufficiently high residue levels for HPLC analysis. Residue levels in the egg yolk samples from the low dose group (1-5F) were also too low for HPLC analysis. Only the 96 h egg white from the high dose group (6-10F) contained sufficiently high residue levels for HPLC analysis. Three components were detected. The metabolite AE 0712556 was the major component and accounted for 0.005 ppm (41.2% TRR). Another major component was assigned as a sulphate conjugate of dihydroxy parent and accounted for 0.003 ppm (22.5% TRR). A further minor unknown component was present at a level of 0.002 ppm (15.7% TRR).

The assignment of radiolabelled components detected in excreta, tissues and egg samples is summarised in the following Tables:

Table 6.2.2- 12 Characterisation and Identification of radioactivity in the Excreta of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	% Dose
Excreta (48 h)	1	Methanol	Unknown	42.1	0.4	0.02
			Unknown	44.9	0.8	0.05
			Unknown	48.0	0.7	0.05
			HS #	49.4	1.1	0.07
			DHS #	51.2	3.2	0.20
			DHS #	52.3	0.8	0.05
			Unknown	53.5	0.6	0.04
			Unknown	55.7	1.0	0.06
			AE C643890*	58.8	19.6	1.23
			AE C638206*	62.7	58.1	3.65
				Total	86.3	5.42
Excreta (335 h)	1	Methanol	Unknown	44.4	0.7	0.05
			Unknown	47.3	0.4	0.02
			HS #	50.0	7.1	0.48
			DHS #	51.0	0.8	0.06
			DHS #	51.9	1.0	0.06
			Unknown	56.2	0.7	0.05
			AE C643890*	59.5	12.3	0.83
			AE C638206*	63.5	65.3	4.39
				Total	88.3	5.94

% TRR = % Total radioactive residue. *= Assigned by co-chromatography and LC-MS. # = Assigned by LC-MS.
HS = Hydroxy sulphate of AE C638206. DHS = Dihydroxy sulphate of AE C638206.

Table 6.2.2- 13 Characterisation and Identification of radioactivity in the Excreta of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at a nominal dose level of 1 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	% Dose
Excreta (48 h)	1	Methanol	Unknown*	44.8	1.7	0.12
			Unknown	48.1	1.6	0.11
			HS #	49.4	1.5	0.10
			DHS #	51.3	6.6	0.44
			DHS #	52.3	1.5	0.10
			Unknown	53.7	1.4	0.09
			Unknown	55.7	1.1	0.07
			AE C643890	58.8	33.9	2.29
			AE C638206	62.7	27.7	1.87
				Total	77.0	5.19
Excreta (335 h)	1	Methanol	Unknown	41.7	0.6	0.04
			Unknown*	44.1	1.5	0.10
			Unknown	48.0	0.6	0.04
			HS #	49.5	1.1	0.07
			DHS #	50.8	22.2	1.44
			DHS #	52.1	2.6	0.17
			Unknown	53.4	3.0	0.20
			AE C643890	58.8	19.2	1.25
			AE C638206	62.7	25.2	1.64
				Total	76.9	4.95

% TRR = % Total radioactive residue. *= Assigned by co-chromatography and LC-MS. # = Assigned by LC-MS.
HS = Hydroxy sulphate of AE C638206, DHS = Dihydroxy sulphate of AE C638206.

Table 6.2.2- 14 Characterisation and Identification of radioactivity in the Liver of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at a nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	Ppm
Liver	1	Methanol	Unknown	7	0.7	0.002
			Unknown	12	0.2	0.001
			Unknown	37	2.7	0.007
			Unknown	43	2.2	0.006
			HS +	45	1.0	0.003
			HS ++	48	1.4	0.004
			DHS ++	50	1.9	0.005
			Unknown	55	0.1	<0.001
			Unknown	58	0.2	0.001
			AE 0712550 *	62	5.9	0.016
			Unknown	67	0.5	0.001
				Total	16.8	0.046
		Enzyme Hydrolysis	Unknown	9-10	0.8	0.002
			Unknown	28-36	19.7	0.053
			Unknown	39-43	18.4	0.051
			Unknown	44-50	7.6	0.021
			Unknown	51	0.2	0.001
				Total	46.8	0.128
		Acid Hydrolysis	Unknown	6-11	1.9	0.005
			Unknown	12-15	0.3	0.001
			Unknown	17-22	0.9	0.003
			Unknown	35-39	0.4	0.001
			Unknown	40-45	1.7	0.005
			Unknown	46-48	1.3	0.004
			Unknown	55	0.1	<0.001
			Unknown	59-61	2.1	0.006
			Unknown	68-70	0.6	0.002
				Total	9.3	0.027
	2	Enzyme Hydrolysis	Unknown	6	1.0	0.003
			Unknown	15-19	3.2	0.009
			Unknown	20-21	1.7	0.005
			Unknown	22-25	6.2	0.017
			Unknown	26-27	2.8	0.008
			Unknown	28-31	7.5	0.020
			Unknown	32-36	7.8	0.022
			Unknown	37-40	5.6	0.015
			Unknown	41-44	4.6	0.013
			Unknown	45-47	2.2	0.006
			Unknown	48-50	1.9	0.005
				Total	44.5	0.123

% TRR = % Total radioactive residue
ppm = µg equivalents.g^{-1}
\+ = assigned by extrapolation from 312 h egg yolk extract
++ = Assigned by SRM LC-MS
* = Assigned by co-chromatography and LC-MS
HS = Hydroxy sulphate of AE C638206
DHS = Dihydroxy sulphate of AE C638206

Table 6.2.2- 15 Characterisation and Identification of radioactivity in the Fat and the Skin & fat of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at a nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	ppm
Abdominal Fat	1	Methanol	Unknown	55	0.8	0.001
			AE 0712556 +	61	47.3	0.012
			AE C638206 *	63	15.6	0.004
			Unknown	67	7.0	0.002
				Total	73.7	0.019
Skin & Fat	1	Methanol	Unknown	53	2.2	0.001
			AE 0712556+	60	29.9	0.007
			AE C638206 *	63	15.8	0.003
			Unknown	67	8.5	0.002
				Total	56.4	0.012

% TRR = % Total radioactive residue
ppm = µg equivalents.g^{-1}
* = Assigned by co-chromatography and LC-MS
+ = assigned by co-chromatography with a reference standard

Table 6.2.2- 16 Characterisation and Identification of radioactivity in the Eggs of laying hens following 14 daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 at a nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	ppm
Egg Yolk (96 h)	1	Methanol	HS *	45	3.9	0.002
			Unknown	48	1.1	<0.001
			DHS *	51	34.0	0.015
			Unknown	54	2.6	0.001
			AE 0712556+	60	9.6	0.004
			AE C638206+	63	10.5	0.005
			Unknown	67	0.6	<0.001
				Total	62.3	0.027
Egg Yolk (312 h)	1	Methanol	HS +	44	7.1	0.006
			DHS +	52	15.3	0.013
			AE 0712556	61	15.9	0.014
			AE C638206	64	3.3	0.003
				Total	41.6	0.036
Egg White (96 h)	1	Methanol	DHS	51	22.5	0.003
			Unknown	58	15.7	0.002
			AE 0712556++	61	41.2	0.005
				Total	79.4	0.010

% TRR = % Total radioactive residue
ppm = µg equivalents.g^{-1}
* = Assigned by extrapolation from sample
+ = Assigned by SRM LC-MS
++ = Assigned by co-chromatography with a reference standard.
HS = Hydroxy sulphate of AE C638206.
DHS = Dihydroxy sulphate of AE C638206.

Conclusion:

Following repeated oral administration of [pyridyl-2,6-^{14}C]-AE C638206 to the laying hen, the recovery of radioactivity was quantitative with means of 95.69% dose and 94.49% dose recovered for the 1 and 10 ppm dose groups respectively. The elimination of radioactivity had reached the mean levels of 95.5% dose for the 1 ppm dose group and 94.3% dose for the 10 ppm dose group by 335 h post the first dose occasion. The total amount of radioactivity recovered in the eggs was 0.13% and 0.09% dose for the 1 and 10 ppm dose groups respectively. In terms of concentration of radioactivity in the eggs, the levels did not exceed mean levels of 0.003 µg equiv./g in the egg whites or 0.014 µg equiv./g for the egg yolks for the 1 ppm diet group and did not exceed mean levels of 0.013 µg equiv./g in the egg whites or 0.089 µg equiv./g for the egg yolks for the 10 ppm diet group. Concentrations of radioactivity in the tissues was also low which can be clearly seen in the results obtained from the group dosed at a level that would be considered to be in excess of a realistic field exposure level (1 ppm in the diet) where none of the tissue concentrations achieved or exceeded 0.05 ppm. Where tissue residues in excess of 0.05 ppm were detected in the hens dosed at the exaggerated level of 10 ppm in the diet (liver) they were shown to be multicomponent with each individual metabolite comprising the residue present at a low level (<0.05 ppm). The results from the 10 ppm dose group liver enzyme hydrolysis HPLC analysis using method 2 indicated that the low level components (0.003 to 0.022 ppm) present were associated with peptides which would also have been the case for the components in the kidney enzyme hydrolysate.

Several metabolite components present in the concentrated excreta, egg yolk, egg white and tissue extracts by HPLC were confirmed by using LC-MS.

In conclusion, following repeated oral administration of [^{14}C]-AE C638206 to the laying hen, there was no evidence of any accumulation of radioactivity in eggs or edible tissues. The compound was found to be mainly excreted and only partially absorbed and that which was absorbed was then extensively metabolised and rapidly eliminated resulting in low to almost undetectable tissue residues with low to very low transfer to eggs

The metabolism of AE C638206 in the hen is proposed to proceed by hydroxylation of the chlorophenyl ring in the meta and para positions to give metabolites AE 0712556 and AE C643890, respectively. Each of these metabolites is conjugated with sulphate or hydroxylated in a second position to give a proposed dihydroxy intermediate, which is further metabolised to a sulphate conjugate. The presence of polar components in the enzyme hydrolysate of liver and kidney that were associated with peptides was also demonstrated.

Assessment and conclusion by applicant:
The study is acceptable.

The following study is currently in progress and will be submitted at the indicated timepoint:

Dossier node	Draft title	Study ID	Planned submission
KCA 6.2.2	[^{14}C]-BAM: Nature of the Residue in Laying Hens (OECD 503)	VC/19/035	November 2020

CA 6.2.3 Lactating ruminants

The calculations show that the dietary burden for cattle exceeds the trigger value of 0.004 mg kg bw/day for both fluopicolide and M-01 (CA 6.4.2). Therefore, metabolism studies covering these compounds are required. The fluopicolide cattle metabolism study was previously reviewed at the EU level.

Following repeated oral administration of [^{14}C]-AE C638206 with a dose equivalent to 1 or 10 ppm in the diet for 7 days to the lactating cow with either the phenyl or the pyridyl radiolabel the overall recoveries of radioactivity were quantitative and ranged from between 76% to a mean of 84%.

Table 6.2.3- 1 Overall Recovery of radioactivity from lactating cows following twice daily oral administrations of [^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Data expressed as percentage of administered dose.

Sample	Phenyl radiolabel		Pyridyl radiolabel	
	1 ppm diet	10 ppm diet	1 ppm diet	10 ppm diet
Urine	16.81	19.34	13.50	10.71
Faeces	57.23	54.94	69.10	67.00
Cage wash	0.87	1.02	1.15	2.09
Final cage wash	0.05	0.06	n.a.*	n.a.*
Milk	0.14	0.13	0.09	0.08
Tissues	0.78	0.54	0.39	0.29
Total	75.88	76.03	84.23	80.17

*n.a. = not applicable as value was included in cage wash result.

The majority of the administered radioactivity was recovered in the urine and faeces for both radiolabels (*ca* 75% dose for the phenyl radiolabel and 80-84% dose for the pyridyl radiolabel) leaving only low levels of radioactivity in the tissues and milk. The levels of radioactivity recovered in the tissues of the phenyl radiolabel groups were consistently higher (approximately double) than those recovered for the pyridyl radiolabel groups. This suggests that the fate of the pyridyl radiolabel differed to some extent to that of the phenyl radiolabel which, in turn, implies that a proportion of the administered AE C638206 had been metabolised allowing the separation of the phenyl and pyridyl rings.

At the 1 ppm dose level the radioactive residues found in the milk varied between 0.0004 to 0.002 µg equiv./g with a tendency towards higher concentrations, albeit very low, for the phenyl radiolabel group. At the 10 ppm dose level this tendency was more pronounced with the concentration of radioactivity in the milk from the phenyl group being, on average, 1.75 times higher than those from the pyridyl dose group. In both groups the concentrations remained low, varying between 0.007 to 0.019 µg equiv./g. The following table summarizes the milk data.

Table 6.2.3- 2 Concentrations of radioactivity in the milk of lactating cows following twice daily oral administrations of [^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Values are expressed in terms of µg equivalents per gram sample.

Time point	Phenyl radiolabel		Pyridyl radiolabel	
	1 ppm diet	10 ppm diet	1 ppm diet	10 ppm diet
Day 1	0.0004	0.008	0.001	0.007
Day 2	0.001	0.014	0.001	0.010
Day 3	0.001	0.017	0.001	0.009
Day 4	0.002	0.018	0.001	0.010
Day 5	0.002	0.019	0.001	0.010
Day 6	0.002	0.018	0.001	0.010
Day 7	0.002	0.018	0.001	0.010
Day 8	0.001	0.014	0.001	0.010

The tissue concentrations for both radiolabels are presented in Table 6.2.1-30.

Table 6.2.3- 3 Concentrations of radioactivity in the tissues of lactating cows following twice daily oral administrations of [^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Data expressed in terms of µg [^{14}C]-AE C638206 equivalents/g tissue

	Phenyl radiolabel		Pyridyl radiolabel	
	1 ppm diet	10 ppm diet	1 ppm diet	10 ppm diet
Liver	0.900	6.443	0.058	0.449
Kidney	0.026	0.302	0.033	0.196
Fat	0.006	0.040	0.004	0.041
Muscle	BLQ	0.024	0.001	0.012
Blood	0.011	0.088	0.010	0.074
Plasma	0.013	0.100	0.011	0.082

The highest tissue concentrations were consistently observed in the liver at both dose levels and using both radiolabels.

Comparison of the concentrations observed in the tissues in the 1 ppm experiments shows that equivalent concentrations were obtained in all the tissues except the liver and muscle. In the case of the muscle the levels in the phenyl radiolabel experiment were below the level of quantification whilst those obtained in the pyridyl dose group were very low (0.001 µg equiv./g) but measurable. For the liver however the concentration observed in the phenyl radiolabel experiment was *ca* 16 times that observed in the pyridyl experiment.

Comparison of the concentrations observed in the tissues in the 10 ppm experiments shows that equivalent concentrations were obtained in the fat blood and plasma. The concentrations observed in the muscle and kidney samples from the phenyl radiolabel experiment were approximately twice those observed for the pyridyl experiment. As seen in the 1 ppm data, the concentration of radioactivity in the liver observed in the phenyl radiolabel experiment was *ca* 14 times that observed in the pyridyl experiment.

The identified metabolites of AE C638206 in the cow are proposed to have been formed by hydroxylation of the chlorophenyl ring in the meta and para positions to give metabolites AE 0712556 and AE C643890 respectively. Each of these metabolites is conjugated with sulphate or glucuronic acid. Alternatively metabolites AE 0712556 or AE C643890 were hydroxylated in a second position to give a proposed dihydroxy intermediate, which is further metabolised to give either a sulphate or glucuronide conjugate. The presence of polar components in the enzyme hydrolysate of liver and kidney that were associated with peptides was also demonstrated by HPLC.

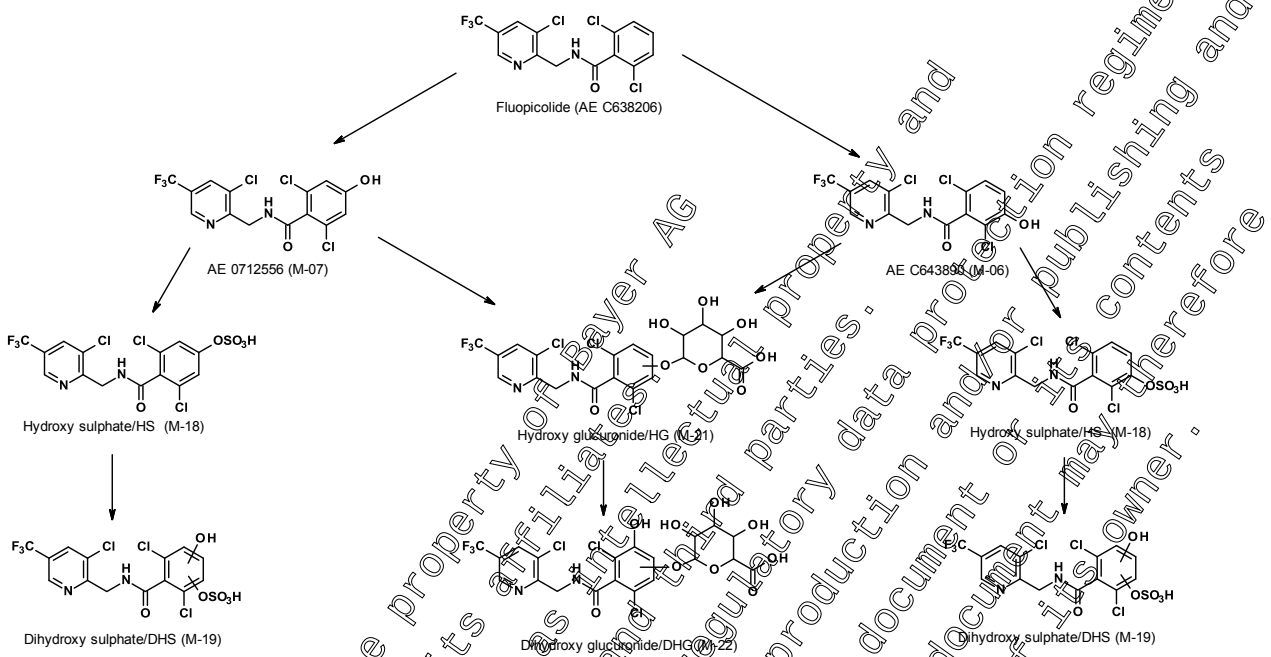
In addition to the identified metabolites complementary work was performed on the unidentified polar fractions in the liver and kidney. Fractionation of the liver and kidney cells showed that the majority of the radioactivity was associated with proteins and amino acids (63% in the liver, 69% in the kidney). It is possible that AE C638206 was being metabolised *via* conjugation with glutathione. The glutathione metabolites produced could then undergo cleavage by ß-lyase leaving metabolites that could bind to proteins and amino acids. There was a lack of significant incorporation of any protein-bound residues into RNA or DNA suggesting that the metabolic pathway was acting as a de-activation mechanism in this case. The pyridyl radiolabel study took an alternative but complementary approach and demonstrated that the bulk of the radioactivity in the unidentified polar fractions was associated with amino acids and peptides by use of a VYDAC HPLC column which could resolve such components (into 14 separate fractions for the liver and to below the LOQ for the kidney).

As was observed in the poultry metabolism studies, there was a tendency for higher radioactivity concentrations to be found in the phenyl radiolabel experiment compared to the pyridyl radiolabel experiment. Given that both radiolabels produced the same hydroxylated metabolites and conjugates thereof it would appear that the difference must be due to differing fates of the phenyl and pyridyl groups following a cleavage of the parent molecule. In both the hen and the cow the highest concentrations of radioactivity were observed in the liver and the livers of both species were found to contain polar fractions that were very difficult to extract and identify but were demonstrated to be associated with some of the liver and kidney proteins. In the case of the hen (and indeed the rat) cleavage products were observed as were metabolites that would have been produced following initial conjugation with glutathione. In the case of the cow the evidence is more circumstantial as the presence of cleavage products and thiomethyl metabolites could not be confirmed. It is assumed however that they had been formed and that the following explanation (already given for the hen) offers the best hypothesis for explaining both the difference in tissue/milk concentrations between the radiolabels and the presence of radioactivity associated with proteins.

The evidence suggests that a proportion of the parent molecule had been cleaved, probably by oxidative N-dealkylation, to form both AE C653711 (BAM) containing the phenyl portion of the parent molecule and AE C657188 (PCA) which contained the pyridyl portion of the parent. When administered to the rat [^{14}C]-PCA was seen to be eliminated *via* the urine unchanged. BAM, on the other hand, underwent significant biotransformation which included conjugation with glutathione that was subsequently metabolised through to a mercapturic acid conjugate, a cysteine conjugate and a thiomethyl metabolite. The rat also produced such metabolites (and many more) after administration of [^{14}C]-AE C638206. It was noteworthy that the majority of the biotransformations occurred on the phenyl ring of AE C638206 as opposed to the pyridyl ring. The investigations into the polar metabolites in the liver and kidney in both studies demonstrated that they were associated with amino acids, peptides and proteins. Such associations are known to occur when amino acid conjugates and thiomethyl groups are formed. Thus, assuming that the majority if not all, of these metabolites were formed on the phenyl ring (either as parent or after cleavage) then it would be expected that higher tissue levels would be observed with the phenyl radiolabel compared to the pyridyl radiolabel as more of the radioactivity would be in association with liver and kidney peptides/proteins. On the other hand, in the pyridyl radiolabel experiment the radiolabelled portion of the molecule that was cleaved would be expected to be eliminated in the urine as PCA resulting in relatively lower tissue radioactivity concentrations.

The proposed metabolic pathway for [^{14}C]-AE C638206 in the lactating cow following repeated administration is presented in Figure 6.2.3-1.

Figure 6.2.3-1: The Proposed Metabolic Pathway for [^{14}C]-AE C638206 in the Lactating Cow



Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.2.3/01
Report Author:	[redacted]
Report Year:	2008
Report Title:	(14C)-AE C638206: Absorption, distribution, metabolism and excretion following repeated oral administration to the lactating cow
Report No:	2014040-D1145
Document No:	M-218626-02-1
Guideline(s) followed in study:	US EPA Sub-division O, Series 171-4b and OPPTS 860.1300; EU 96/68/EC Annex I, Section 6.2
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted (DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The objectives of this study were to determine the routes and rates of excretion of [phenyl-U-^{14}C]-AE C638206 and/or its radiolabelled metabolites following a 7 day repeat dose regimen in the lactating cows at two dose levels (1 & 10 ppm diet). To provide information on the levels [phenyl-U-^{14}C]-AE C638206 and/or its radiolabelled metabolites in excreta, milk and selected tissues following repeat administrations of [phenyl-U-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm of daily food consumption. To investigate the number, quantity and identity of radiolabelled metabolites present in tissues, milk, and excreta. To provide an indication, from the levels of radioactivity in excreta, milk and selected tissues, of the material balance.

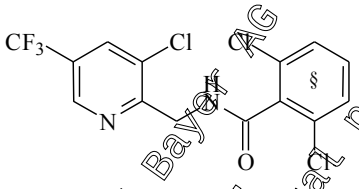
Material and Methods

Species, strain:	Cow, Holstein Friesian
Source:	[redacted]
Number and sex:	2 lactating females
Age/body weight:	*ca* 6.5 years/572-582 kg on arrival.
Acclimatisation:	The cows were acclimatised for up to 17 days. During the last 3 days of acclimatisation, the cows were placed in individual metabolism cages suitable for the separate collection of urine and faeces and acclimatised for 2 hours per day. During the initial acclimatisation period consumption of concentrate and milk production was measured. During the last few days of acclimatisation, measurement of food consumption was extended to include hay. The appearance and behaviour of the animals were observed twice daily (*am* and *pm*). Prior to dosing, the apparatus for the separate collection of urine and faeces was attached to the rear end of the cows.
Animal identification:	On receipt, ear tags with the supplier's number identified the cows. During the arrival procedure numbered collars containing an arbitrarily allocated stock number uniquely identified them. An individual subject code was allocated during the initial acclimatisation period. In addition to the above, metabolism cages were identified by the presence of coloured cards giving information including study number, subject code and animal number. The study room was identified by a card on the outside door giving information including room number and study number.
Environmental conditions:	The cows were housed in the livestock unit which was maintained at a temperature of between 16 and 20°C and humidity between 46 and 76% (temperature and humidity were recorded daily). Fluorescent lighting was cycled 16 h light (07:00 - 23:00) and 8 h dark. The unit is designed so that there are 10 air changes per h.
Food and water:	The cows were offered a total of 3 kg of a mixture of a commercially available concentrate (261 – Kestrel, Farmway Limited) twice daily after both morning and afternoon milking. 101F manifested signs of bloat during the acclimatisation period and on veterinary advice the amount of concentrate offered was reduced to 2 kg twice daily. Consumption of concentrate was recorded daily. Hay was offered *ad libitum*. Consumption was recorded during the last 3 days of acclimatisation and until termination of the study. Mains water was available *ad libitum*. Alcontrol Laboratories (Bradford, England) undertook periodic analysis of the drinking water for heavy metals and chlorinated hydrocarbons. The diet and water were considered not to have contained any contaminant at a level that might have affected the integrity or outcome of the study.

Test Material:

Non-radiolabelled: Batch: R001737,
Purity = 99.3%.

Radiolabelled: [phenyl-U-^{14}C]-AE C638206.
Batch: CFQ12747.
Specific activity: 5.572 MBq/mg (150.6 µCi/mg).
Radiopurity: >99%.



§ = position of radiolabel.

Treatment:

Capsules containing [^{14}C]-AE C638206 were administered orally, with the aid of a balling gun, twice daily following the morning and afternoon milking for 7 consecutive days. Following dosing, a small volume of water was injected into the mouth to aid swallowing. Cow 101F (group A) received a nominal dietary concentration of 1 ppm, equivalent to 30 MBq/day (14 mg AE C638206/day based on an assumed consumption of 14 kg dry matter/day), and cow 201F (group B) received a nominal dietary concentration of 10 ppm, equivalent to 240 MBq/day (160 mg AE C638206/day based on an assumed consumption of 16 kg dry matter/day). Half the daily dose was administered in the morning and the other half in the afternoon.

Sampling:

The cows were milked twice daily (*am* and *pm*) prior to dose administration. Urine, faeces and cage wash (cages were rinsed with a minimal volume of water after collection of urine and faeces) were collected at 24 h intervals until necropsy. At approximately 23.25 h to 23.75 h after the last dose administration, the cows were removed from the metabolism cages and killed by stunning with a captive bolt followed by exsanguination by severance of the major blood vessels of the neck. A terminal sample of blood was collected. A portion of blood was centrifuged to prepare plasma. The metabolism cages were rinsed with water then methanol to provide final cage washes. The following organs or tissues were taken or sampled: Muscle (hind and forequarter), Fat (renal and omental), Liver (whole organ) and Kidneys (whole organ).

Radioassay:

With the exception of milk, which was assayed in triplicate, radioassays were performed in at least duplicate. Radioactivity was measured for 5 min or for 2 sigma % using Packard Tri-Carb liquid scintillation counters (Canberra Packard, Pangbourne, Berkshire, UK) with the facilities for computing quench-corrected disintegrations per minute (dpm). Efficiency correlation curves were prepared for organic, aqueous and combusted sample types and were routinely checked by the use of [^{14}C]-toluene quenched standards obtained from Perkin Elmer Life Sciences Ltd, Pangbourne, Berkshire, UK). The spectrometer was recalibrated if a deviation of greater than 3% was observed when counting quality control standards.

Chromatography:

Excreta, milk and tissues were extracted by various methods including solvent extraction, protease hydrolysis and acid hydrolysis and the extracts were analysed by two HPLC systems for metabolite quantification. Both systems were reverse-phase gradient elution methods using a Columbus X-Terra C18 (250 x 4.6 mm, 5 µm) column. Identification work was performed with LC-MS and comparison with authentic standards.

Findings:

Following twice-daily oral administrations of [phenyl-U-^{14}C)-AE C638206 for 7 days at a dose level corresponding to 1 or 10 ppm in the diet, 75% of the dose was recovered in the excreta.

Table 6.2.3- 4 Recovery of radioactivity from lactating cows following twice daily oral administrations of [phenyl-U-^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Sample	Per cent of administered dose	
	Cow N°101F (1 ppm)	Cow N° 201F (10 ppm)
Urine	16.81	19.34
Faeces	57.23	54.94
Cage wash	0.868	1.022
Final cage wash	0.069	0.056
Milk am	0.073	0.068
Milk pm	0.068	0.065
Tissues	0.785	0.538
Total	75.88	76.03

The concentrations of radioactivity in milk were above the limit of quantification at all time points, reaching a plateau with a maximum of 1.8 and 18.8 ng equivalents/g at the low and high dose respectively at 5 days after the first dose.

Table 6.2.3- 5 Concentrations of radioactivity in Milk from lactating cows following twice daily oral administrations of [phenyl-U-^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Time point	ng equivalents of (^{14}C)-AE C638206/g			
	Cow N°101F (1 ppm)		Cow N° 201F (10 ppm)	
	am	pm	am	pm
Pre-dose	-	NS	-	NS
Day 2	BLQ	0.890	3.533	11.52
Day 3	1.080	1.268	12.33	16.27
Day 4	1.377	1.433	16.95	17.55
Day 5	1.413	1.754	17.55	18.69
Day 6	1.750	1.770	18.27	18.83
Day 7	1.572	1.428	17.82	17.48
Day 8	1.483	1.680	17.70	18.34
Day 9	1.356	-	14.05	-

NS – No sample
BLQ – Below limit of quantification

The concentrations of radioactivity in the tissues are shown in Table 6.2.1-16. At both dose-levels, the highest level of radioactivity was found in the liver. Fat and muscle contained levels of radioactivity below that found in the systemic circulation (blood).

Table 6.2.3- 6 Concentrations of radioactivity in Tissues from lactating cows following twice daily oral administrations of [phenyl-U-^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Sample	ng equivalents of (^{14}C)-AE C638206/g tissue	
	101F (1 ppm)	201F (10 ppm)
Plasma	13.41	100.4
Blood	10.55	87.58
Renal Fat	5.713	40.04
Liver	89.95	644.3
Kidney	26.27	302.1
Omental Fat	5.079	42.79
Muscle Hindquarter	BLQ	22.77
Muscle Forequarter	BLQ	25.15

BLQ – Below limit of quantification

The major metabolite identified in the excreta was AE C643890, an hydroxylated analogue of AE C638206, which accounted for 39% of the applied radioactivity in the radiotrace of urine. A second hydroxylated analogue, AE 0712556, accounted for a further 8.5%.

AE C638206 was not detected in urine but was the major component in faeces, accounting for 67% of the radioactivity. Faeces also contained AE C643890 and AE 0712556 (8.1% and 4.3% respectively).

At the high dose, the concentration of radioactive residues in the edible tissues ranged from 23 ppb in hindquarter muscle to 644 ppb in the liver. Residues in the fat, milk and muscle were all below the concentration requiring extensive analysis (<50 ppb). The major compound identified in these samples was unchanged AE C638206, which accounted for 37% of the TRR in the milk and 78% in the fat.

Table 6.2.3- 7 Identification/Characterisation of radioactivity in Excreta and Tissues from a lactating cow following twice daily oral administrations of [phenyl-U-^{14}C]-AE C638206 for 7 days at the nominal dose level of 10 ppm in the diet

Tissue	Residue level (ppb)	% Extracted	% Total ^{14}C-residue identified/characterised					
			AE C638206	AE C643890	AE 0712556	AE C653711	Polar§	Non-extracted
Urine		NA	-	39	8.5	-	47	NA
Faeces		21.6	14.0	1.7	0.92	-	1.7	78.4
Milk	19	85.9	36.0		-	3.9*	37.8	14.1
Fat	41	84.9	78.4	-	-	-	-	16.8
Muscle	24	28.2	5.1	-	-	-	13.2	74.2
Liver	644	89.9	0.9	1.6	1.2	-	79.7	10.9
Kidney	302	92.4	0.5	0.8	3.3	-	77.5	7.6

All the data presented in the above table were produced from experimental measurements and have not been normalised.
§ In most cases there were a number of areas of radioactivity in the polar region, each of which could contain more than one metabolite.
NA = Not Applicable
* The presence of this metabolite could not be confirmed in a second system or by HPLC/MS.

The residues in the liver and kidney proved to be very intractable. A variety of different methods was employed including solvent extraction, acid or base hydrolysis, enzyme deconjugation, and protease digestion. The majority of the radioactivity was difficult to extract into a form that could be analysed by HPLC, and appeared to consist mainly of polar compounds, even though 85-92% of the radioactivity could be extracted into solvent after protease digestion. A significant proportion of the residues in the liver and kidney eluted just before the mixed standards in HPLC system 1, in a peak that eluted at the same time as the radioactivity present in the bile.

The cow readily excreted the radioactive dose, and the total amount of dose remaining in the liver and kidneys was low. It is therefore likely that the bile was the excretion route for these unidentified polar residues.

Fractionation of the liver and kidney cells showed that the majority of the radioactivity was associated with proteins and amino acids (63% in the liver, 69% in the kidney). It is possible that AE C638206 was being metabolised *via* conjugation with glutathione. The glutathione metabolites produced could then undergo cleavage by ß-lyase leaving metabolites that could bind to proteins and amino acids. There was a lack of significant incorporation of any protein-bound residues into RNA or DNA suggesting that the metabolic pathway was acting as a de-activation mechanism in this case.

Conclusions:

Following the daily oral dosing of lactating cows with a dose equivalent to either 1 or 10 ppm AE C638206 in the diet for 7 days, the mean recovery of radioactivity was approximately 75% of the administered dose. The majority of the administered radioactivity was excreted with 74.81% and 75.30% of the dose being recovered in the excreta for the 1 and 10 ppm cows respectively. At *ca.* 24 h after the last dose the concentrations of radioactivity in all tissues were above the limit of quantification and were 7-11 times greater at the high dose. At the high dose, the concentrations of radioactivity in the tissues varied between 644.3 ng equivalents/g (644 ppb) in liver to 22.77 ng equivalents (23 ppb) in hindquarter muscle. In the milk, the level of radioactive residues reached a steady state with a maximum value of 18.8 ng equivalents/g (19 ppb) 5 days after the first dose at the high dose. In the muscle, fat and milk, unchanged AE C638206 was the major identified residue. In the liver and kidney, the hydroxylated metabolite AE C643890 was the major identified component, though the majority of the residue consisted of unidentified polar material that appeared to be associated with proteins and amino acids.

Assessment and conclusion by applicant:

The study is acceptable

Data Point:	KCA 6.2.3/02
Report Author:	[redacted]
Report Year:	2009
Report Title:	The distribution and metabolism of (14C)-AE C638206 in the lactating cow
Report No:	21582
Document No:	M-233391-02-1
Guideline(s) followed in study:	US EPA, Sudivision O, Series 171-4, OPPTS 860.1300, EU 91/414/EEC as amended by 96/58/EC Annex 1, Section 6.2
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive summary

The objectives of this study were to determine the routes and rates of excretion of [pyridyl-2,6-^{14}C]-AE C638206 and/or its radiolabelled metabolites following a 7 day repeat dose regimen in the lactating ruminants at two dose levels (1 & 10 ppm diet). To provide information on the levels [pyridyl-2,6-^{14}C]-AE C638206 and/or its radiolabelled metabolites in excreta, milk and selected tissues following repeat administrations of [pyridyl-2,6-^{14}C]-AE C638206 at the nominal dose levels of 1 and 10 ppm of daily food consumption. To investigate the number, quantity and identity of radiolabelled metabolites present in tissues, milk, and excreta. To provide an indication, from the levels of radioactivity in excreta, milk and selected tissues, of the material balance.

Material and Methods:

Species, strain: Cow, Holstein Friesian

Source: [redacted]

Number and sex: 2 lactating females

Age/body weight: 3-7 years/554-676 kg during acclimatisation.

Acclimatisation: The animals were acclimatised for at least 7 days in the experimental unit during which time milk yield was recorded. During this time the animals were observed for signs of ill health and examined by a veterinary surgeon prior to acceptance on to the study. During the acclimatisation period the animals were group housed in a loose pen with straw bedding. The animals were each fitted with a urinary bladder catheter to facilitate urine collection and transferred to individual metabolism cages on the day prior to dosing to allow faeces collection

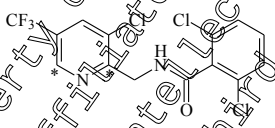
Animal identification: A numbered collar.

Environmental conditions: During the acclimatisation and study periods, the animals were maintained on a 12 h light/ 12 h dark cycle and room temperature and relative humidity were recorded daily. Temperature and humidity recorded during the acclimatisation and study periods ranged from 11-18°C and 44-94%, respectively.

Food and water:	The animals were offered *ca* 14 kg of good quality meadow hay per day. The animals were also offered a weighed amount (*ca* 3 kg) of non-medicated protein concentrate (Dairy Nuts, Billington Agriculture, Liverpool, England) twice daily after dosing. Domestic mains quality water was available *ad libitum*.

Test Material:

Non-radiolabelled:	Batch: R001737, Purity = 99.3%.
Radiolabelled:	[pyridyl-2,6-^{14}C]-AE C638206.
Batch:	GAR2034/4.
Specific activity:	6.77 MBq/mg (183 µCi/mg).
Radiopurity:	>99%.



* = position of radiolabel in 2 and 6 positions of the pyridine ring

Treatment:

The daily dose for each cow was administered over 7 consecutive days in 2 equal portions, one after morning milking (*ca* 0800 h) and one following afternoon milking (*ca* 1600 h). Cow 1F was dosed at the low dose level and cow 2F at the high dose level. The capsules were administered orally using a bolus gun. The animals were offered protein concentrate immediately after dosing.

Sampling:

Urine and faeces were collected at 24 h intervals following administration of the first daily dose up until the time of killing. The crates were washed with water at the end of the study period and the washings retained for total radioactivity analysis. Milk samples were collected from each animal in the morning prior to administration of the first dose and twice, throughout the study period, immediately prior to the morning (*ca* 0800 h) and afternoon (*ca* 1600 h) doses. The final milk collection was made immediately prior to kill. The weighing of urine, faeces, cage wash and milk samples were recorded and total radioactivity measured. Approximately 23 h after administration of the final dose, the cows were stunned using a captive bolt, pithed and exsanguinated by severance of the major neck vessels. The following biological fluids and tissues were removed and assayed for total radioactivity: Whole Blood, Omental Fat, Plasma, Renal Fat, Kidneys, Skeletal Muscle (mixture of forequarter, hindquarter and loin) and Liver.

Radioassay:

Each vial containing scintillant was analysed for 5 min, together with representative standard and blank samples on a liquid scintillation analyser (Packard 1600TR Liquid Scintillation Analyser) with automatic quench correction using an external standard method. Scintillation vials were allowed to heat and light stabilise prior to analysis. Blanks were subtracted from the counts to give net dpm. per sample.

A limit of quantification of 30 dpm. above background has been instituted in these laboratories. If results arose from data less than 30 dpm. above background, the fact is noted in the results section of the report.

Chromatography:

Excreta, eggs and tissues were extracted by various methods including solvent extraction, protease hydrolysis and acid hydrolysis and the extracts were subjected to one or two HPLC systems for metabolite quantification. The first being a reverse-phase gradient elution using an X-Terra C18 (250 x 4.6 mm, 5 µm) column and the second using a VYDAC Protein and Peptide C18 (250 x 4.6 mm, 5 µm) column. Identification work was performed with LC-MS and comparison with authentic standards.

Findings:

The major route of elimination for both dose levels was *via* faeces, with 69.1% (low dose) and 67.0% (high dose) of the administered dose recovered. Excretion in urine accounted for 13.5% (low dose) and 10.7% (high dose) of the administered dose. Overall recoveries of radioactivity were 84.23% and 80.17% for the 1 ppm and 10 ppm cows respectively.

Table 6.2.3- 8 Recovery of radioactivity from lactating cows following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose levels of 1 and 10 ppm in the diet

Sample	Recovery of Total Radioactivity (% of Administered Dose)	
	Target dose level: 1 ppm in diet	Target dose level: 10 ppm in diet
Urine	13.50	10.71
Faeces	69.10	67.00
Cage Wash	1.15	2.09
Milk	0.09	0.08
Tissues	0.39	0.29
Total	84.23	80.17

The concentrations of total radioactivity in milk were low for both dose levels, with a maximum concentration of 0.010 µg equiv.g^{-1} reached at 32 h post dose at the 10 ppm dose level. For the 1 ppm dose level, levels did not rise above 0.001 µg equiv.g^{-1}. Therefore no identification was necessary.

The highest tissue residue levels were found in the liver, kidney, renal fat, whole blood and plasma, with low residue levels found in omental fat and muscle. The overall distribution of total radioactivity within the tissues was broadly similar for both dose levels. Comparison of residue levels in tissues at the high and low dose level showed concentrations at the high dose were lower (only a *ca* seven-fold increase observed) than expected compared to a 10-fold increase in dose level, with the exception of muscle (twelve-fold) and renal fat (fourteen-fold).

Table 6.2.3- 9 Concentrations of radioactivity in Tissues from lactating cows following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at nominal dose levels of 1 and 10 ppm in the diet

Sample	Mean Tissue Concentration of Radioactivity (µg.equiv.g^{-1})	
	Tissues taken 175 h post dose 1	
	Target dose level: 1 ppm in diet	Target dose level: 10 ppm in diet
Liver	0.058	0.449
Kidney	0.033	0.196
Skeletal Muscle	0.001	0.012
Renal Fat	0.003	0.042
Omental Fat	0.005	0.039
Plasma	0.011	0.082
Whole Blood	0.010	0.074

Radioactivity was extracted from samples of faeces (48 h and 175 h), liver, kidney, abdominal fat, renal fat, skeletal muscle and milk (32 h and 175 h) at the high dose level and from faeces (48 h and 175 h), liver, kidney and renal fat at the low dose level with solvent and, where appropriate, additional enzymatic and hydrolytic methods (liver and kidney).

Extraction efficiencies for the high dose samples were 76.9% TRR (48 h faeces), 85.3% TRR (175 h faeces), 88.8% TRR (32h milk), 82.8% TRR (175h milk), 68.3% TRR (liver), 99.9 % TRR (kidney), 35.5 % TRR (muscle), 88.4% TRR (renal fat), 88.2% TRR (omental fat). The low extraction efficiency for muscle is due to the very low initial residue levels (0.012 µg equiv.g^{-1}, respectively).

Extraction efficiencies for the low dose samples were 69.5% TRR (48 h faeces), 70.6% (175 h faeces), 75.9% TRR (liver), 48.8% TRR (kidney) and 77.8% TRR (renal fat), respectively. In the case of the low dose kidney, only the solvent extracts were processed further due to low residue levels in the enzyme and acid hydrolysates. For low dose liver, the acid hydrolysate was not processed further.

Concentrated tissues (liver, kidney and renal fat), urine and faeces and extracts were analysed by HPLC and selected samples were further analysed by Liquid Chromatography-Mass Spectroscopy (LC-MS). Authentic reference standards were also analysed and co-chromatography was used as a means of tentative identification. LC-MS was used as a means of confirming assignments made by co-chromatography or to provide evidence concerning the likely structures of metabolites.

Radio-HPLC profiles of faeces extracts from cow 1 (low dose) and cow 2 (high dose) collected 48 h and 175 h after dose administration were broadly consistent. The major component in all 4 samples was AE C638206 which accounted for 1.64 to 5.40% of the dose (45.3 to 60.3% TRR). The metabolite AE C643890 was detected in 3 of the samples and by represented 0.02 to 0.08% of dose (0.6 to 1.7% TRR). An unknown metabolite in 2 of the samples represented 0.05 to 0.10% dose (1.0% TRR).

Radio-HPLC profiles of urine from cow 1 (low dose) and cow 2 (high dose) collected 48 h and 175 h after dose administration were broadly consistent. Up to 11 components in total were detected. AE C643890 was present in all 4 samples and was the major component in the high dose urine samples. This metabolite accounted for 0.10 to 0.49% of dose (9.3 to 32.4% TRR). The metabolite AE 0712556 was detected in only the high dose urines and accounted for up to 0.15% dose (9.7% TRR). Metabolites with retention times of approximately 41, 44, 47 and 50 min was present in all 4 samples at levels of 0.02 to 0.46% of dose (17.3 to 39.0% TRR). These metabolites were characterised as sulphate and glucuronide conjugates of hydroxylated AE C638206 and were more significant in low dose urine.

Solvent extract from the high dose cow liver was shown to contain 4 radiolabelled components. Parent, AE C638206 was detected at a level of 0.013 ppm (2.9% TRR) and the hydroxylated metabolites AE C643890 and AE 0712556 were present and together represented 0.018 ppm (4.0% TRR). The remaining metabolites had retention times of 43 and 47 min and were characterised as a glucuronide conjugate of hydroxylated parent and a sulphate conjugate of hydroxylated parent, respectively. These conjugated metabolites represented up to 0.022 ppm (4.9% TRR). Initially the enzyme hydrolysate was found to contain 2 components. These were present at levels of 0.003 ppm (0.6% TRR) and 0.169 ppm (37.7% TRR). The later eluting region was poorly resolved and tailing. Using a second HPLC method specific for the separation of peptides, the enzyme hydrolysate was subsequently shown to contain 14 components, accounting for levels of 0.004 to 0.039 ppm (0.9 to 8.7% TRR). The 6M HCl hydrolysate was found to contain 4 components, with retention times ranging from 6 to 46 min, at levels of 0.003 to 0.007 ppm (0.7 to 1.5 % TRR).

Only the enzyme hydrolysate from the low dose cow liver contained sufficiently high residue levels for HPLC analysis. A single radiolabelled component eluting over a 5 min period (39-44 min) was detected and accounted for 33.2% TRR (0.019 ppm). Using a HPLC method specific for peptide analysis, the broad region of radioactivity was resolved into several components, all at levels <LOQ.

The solvent extract from the high dose cow kidney was found to contain 7 radiolabelled components. Parent AE C638206 accounted for 0.003 ppm (1.8% TRR) and the hydroxylated metabolites AE C643890 and AE 0712556 were present and together represented 0.005 ppm (2.6% TRR). Three of the remaining 5 metabolites were characterised as glucuronide conjugates of hydroxylated parent and represented 0.009 ppm to 0.019 ppm (4.7 to 10.0% TRR). The remaining unknown metabolites were present at levels less than 0.005 ppm

Initially, the enzyme hydrolysate from this sample was found to contain 2 components, with retention times of 39 min (close to AE C653598) and 42 min (close to AE C651905). These were present at levels of 0.010 ppm (5.1% TRR) and 0.024 ppm (12.5% TRR). Using a second HPLC method specific for the separation of peptides, these were resolved into a number of components, all at levels <LOQ.

The 6 M HCl hydrolysate was found to contain a single radiolabelled component and accounted for 0.074 ppm (37.9 % TRR).

The solvent extracts from the high and low dose cow renal fat extracts were shown to contain only parent AE C638206 which accounted for 73.4% TRR (0.031 ppm) and 64.4% TRR (0.003 ppm), respectively.

A summary of the results obtained for excreta and tissues is presented in the following tables:

Table 6.2.3- 10 Characterisation and Identification of radioactivity in the Excreta of the lactating cow following following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	% Dose
Urine (48 h)	1	NA	Unknown	7	0.6	0.01
			Unknown	13	2.2	0.03
			Unknown	26	0.6	0.01
			Unknown	38	0.7	0.01
			DHG #	41	5.9	0.09
			HG #	45	23.3	0.37
			HS #	47	16.0	0.25
			DHS/HS #	50	8.2	0.13
			Unknown	56	1.6	0.03
			AE C643890 *	59	31.2	0.49
			AE 0712556 *	62	9.7	0.15
				Total	100.0	1.57
Urine (175 h)	1	NA	Unknown	11	2.5	0.02
			Unknown	19	0.4	<0.01
			DHG #	41	5.6	0.05
			HG #	44	17.3	0.15
			HS #	46	21.6	0.19
			DHS/HS #	50	9.8	0.08
			Unknown	56	9.9	0.09
			AE C643890 *	60	32.4	0.28
			AE 0712556 *	64	0.4	<0.01
				Total	99.9	0.86
Faeces (48 h)	1	Methanol	Unknown	56.9	1.0	0.10*
			AE C643890	59.4	0.8	0.08*
			AE C638206	63.3	56.5	5.40*
				Total	58.3	5.58
Faeces (175 h)	1	Methanol	AE C643890	59.7	0.6	0.02*
			AE C638206	63.2	60.3	2.43*
				Total	60.9	2.45

% TRR = % Total radioactive residue
NA = Not applicable
* = Assigned by co-chromatography and LC-MS
# = Assigned by LC-MS
DHG = Dihydroxy glucuronide of AE C638206
HG = Hydroxy glucuronide of AE C638206
HS = Hydroxy sulphate of AE C638206
DHS = Dihydroxy sulphate of AE C638206

Table 6.2.3- 11 Characterisation and Identification of radioactivity in the Liver of the lactating cow following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	ppm
Liver	1	Methanol	HG +	43	4.9	0.022
			HS +	47	2.4	0.011
			AE C643890/ AE 0712556 *	61	4.0	0.018
			AE C638206 *	64	2.9	0.013
				Total	14.2	0.064
		Enzyme Hydrolysis	Unknown	9	0.6	0.003
			Unknown	34-48	37.7	0.169
				Total	38.3	0.172
		Acid Hydrolysis	Unknown	6	1.5	0.007
			Unknown	10	0.7	0.003
			Unknown	21	1.1	0.005
			Unknown	46	0.9	0.004
				Total	4.2	0.019
	2	Enzyme Hydrolysis	Unknown	5	0.9	0.004
			Unknown	15	1.0	0.005
			Unknown	18	1.4	0.006
			Unknown	20	2.1	0.009
			Unknown	24	8.7	0.039
			Unknown	28	5.6	0.025
			Unknown	31	2.3	0.010
			Unknown	34	2.8	0.013
			Unknown	36	2.3	0.010
			Unknown	38	2.3	0.010
			Unknown	40	2.4	0.011
			Unknown	42	1.7	0.008
			Unknown	45	3.7	0.017
			Unknown	48	1.1	0.005
				Total	38.3	0.172

% TRR = % Total radioactive residue
ppm = µg equivalents.g^{-1}
* = Assigned by co-chromatography and LC-MS
+ = Assigned by SRM LC-MS
DHG = Dihydroxy glucuronide of AE C638206
HG = Hydroxy glucuronide of AE C638206
HS = Hydroxy sulphate of AE C638206
DHS = Dihydroxy sulphate of AE C638206

Table 6.2.3- 12 Characterisation and Identification of radioactivity in the Kidney and Renal Fat of the lactating cow following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose level of 10 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	ppm
Kidney	1	Methanol	Unknown	34	1.6	0.003
			Unknown	37	2.8	0.005
			DHG +	42	10.0	0.019
			HG +	44	4.7	0.009
			DHS/HS + AE C643890/ AE 0712556 *	51	5.2	0.010
				60	2.6	0.005
			AE C638206 *	64	1.8	0.003
				Total	28.7	0.054
		Enzyme Hydrolysis	AE C653598	39	5.1	0.010
			Unknown	41-42	12.5	0.024
				Total	17.6	0.034
		Acid Hydrolysis	Unknown	24-	37.9	0.074
	2	Enzyme Hydrolysis	All components less than LOQ			
Renal Fat	1	Methanol	AE C638206 *	64	73.4	0.031

% TRR = % Total radioactive residue
ppm = µg equivalents.g^{-1}
* = Assigned by co-chromatography and LC-MS
+ = Assigned by SRM LC-MS
DHG = Dihydroxy glucuronide of AE C638206
HG = Hydroxy glucuronide of AE C638206
HS = Hydroxy sulphate of AE C638206
DHS = Dihydroxy sulphate of AE C638206

Table 6.2.3- 13 Characterisation and Identification of radioactivity in the Excreta of the lactating cow following twice daily oral administrations of [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose level of 1 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	% Dose
Urine (48 h)	1	NA	Unknown	11	2.0	0.04
			DHG +	41	4.8	0.10
			HG +	44	22.4	0.46
			HS +	46	39.0	0.81
			DHS/HS +	50	4.5	0.09
			Unknown	55	1.5	0.03
			AE C643890 *	59	9.3	0.19
				Total	83.5	1.72
Urine (175 h)	1	NA	Unknown	11	2.7	0.01
			DHG +	40	5.2	0.02
			HG +	44	22.1	0.10
			HS +	46	35.6	0.16
			DHS/HS +	50	4.7	0.02
			Unknown	56	7.5	0.03
			AE C643890 *	60	22.1	0.10
				Total	99.9	0.44
Faeces (48 h)	1	Methanol	AE C638206 *	63.3	45.3	4.51
Faeces (175 h)	1	Methanol	Unknown	56.0	1.0	0.03
			AE C643890 *	59.9	1.7	0.05
			AE C638206 *	63.2	58.4	2.68
				Total	106.4	7.27

% TRR = % Total radioactive residue
NA = Not applicable
+ = assigned by extrapolation of assignment made in 48 hour urine
* = Assigned by co-chromatography with a reference standard
DHG = Dihydroxy glucuronide of AE C638206
HG = Hydroxy glucuronide of AE C638206
HS = Hydroxy sulphate of AE C638206
DHS = Dihydroxy sulphate of AE C638206

Table 6.2.3- 14 Characterisation and Identification of radioactivity in the Liver and Renal Fat of the lactating cow following twice daily oral administrations [pyridyl-2,6-^{14}C]-AE C638206 for 7 days at the nominal dose level of 1 ppm in diet

Sample	HPLC Method	Extractable Fraction	Component	Retention Time (min)	Individual components as:	
					% TRR	ppm
Liver	1	Enzyme Hydrolysis	Unknown	39-44	33.2	0.019
	2	Enzyme Hydrolysis	All components less than LOQ			
Renal Fat	1	Methanol	AE C638206 +	63	64.4	0.003

% TRR = % Total radioactive residue, ppm = µg equivalents.g^{-1}, + = Assigned by co-chromatography with a reference standard.

Conclusion:

Following repeated oral administration of [^{14}C]-AE C638206 to the lactating cow, the recovery of radioactivity was quantitative with 83.84% dose and 79.88% dose recovered for the 1 and 10 ppm cows respectively. The elimination of radioactivity had reached the levels of 82.6% dose for the 1 ppm cow and 77.7% dose for the 10 ppm cow by 175 h post the first dose occasion. The total amount of radioactivity recovered in the milk was 1.15% and 2.09% dose for the 1 and 10 ppm cows respectively. In terms of concentration of radioactivity in the milk, levels did not exceed 0.001 µg equiv./g for the cow dosed at 1 ppm diet and did not exceed 0.010 µg equiv./g for the cow dosed at 10 ppm diet. Concentrations of radioactivity in the tissues were also low which can be clearly seen in the results obtained from the animal dosed at a level that would be considered to be in excess of a realistic field exposure level (1 ppm in the diet) where only the liver exceeded 0.05 ppm (0.058 ppm). Where tissue residues in excess of 0.05 ppm were detected in the cow dosed at the exaggerated level of 10 ppm in the diet (liver and kidney) they were shown to be multicomponent with each individual metabolite comprising the residue present at a low level (<0.05 ppm).

Several metabolite components present in the urine and concentrated tissue extracts by HPLC were confirmed by using LC-MS however.

In conclusion, following repeated oral administration of [^{14}C]-AE C638206 to the lactating cow, there was no evidence of any accumulation of radioactivity in milk or edible tissues. The compound was found to be extensively metabolised and rapidly eliminated resulting in low to almost undetectable tissue residues and low to very low transfer to milk

The metabolism of AE C638206 in the cow is proposed to proceed by hydroxylation of the chlorophenyl ring in the meta and para positions to give metabolites AE 0712556 and AE C643890 respectively. Each of these metabolites is conjugated with sulphate or glucuronic acid. Alternatively, metabolites AE 0712556 or AE C643890 were hydroxylated in a second position to give a proposed dihydroxy intermediate, which is further metabolised to give either a sulphate or glucuronide conjugate. The presence of polar components in the enzyme hydrolysate of liver and kidney that were associated with peptides was also demonstrated.

Assessment and conclusion by applicant:

The study is acceptable

The following study is currently in progress and will be submitted at the indicated timepoint:

Dossier node	Draft title	Study ID	Planned submission
KCA 6.2.3	[^{14}C]-BAM: Nature of the Residue in a Lactating Goat (OECD 503)	VC/19/034	November 2020

CA 6.2.4 Pigs

The available animal metabolism studies (for poultry, ruminants and rats) show that fluopicolide appears to undergo hydroxylation and conjugation to sulfate or glucuronic acid, oxidative N-dealkylation and conjugation to glutathione, followed by the subsequent biotransformation of the glutathione in all three species.

As the general metabolic pathways are similar for each of the tested animals, the use of a fourth species is not required to understand the metabolism of fluopicolide. Therefore, a metabolism study for pigs is not triggered.

For M-01, the corresponding ^{14}C-radiolabeled metabolism studies for laying hens and lactating goats are currently in-progress. Once the results of these studies are available and the reports have been finalised, this section will be updated to consider the extrapolation of these data to address the metabolism for pigs.

CA 6.2.5 Fish

As a new data requirement according to Regulation (EC) No 283/2013, metabolism studies on fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications. The working document on the nature of pesticide residues in fish (SANCO/11187/2013 rev. 3 of 31 January 2013) further specifies that metabolism studies in fish are required only if an active substance has a log P_{OW} equal or greater than 3. For substances with rather low lipophilicity (log P_{OW}<3), accumulation of residues in fish via the diet is known to be negligible.

However, in the European Commission Summary Report of the Standing Committee on plants, animals, food and feed held in Brussel on 24 November -25 November 2014 it was emphasized that the Commission working document on the nature of pesticide residues in fish was discussed in 2013 and it was concluded that it is not yet finalized and ready to be noted as a guidance document. The Commission emphasized that for the time being there are no agreed test guidelines and that hence the pertinent data requirements can be waived. This was also clarified in general at the meeting of the Committee's section on Plant Protection Products - Legislation on 09/10 October 2014, and laid down in document SANCO/10181/2013 Rev 2.1. Such test guidelines must be published in the form of an update of the respective Commission Communications.

Nevertheless, the following data is available for fluopicolide to support that there is no need for a new metabolism study in fish.

A bioaccumulation and metabolism study for [2,6-^{14}C-pyridinyl]-Fluopicolide in bluegill sunfish is available ([redacted] 2003; M-241273-01-1). The bioaccumulation of the fluopicolide residues in fish was determined using a continuous flow-through set-up over 45 days (which included a 24-day uptake period and a 21-day depuration period).

This fish bioaccumulation study was previously assessed during the original EU inclusion for fluopicolide (DAR, 2005) and has been summarised fully within Document MCA section 8.2.2.3 of this dossier. A brief summary of the study results is described within the following paragraph:

The study showed that fluopicolide accumulates rapidly in fish tissues, principally in the non-edible portions, regardless of the exposure concentration. The steady state bioconcentration factors (BCFs) for the low treatment (0.8 µg/L) were 48x, 117x and 197x in edible, whole fish, and non-edible, respectively. For the high treatment (8.0 µg/L) were 40x, 104x, and 175x in edible, whole fish and non-edible, respectively. Fluopicolide cleared rapidly from fish tissues regardless of the exposure concentration. The depuration appeared to be biphasic with the "fast" phase as the major component. Based on a one-compartment model with whole fish, the calculated BCFs were 121x and 102x for the low and high treatment, respectively. The time to reach 90% of the steady state was about 2 days for both treatments. The depuration half-life was about 0.5 day for both treatments.

The major residue in all fish tissues was unchanged parent fluopicolide – as shown in Table 6.2.5- 2.

Table 6.2.5- 1 Summary of identified metabolites in fish tissues sampled at day 28. Values in mg/kg tissue and % of total tissue radioactivity (in parenthesis)

Treatment	Tissue type	Residue in analysed extracts		Fluopicolide residues		% Identified	Largest single unidentified component	
		mg/kg	%	mg/kg	%		mg/kg	%
Low	Edible	0.039	87.6	0.039	87.6	100	-	
(0.8 µg/L)	Non-edible	0.158	91.4	0.128	73.8	73.8	0.013	7.8
High	Edible	0.271	85.5	0.271	85.5	100	-	-
(8.0 µg/L)	Non-edible	1.228	91.8	0.908	67.9	67.9	0.169	12.7

While the bioaccumulation study noted that fluopicolide rapidly accumulates within the tissues of fish, the study also shows that the fluopicolide residue levels rapidly clear from the fish tissues during the depuration phase. No metabolites of fluopicolide were identified and only fluopicolide was present within the edible portions of the analysed fish. As a low BCFs were obtained during the study for the low and high treatment rates, it can be concluded there is no indication of any significant accumulation of residues within fish tissues.

A calculation of the dietary burden for fish has been undertaken in Appendix 1 of this document. The results show that high fluopicolide intakes are expected for fish (>0.1 mg/kg) based on the residues expected with the treated and succeeding crops: 0.726 mg/kg for the common carp and 0.483 mg/kg for rainbow trout. For M-01, low exposures for fish through the diet are expected: 0.089 mg/kg for the common carp and 0.068 mg/kg for rainbow trout.

The physical-chemical properties data (contained within KCA 2.7) show that fluopicolide and its metabolites have a low liability to bioaccumulation, as the log POW values are <3 (refer to Table 6.2.5-2). The available data on the residue behaviour of fluopicolide in animals shows that the compound does not accumulate in tissues.

Table 6.2.5- 2 Summary of the partition coefficients for fluopicolide and its metabolites (M-01, M-02, M-03, M-05, M-10, M-14, and M-15)

Test item	Method	Results	Study reference
Fluopicolide	EEC Method A8 (HPLC method)	Log Pow = 2.9 at pH 4/7/9 and 20°C	[redacted] 2003; M-231643-01-1
M-01 AE C653711	OECD 117 (HPLC method)	Log Pow = 0.51 at an unspecified pH and temperature	[redacted] 2000; M-234334-01-1
	OECD 117 (HPLC method)	Log Pow = 0.7 at pH 5/7/9 and 25°C	[redacted] 2014; M-496102-01-1
M-02 AE C657188	EEC Method A8 (shake flask method)	Log Pow = 1.1 at pH 2 and 23°C Log Pow = -2.0 at pH 7 and 23°C Log Pow = -2.16 at pH 9 and 23°C	[redacted] 2004; M-228264-01-1
	OECD 107 (shake flask method)	Log Pow = -1.55 pH 5 at 24 °C Log Pow = -2.0 pH 7 at 24 °C Log Pow = -2.2 pH 9 at 24 °C	[redacted] 2019; M-650978-01-1
M-03 AE 0608000	EEC Method A8 (HPLC method)	Log Pow = 2.36 at pH 2 and 20°C Log Pow = 2.34 at pH 7 and 20°C Log Pow = 2.34 at pH 9 and 20°C	[redacted] 2003; M-219294-01-1
M-05 AE 1344122	OECD 107 (shake flask method)	Log Pow = -1.9 pH 5 at 24°C Log Pow = -2.1 pH 7 at 24°C Log Pow = -2.4 pH 9 at 24°C	[redacted] 2015; M-510179-01-1
M-10 AE 1344123	OECD 107 (shake flask method)	Log Pow = -4.2 pH 5 at 23 °C Log Pow = -4.3 pH 7 at 23 °C Log Pow = -4.5 pH 9 at 23 °C	[redacted] 2019; M-521962-01-1
M-14 AE 1388273	OECD 107 (shake flask method)	Log Pow = 0.1 pH 5 at 23 °C Log Pow = -0.1 pH 7 at 23 °C Log Pow = -1.3 pH 9 at 23 °C	[redacted] 2015; M-507659-01-1
M-15 AE 1413903	OECD 107 (shake flask method)	Log Pow = -0.7 pH 5 at 23 °C Log Pow = -0.6 pH 7 at 23 °C Log Pow = -0.6 pH 9 at 23 °C	[redacted] 2018; M-619411-01-1

While relatively high intakes for fluopicolide within the fish diet are expected, the physical chemical properties and the bioaccumulation study for this substance show that it is unlikely to persist at significant levels within fish tissues. As the overall low probability for the intake of fluopicolide as well as its biotransformation, residues of the active substances fluopicolide in fish are considered to be of no concern and no accumulation in the food chain is to be expected.

CA 6.3 Magnitude of residue trials in plants

Residue definition (EFSA Journal 2019;17(7):5748)

Monitoring residue definition for food of plant origin:	Fluopicolide
Risk assessment residue definition for food of plant origin:	Definition 1: Fluopicolide Definition 2: Metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01)

In the original Annex II dossier for Annex I inclusion of fluopicolide under Directive 91/414/EEC, the uses of fluopicolide were supported on grapes and potato.

In the approval renewal of fluopicolide, the representative uses are proposed on potato, lettuce, cucumber and winter oilseed rape as recorded in Table 6.3-2. Summarises of the supporting data for these commodities are presented within sections CA 6.3.2 (for potatoes), CA 6.3.3 (for lettuce), CA 6.3.4 (for cucumbers), and CA 6.3.5 (for oilseed rape).

An overview of the available data to support each GAP is provided within the following Table.

Table 6.3- 1: Summary of the residue trials data to support the representative uses

Crop	**Residue levels** (mg/kg) **observed in the supervised residue trials relevant to the supported GAPs**	**Residue component**	**MRL*** proposals (mg/kg)	**HR** (mg/kg) (c)	**STMR** (mg/kg) (d)
GAP: 1 - 4 applications at 0.1 kg a.s. /ha (FLC); BBCH 21-89; application interval = 7 days; PHI = 7 days					
Potato	NEU: 19 x <0.01 SEU: 15 x <0.01	Fluopicolide	<0.01	<0.01	<0.01
	NEU: 19 x <0.01 SEU: 15 x <0.01	M-01	n.a.	<0.01	<0.01
	NEU: 19 x <0.01 SEU: 15 x <0.01	M-02	n.a.	<0.01	<0.01
GAP: 1 - 3 applications at 0.1 kg a.s. /ha (FLC); BBCH 21-89; application interval = 7 days; PHI = 7 days					
Potato	NEU: 3 x <0.01; 2 x 0.01 SEU: 3 x <0.01; 2 x 0.013	Fluopicolide	0.02	0.013	<0.01
	NEU: 5 x <0.01 SEU: 5 x <0.01	M-01	n.a.	<0.01	<0.01
	NEU: 5 x <0.01 SEU: 5 x <0.01	M-02	n.a.	<0.01	<0.01
GAP: 1 - 2 applications at 0.1 kg a.s. /ha (FLC); BBCH 21-89; application interval = 7 days; PHI = 7 days					
Potato	NEU: 2 x <0.01 SEU: 2 x <0.01	Fluopicolide	<0.01	<0.01	<0.01
	NEU: 2 x <0.01 SEU: 2 x <0.01	M-01	n.a.	<0.01	<0.01
	NEU: 2 x <0.01 SEU: 2 x <0.01	M-02	n.a.	<0.01	<0.01

Crop	Residue levels (mg/kg) observed in the supervised residue trials relevant to the supported GAPs	Residue component	MRL* proposals (mg/kg)	HR (mg/kg) (c)	STMR (mg/kg) (d)
GAP: 1 - 2 applications at 0.1 kg a.s. /ha (FLC); BBCH 41-49; application interval = 7 days; PHI = 7 days					
Lettuce	NEU: 0.03, 0.17, 0.19, 0.19, 0.28, 0.36, 0.52, 0.63, 0.73 ,0.87 SEU: 0.28, 0.30, 0.49, 0.68, 0.76, 0.76, 0.99, 1.6, 1.7, 1.9	Fluopicolide	3	1.9	0.58
	NEU: 5 x <0.01, 0.01, 0.011, 2 x 0.012, 0.013 SEU: 3 <0.01, 0.01, 0.012, 0.014, 0.02, 0.021, 2 x 0.028	M-01	n.a.	0.028	0.011
	NEU: 10 x <0.01 SEU: 10 x <0.01	M-02	n.a.	<0.01	<0.01
GAP: 1 application at 0.1 kg a.s. /ha (FLC); BBCH 13-49; PHI = 7 days					
Lettuce	NEU: 2 x 0.1, 0.17, 0.21, 0.37, 0.48, 0.72, 0.87, 0.96 SEU: 0.092, 0.099, 0.13, 0.52, 0.62, 0.73, 1.2, 1.2, 1.5	Fluopicolide	3	1.5	0.5
	NEU: 6 x <0.01, 0.012, 2 x 0.015 SEU: 4 x 0.01, 2 x 0.011, 2 x 0.014, 0.024	M-01	n.a.	0.024	0.01
	NEU: 9 x <0.01 SEU: 9 x <0.01	M-02	n.a.	<0.01	<0.01
GAP: 1 - 3 applications at 0.1 kg a.s. /ha (FLC); BBCH 21-89; application interval = 7 days; PHI = 7 days					
Cucumber	Inter-zonal (greenhouse - indoor): 2 x 0.02, 2 x 0.03, 2 x 0.04, 0.08, 0.09	Fluopicolide	0.15	0.09	0.035
	Inter-zonal (greenhouse - indoor): 8 x <0.01	M-01	n.a.	<0.01	<0.01
	Inter-zonal (greenhouse - indoor): 8 x <0.01	M-02	n.a.	<0.01	<0.01
GAP: Applied to seeds at a nominal rate of 0.2 kg a.s. /100 kg seed; BBCH 00; PHI = not applicable					
Oilseed rape	Inter-zonal (seed treatment): 10 x <0.01	Fluopicolide	0.01*	<0.01	<0.01
	Inter-zonal (seed treatment): 10 x <0.01	M-01	n.a.	<0.01	<0.01
	Inter-zonal (seed treatment): 10 x <0.01	M-02	n.a.	<0.01	<0.01

NEU: Northern European trials zone
SEU: Southern European trials zone
n.a.: Not applicable – not part of the residue definition for monitoring
* Proposals are based on primary crop supervised trials only and do not take into consideration the data from the rotational crop studies (CA 6.6). Consolidated MRL proposals (taking all data into consideration) are presented and justified within section CA 6.7.2 of this document.

Table 6.3- 2: Summary of the supported critical GAP.

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	g a.s./ha min-max (l)	Water L/ha min-max	g a.s./hl min-max (l)		
Potato	EU	FLC+PCH SC 687.5	F	*Phytophthora infestans* (PHYTIN)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 21 - 89	1 - 4	7	FLC: 100 PCH: 1000	100 - 1000	FLC: 10 – 100 PCH: 100 - 1000	7	*
Potato	EU	FLC+PCH SC 687.5	F	*Phytophthora infestans* (PHYTIN)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 21 - 89	1 - 3	7	FLC: 100 PCH: 1000	100 - 1000	FLC: 10 – 100 PCH: 100 - 1000	7	**
Potato	EU	FLC+PCH SC 687.5	F	*Phytophthora infestans* (PHYTIN)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 21 - 89	1 - 2	7	FLC: 100 PCH: 1000	100 - 1000	FLC: 10 – 100 PCH: 100 - 1000	7	**
Lettuce	EU	FLC+PCH SC 687.5	F	*Bremia lactucae* (BREMLA)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 41 - 49	1 - 2	7	FLC: 100 PCH: 1000	200 - 1000	FLC: 10 -50 PCH: 100 -500	7	

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	g a.s./ha min-max (l)	Water L/ha min-max	g a.s./hL min-max (l)		
Lettuce	EU	FLC+PCH SC 687.5	F	*Bremia lactucae* (BREMLA)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 13 - 49	1 - 1	n.a.	FLC: 100 PCH: 1000	200 - 1000	FLC: 10 - 50 PCH: 100 - 500	7	
Cucumber	EU	FLC+PCH SC 687.5	G	*Pseudoperonospora cubensis* (PSPECU)	SC	FLC: 62.5 g/L PCH: 625 g/L	Foliar spray	BBCH 21 - 89	1 - 1	-	FLC: 100 PCH: 1000	1000 - 1250	FLC: 8 - 10 PCH: 80 - 100	1	†
Rape, winter	EU	FLC+FXA FS 350	F	*Plenodomus lingam* (LEPTMA), *Peronospora parasitica* (PERONA), *Alternaria brassicae* (ALTEBA), *Rhizoctonia spp.* (RHIZSP)	FS	FLC: 200 g/L FXA: 150 g/L	Seed treatment	BBCH 00	1 - 1	n.a.	FLC: 5 – 12 FXA: 3.75 - 9	n.a.	FLC: = FXA: 150 g a.s./100 kg seeds	n.a.	††

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds

(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of applications possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)

(m) PHI - minimum pre-harvest interval

* Additional fall-back GAPs are noted:
1) Applied once in two years (fall-back GAP)
2) Applied once in three years (fall-back GAP)

** While the 4 x 100 g a.s./ha application scenario is the most critical, the risk assessment in other technical areas will determine the viability of this use. Additional fall-back GAPs with applications of 3 x 100 g a.s./ha or 100 g a.s./ha , may be necessary. Additional fall-back measures may also apply:
1) Applied once in two years (fall-back GAP)
2) Applied once in three years (fall-back GAP)

† Grown in a high-tech greenhouse: soil-based application

†† Application per treatment: 2.5 - 6 kg seeds/ha

n.a. Not applicable

FLC: Fluopicolide

FXA: Fluoxastrobin

PCH: Propamocarb-hydrochloride

FLC+PCH SC 687.5 = representative formulation Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)

FLC+FXA FS 350 = representative formulation Fluopicolide + Fluoxastrobin FS 350 (200+150 g/L)

CA 6.3.1 Grapes

Not applicable, see GAP in Section CA 6.3

CA 6.3.2 Potato

The critical Good Agricultural Practice (cGAP) supported at the European level in the Annex I renewal (AIR) process consists of 1-4 foliar spray applications at 100 g a.s./ha fluopicolide in northern Europe and southern Europe, with a minimum spray interval of 7 days and a PHI of 7 days.

Table 6.3.2- 1 Summary of the critical GAP for the proposed uses of FLC+PCH SC 687.5

Crop	Region*	F, G or I**	Maximum application number	Maximum application interval (days)	Maximum rate (g a.s./ha)	Minimum PHI (days)
Potato	N-EU and S-EU	F	1-4	7	100	7
Potato	N-EU and S-EU	F	1-3	7	100	7
Potato	N-EU and S-EU	F	1-2	7	100	7

* EU-N northern Europe EU-S southern Europe ** F Field; G Greenhouse; I Indoor

Trials available to support the European GAP relevant for the active substance renewal are summarised in Table 6.3.2- 2 and Table 6.3.2- 3.

Table 6.3.2- 2 Residue trials conducted per geographical region and formulation

Region	Crop	Formulation	Number of trials						Document No	Dossier Ref.
			Vegetation period					Total		
			2001	2002	2003	2009	2010			
1-4 x 100 g a.s /ha, BBCH 21-89, Application interval: 7 days, PHI: 7 days (foliar application)										
NEU & SEU	Potato	SC 687.5 AE B06G752 04 SC61 A1 (688 SC) AE B066752 04 SC61 A102 AE C638206 00 SE10 A303		8 (NEU) 8 (SEU)	4 (NEU) 4 (SEU)	3 (NEU) 3 (SEU)	4 (NEU)	19 (NEU) 15 (SEU)	M-231883-01-1 M-231939-01-1 M-232146-01-1 M-232144-01-1 M-236086-01-1 M-237282-01-1 M-398344-01-1 M-401823-02-1	6.3.2/05 6.3.2/06 6.3.2/02 6.3.2/01 6.3.2/10 6.3.2/09 6.3.2/08 4.1.2/63

Region	Crop	Formulation	Number of trials						Document No	Dossier Ref.
			Vegetation period					Total		
			2001	2002	2003	2009	2010			
1-3 x 100 g a.s /ha, BBCH 21-89, Application interval: 7 days, PHI: 7 days (foliar application)										
NEU & SEU	Potato	AE C638206 00 SE10 A303	5 (NEU) 5 (SEU)					5 (NEU) 5 (SEU)	M-214893-02-1 M-214897-01-1	6.3.2/03
1-2 x 100 g a.s /ha, BBCH 21-89, Application interval: 7 days, PHI: 7 days (foliar application)										
NEU & SEU	Potato	SC 687.5					2 (NEU) 2 (SEU)	2 (NEU) 2 (SEU)	M-420098-01-1	6.3.2/07

NEU – Northern European field trials zone
SEU – Southern Europe field trials zone

Table 6.3.2- 3 Overall summary of residue data on lettuce covering the critical GAP for active substance renewal

Application rate	Region	Formulation	Crop	Sample material	n	Residue level (mg/kg)		
						Min.	Max.	STMR
1-4 applications at 100 g/ha	N-EU	SC 687.5 AE B06G752 04 SC61 A1 (688 SC)	Potato	Tuber	19	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)
1-4 applications at 100 g/ha	S-EU	AE B066752 04 SC61A102 AE C638206 00 SE10 A303	Potato	Tuber	15	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)
1-3 applications at 100 g/ha	N-EU	AE C638206 00 SE10 A303	Potato	Tuber	5	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)
1-3 applications at 100 g/ha	S-EU	AE C638206 00 SE10 A303	Potato	Tuber	5	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	0.013 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)
1-2 applications at 100 g/ha	N-EU	687.5 SC	Potato	Tuber	2	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)
1-2 applications at 100 g/ha	S-EU	687.5 SC	Potato	Tuber	2	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)

NEU – Northern Europe
SEU – Southern Europe

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.3.2/01
Report Author:	[redacted]
Report Year:	2003
Report Title:	Residue behaviour in potatoes European Union (Northern zone) 2002 Propamocarb hydrochloride + AE C638206 water miscible suspension concentrate (SC) 625 g/L + 62.5 g/L Code: AE B066752 04 SC61 A102
Report No:	C032828
Document No:	M-232144-01-1
Guideline(s) followed in study:	EU Commission Working Document 7029/VI/95 rev. 5 - 22/07/97 US EPA OCSPP Guideline #860.1500 Crop Field Trials
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 magnitude of the residue trials were conducted on potatoes in the Northern European residue trials zone (Northern France, Germany and The United Kingdom) during 2002. Four applications of AE AE B066752 04 SC61 A102 (a product containing 62.5 g/of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE B066752 04 SC61 A102 (62.5 g/L of fluopicolide)

   Batch no.: GP220159

   Active Ingredient / Purity: 95%

   Storage: Not stated in the report

   Expiry date: February 2002

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Northern European residue trials zone (Northern France, Germany and The United Kingdom) during 2002. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 4 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE B066752 04 SC61 A102*	4	0.10 kg a.s. / ha	7 days	BBCH 48 (for two trials), 91 – 97 (for the remaining two trials)	7 days

* Product contains 62.5 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 5 Trial details and regions

Trial No.	Country	Location	Crop variety
02R286-1	Germany	04808 Falkenhain	Princess
02R286-2	United Kingdom	CB7 4UP Cambridgeshire	Maris Piper
02R286-3	France (North)	80700 Cremery	Bintje
02R286-4	France (North)	02400 Lucy le Bocage	Bintje

The product was sprayed onto to potatoes using bicycle sprayers, wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 6 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 7 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	88,91, 100, 103, 104, 113	100	9.2	0.01
	0.1	83,84,91,93,94	89	5.8	
	0.2	90	90	-	
		Overall recovery (n=12)	**95**	**9.4**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 8 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	74,81,82,84,86,103	85	11.4	0.01
	0.1	78, 80, 85, 87, 106	87	12.8	
	0.2	81	81	-	
		Overall recovery (n=12)	**86**	**11.2**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalents.

Table 6.3.2- 9 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93,95,95,98,99, 108	98	5.5	0.01
	0.1	90,91,92,94,95	92	2.2	
	0.2	88	88		
		Overall recovery (n=12)	**95**	**5.5**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 182 days.

Acceptable storage stability data are available (presented within this document under point CA6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (625 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2-10 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	02R286	02R286-1	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R286	02R286-2	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R286	02R286-3	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R286	02R286-4	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Northern France, Germany and the United Kingdom). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

The residue trials results are considered to have been acceptably generated and these values are presented within the 'Summary of residues data from the supervised residue trials' section of this dossier (page 114), to check compliance with the current EU MRLs and for use in the risk assessment.

Assessment and conclusion by applicant:
Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.2/02
Report Author:	[redacted]
Report Year:	2003
Report Title:	Residue behaviour in potatoes European Union (Southern zone) 2002 Propamocarb hydrochloride + AE C638206 water miscible suspension concentrate (SC) 625 g/L + 62.5 g/L Code: AE B066752 04 SC61 A102
Report No:	C032829
Document No:	M-232146-01-1
Guideline(s) followed in study:	EU Commission Working Document 7029/VI/95 rev. 5 - 22/07/97 US EPA OCSPP Guideline # 860.1500 Crop Field Trials
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue open-field trials were conducted in southern Europe (Southern France, Italy and Spain) on potatoes, during 2002. Four applications of AE C638206 00 SE10 A303 (a product containing 95 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE B066752 04 SC61 A102 (62.5 g/L of fluopicolide)
   Batch no.: OP220159
   Active Ingredient / Purity: 99.5%
   Storage: Not stated in the report
   Expiry date: February 2002

2. **Test commodity:** Potato
   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Southern European residue trials zone (Southern France, Italy and Spain) during 2002. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 11 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE B066752 04 SC61 A102*	4	0.10 kg a.s. /ha	7 days	BBCH 47 (for one trial), 91 – 95 (for the remaining three trials)	7 days

* Product contains 625 g/L propamocarb hydrochloride and 62.5 g/L fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 12 Trial details and regions

Trial No.	Country	Location	Crop variety
02R287-1	France (South)	69380 Chazay	Bintje
02R287-2	France (South)	47400 Gontaud-de-Nogaret	Charlotte
02R287-3	Italy	70056 Molfetta	Spunta Olandese
02R287-4	Spain	41310 Brenes	Spunta

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 13 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 14 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	88,94, 100, 103, 104, 110	99	8.4	0.01
	0.1	83,84,91,93,94	89	5.8	
	0.2	91	91	-	
		Overall recovery (n=12)	**94**	**8.8**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 15 Procedural recoveries for AE C657188

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	74,81,82,84,86,99	84	9.8	0.01
	0.1	78, 80, 85, 87, 106	87	12.8	
	0.2	83	83	-	
		Overall recovery (n=12)	**85**	**10.4**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 16 Procedural recoveries for AE C653711

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93,95,95,98,99, 112	99	7.0	0.01
	0.1	90,91,92,94,95	92	2.2	
	0.2	91	91		
		Overall recovery (n=12)	**95**	**6.2**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 262 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (625 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 17 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	02R287	02R287-1	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R287	02R287-2	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R287	02R287-3	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R287	02R287-4	AE B066752 04 SC61 A102	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Southern European residue trials zone (Southern France, Italy and Spain). Residues in potato trials were all found to be very low within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg

Metabolite M-01: 4 x <0.01 mg/kg

Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.2.2/03
Report Author:	[redacted]
Report Year:	2003
Report Title:	Decline of residues in potatoes European Union (Northern zone) 2001 AE C638206 Suspo-emulsion (SE) 95 g/L Code: AE C638206 00 SE10 A303
Report No:	C028239
Document No:	M-214893-02-1
Guideline(s) followed in study:	EU (=EEC): 7029/VI/95 rev. 5, 22/07/97
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of five residue open-field trials were conducted in northern Europe (Northern France, Germany and The United Kingdom) on potatoes, during 2001. Three applications of AE C638206 00 SE10 A303 (a product containing 95 g/L of fluopicolide) were made at a target rate of 0.125 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE C638206 00 SE10 A303 (95 g/L of fluopicolide)

   Batch no.: OP200271

   Active Ingredient / Purity: 96%

   Storage: Not stated in the report

   Expiry date: March 2002

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 5 residue decline trials on potatoes in the Northern European residue trials zone (Northern France, Germany and The United Kingdom) during 2001. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 18 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE C638206 00 SE10 A303*	3	0.125 kg a.s. / ha	7 days	BBCH 47-49 (for three trials), 72 – 75 (for the remaining two trials)	7 days

* Product contains 95 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 19 Trial details and regions

Trial No.	Country	Location	Crop variety
01R282-1	Germany	04808 Falkenhain	Secura
01R282-2	United Kingdom	NR147DU Suffolk	Premier
01R282-3	United Kingdom	CB7 4UP Cambridgeshire	Maris Piper
01R282-4	France (North)	51 520 La Veuve	Monalisa
01R282-5	France (North)	62 123 Series Au Bois	Desiree

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 20 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.1- 21 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	98,101,90,101, 104	99	5.4	0.01
	0.05	117, 119, 102,99,94,86	103	12.6	
	0.1	105,105,95,94,92	98	6.4	
		Overall recovery (n=16)	**100**	**8.9**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.1- 22 Procedural recoveries for AE C657188

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	65, 63, 77, 66	68	9.3	0.01
	0.05	68, 68	68	-	
	0.1	83, 82, 73, 79, 86, 90, 67, 79,72	79	9.2	
		Overall recovery (n=15)	**75**	**11.3**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.1- 23 Procedural recoveries for AE C653711

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	89,94, 107,97, 101	98	7.0	0.01
	0.05	101, 102,97,93,98,96	98	3.4	
	0.1	103, 100,97, 104,95	100	3.8	
		Overall recovery (n=16)	**98**	**4.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 458 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.1- 24 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	01R282	01R282-1	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<u><0.01</u>	<u><0.01</u>	<u><0.01</u>
					14	<0.01	<0.01	<0.01

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	01R282	01R282-2	AE C638206 00 SE10 A303	Potato (tuber)	0	0.01	<0.01	<0.01
					1	0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
N-EU	01R282	01R282-3	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
N-EU	01R282	01R282-4	AE C638206 00 SE10 A303	Potato (tuber)	0	0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	0.01	<0.01	<0.01
					7	0.01	<0.01	<0.01
					14	0.01 (1)	<0.01	<0.01
N-EU	01R282	01R282-5	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01

(1) Higher residue value observed at the later timepoint (PHI 14 days), so this trial value has been selected (in accordance with the EFSA 'Residues trials and MRL calculations' guidance document).

III. CONCLUSION

Five independent (decline) residue trials have been conducted in the Northern European residue trials zone (Northern France, Germany and The United Kingdom). Residues in potato trials were all found to be very low within the sampled tubers:

Fluopicolide: 3 x <0.01, 2 x 0.01 mg/kg

Metabolite M-01: 5 x <0.01 mg/kg

Metabolite M-02: 5 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.3.2/04
Report Author:	[redacted].
Report Year:	2003
Report Title:	Decline of residues in potatoes European Union (Southern zone) 2001 AE C638206 suspo-emulsion (SE) 95 g/L Code: AE C638206 00 SE10 A303
Report No:	C028241
Document No:	M-214897-01-1
Guideline(s) followed in study:	EU (=EEC): 7029/VI/95 rev.5 - 22/07/97
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of five residue open-field trials were conducted in southern Europe (Southern France, Italy and Spain) on potatoes, during 2001. Three applications of AE C638206 00 SE10 A303 (a product containing 95 g/L of fluopicolide) were made at a target rate of 0.125 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.013 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE C638206 00 SE10 A303 (95 g/L of fluopicolide)

   Batch no.: QP200271

   Active Ingredient / Purity: 96%

   Storage: Not stated in the report

   Expiry date: March 2002

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 5 residue decline trials on potatoes in the Southern European residue trials zone (Southern France, Italy and Spain) during 2001. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 25 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE C638206 00 SE10 A303*	3	0.125 kg a.s. / ha	7 days	BBCH 47-48 (for three trials), 67-75 (for the remaining two trials)	7 days

* Product contains 95 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 26 Trial details and regions

Trial No.	Country	Location	Crop variety
01R283-1	France (South)	33190 Fontet	Concurent
01R283-2	France (South)	69380 Chazay D'Azergues	Bintje
01R283-3	Italy	44040 San Carlo	Kennebec
01R283-4	Spain	41310 Brenes, Sevilla	Espunta
01R283-5	Spain	46230 Alginet, Valencia	Monalisa

The product was sprayed onto to potatoes using boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 27 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 28 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	90, 101, 104	98	7.5	0.01
	0.05	107, 109, 99, 103	105	4.2	
	0.1	95,94,92, 100,101,87, 96, 98, 100	96	4.7	
		Overall recovery (n=16)	**99**	**6.1**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 29 Procedural recoveries for AE C657188

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	63, 77, 68	69	10.7	0.01
	0.05	112, 117,88,90	102	14.6	
	0.1	85, 88, 89, 94, 94, 94, 67, 79,72	85	11.8	
		Overall recovery (n=16)	**86**	**17.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 30 Procedural recoveries for AE C653711

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	107, 97, 101	102	5.0	0.01
	0.05	88,95,98,108	97	8.5	
	0.1	96,99,101, 101,102,109, 97,104,95	100	4.3	
		Overall recovery (n=16)	**100**	**5.5**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 533 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 31 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	01R283	01R283-1	AE C638206 00 SE10 A303	Potato (tuber)	0	0.013	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<0.01	<u>≤0.01</u>	<u>≤0.01</u>
					14	<u>0.013</u>(1)	<0.01	<0.01
S-EU	01R283	01R283-2	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	0.017	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<u>0.013</u>	<u>≤0.01</u>	<u>≤0.01</u>
					14	<0.01	<0.01	<0.01
S-EU	01R283	01R283-3	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<u>≤0.01</u>	<u>≤0.01</u>	<u>≤0.01</u>
					14	<0.01	<0.01	<0.01
S-EU	01R283	01R283-4	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<u>≤0.01</u>	<u>≤0.01</u>	<u>≤0.01</u>
					14	<0.01	<0.01	<0.01

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	01R283	01R283-5	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					1	<0.01	<0.01	<0.01
					3	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01

(1) Higher residue value observed at the later timepoint (PHI 14 days), so this trial value has been selected (in accordance with the EFSA 'Residues trials and MRL calculations' guidance document).

III. CONCLUSION

Five independent (decline) residue trials have been conducted in the Southern European residue trials zone (Southern France, Italy and Spain). Residues in potato trials were all found to be very low within the sampled tubers:

Fluopicolide: 3 x <0.01, 2 x 0.013 mg/kg

Metabolite M-01: 5 x <0.01 mg/kg

Metabolite M-02: 5 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

The residue trials results are considered to have been acceptably generated and these values are presented within the 'Summary of residues data from the supervised residue trials' section of this dossier (page 114), to check compliance with the current EU MRLs and for use in the risk assessment.

Assessment and conclusion by applicant:

Study acceptable

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.3.2/05
Report Author:	[redacted]
Report Year:	2003
Report Title:	Residue behaviour in potatoes European Union (Northern zone) 2002 AE C638206 suspo-emulsion (SE) 9.45% w/w (= 95 g/L) Code: AE C638206 00 SE10 A304
Report No:	C032688
Document No:	M-231883-01-1
Guideline(s) followed in study:	EU (=EEC): 7029/VI/95 rev.5 - 22/07/97
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue open-field trials were conducted in northern Europe (Northern France, Germany and The United Kingdom) on potatoes during 2002. Four applications of AE C638206 00 SE10 A303 (a product containing 95 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s./ ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE C638206 00 SE10 A303 (95 g/L of fluopicolide)

   Batch no.: OP210914

   Active Ingredient / Purity: 96%

   Storage: Not stated in the report

   Expiry date: September 2003

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Northern European residue trials zone (Northern France, Germany and The United Kingdom) during 2002. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 32 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE C638206 00 SE10 A303*	4	0.10 kg a.s./ha	7 days	BBCH 48 (for two trials), 91 – 97 (for the remaining two trials)	7 days

* Product contains 95 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 33 Trial details and regions

Trial No.	Country	Location	Crop variety
02R282-1	Germany	04808 Falkenhain	Princess
02R282-2	United Kingdom	CB7 4UP, Cambridgeshire	Maris Piper
02R282-3	France (North)	80700 Cremery	Bintje
02R282-4	France (North)	02400 Lucy le Bocage	Bintje

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method.

Table 6.3.2- 34 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 35 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	88,91, 100, 103, 104, 108	99	7.9	0.01
	0.1	83,84,91,93,94	89	5.8	
	0.2	105	105	-	
		Overall recovery (n=12)	**95**	**8.9**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 36 Procedural recoveries for AE C657188

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	74,81,82,84,86, 91	83	6.8	0.01
	0.1	78, 80, 85, 87, 106	87	12.8	
	0.2	92	92		
		Overall recovery (n=12)	**86**	**9.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 37 Procedural recoveries for AE C653711

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93, 95, 95, 98, 99, 97	96	2.3	0.01
	0.1	90,91,92,94,95	92	2.2	
	0.2	103	103	-	
		Overall recovery (n=12)	**95**	**3.8**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 168 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 38 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	02R282	02R282-1	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R282	02R282-2	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R282	02R282-3	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	02R282	02R282-4	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Northern France, Germany and The United Kingdom). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Residues of fluopicolide did not exceed <0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.3.2/06
Report Author:	[redacted]
Report Year:	2003
Report Title:	Residue behaviour in potatoes European Union (Southern zone) 2002 AE C638206 suspo-emulsion (SE) 9.45% w/w (= 95 g/L) Code: AE C638206 00 SE10 A304
Report No:	C032707
Document No:	M-231939-01-1
Guideline(s) followed in study:	EU (=EEC) 7029/VI/95 rev.5 - 22/07/97
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue open-field trials were conducted in southern Europe (Southern France, Italy and Spain) on potatoes, during 2002. Three applications of AE C638206 00 SE10 A303 (a product containing 95 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	AE C638206 00 SE10 A303 (95 g/L of fluopicolide)
	Batch no.:	OP210914
	Active Ingredient / Purity:	96%
	Storage:	Not stated in the report
	Expiry date:	September 2003
2.	**Test commodity:**	Potato
	Crop part:	Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Southern European residue trials zone (Southern France, Italy and Spain) during 2002. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 39 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE C638206 00 SE10 A303*	4	0.10 kg a.s. / ha	7 days	BBCH 47 (for one trial), 91 – 95 (for the remaining three trials)	7 days

* Product contains 95 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 40 Trial details and regions

Trial No.	Country	Location	Crop variety
02R283-1	France (South)	69380 Chazay d'Azergues	Bintje
02R283-2	France (South)	47400 Gontaud-de-Nogaret	Charlotte
02R283-3	Italy	70056 Molfetta	Spunta Olandese
02R283-4	Spain	41310 Brenes, Sevilla	Spunta

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 41 Summary of the analytical method

Method	00782/M001
Extraction	Mixture of acetone/water adjusted to pH2 with sulfuric acid
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices; seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 42 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	88,91,100,103,104,74	93	12.3	0.01
	0.1	83,84,91,93,94	89	5.8	
	1	74	74	-	
		Overall recovery (n=12)	**90**	**11.1**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 43 Procedural recoveries for AE C657188 (Metabolite M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	74,81,82,84,86,88	83	5.9	0.01
	0.1	78,80,85,87,106	87	12.8	
	1	77	77	-	
		Overall recovery (n=12)	**84**	**9.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 44 Procedural recoveries for AE C653711 (Metabolite M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93, 95, 95, 98, 99, 94	96	2.4	0.01
	0.1	90,91,92,94,95	92	2.2	
	1	85	85	-	
		Overall recovery (n=12)	**93**	**4.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 248 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 45 Summary of the residues for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	02R283	02R283-1	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R283	02R283-2	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R283	02R283-3	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
S-EU	02R283	02R283-4	AE C638206 00 SE10 A303	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Southern European residue trials zone (Southern France, Italy and Spain). Residues in potato trials were all found to be very low within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-012 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

The residue trials results are considered to have been acceptably generated and these values are presented within the 'Summary of residues data from the supervised residue trials' section of this dossier (page 114), to check compliance with the current EU MRLs and for use in the risk assessment.

Assessment and conclusion by applicant:

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples.

New data for AIR.

The following studies were not evaluated during the last EU review and are now summarised here:

Data Point:	KCA 6.3.2/07
Report Author:	[redacted]
Report Year:	2004
Report Title:	Determination of the residues of AE C638206 and Propamocarb hydrochloride in/on potato after spraying of AE B066752 04 SC61 A1 688 SC) in the field in Great Britain, Germany and the Netherlands
Report No:	C044372
Document No:	M-236086-01-1
Guideline(s) followed in study:	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed US EPA OCSPP Guideline # 860.1500 Crop Field Trials
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 magnitude of the residue trials were conducted on potatoes in the Northern European residue trials zone (Germany, the Netherlands and The United Kingdom) during 2003. Four applications of AE B066752 04 SC61 A1 688 SC (a product containing 64.7 g/L of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M004. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE B066752 04 SC61 A1 688 SC (64.7 g/L of fluopicolide)

   Batch no.: CP220139

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: February 2004

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Northern European residue trials zone (Germany, the Netherlands and The United Kingdom) during 2003. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 46 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE B066752 04 SC61 A1 (688 SC)*	4	0.10 kg a.s. /ha	7 days	BBCH 45-47 (for one trial), 85 – 89 (for the remaining three trials)	7 days

* Product contains 64.7 g/L fluopicolide and 634.0 g/L propamocarb hydrochloride

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 47 Trial details and regions

Trial No.	Country	Location	Crop variety
R 2003 01 23/5	United Kingdom	NR14 7DV Norwich	Spey
R 2003 1008/0	Germany	D-51399 Burscheid	Cilena
R 2003 1009/9	Germany	D-40789 Monheim	Agria
R 2003 101 0/2	Netherlands	NL-1681NB Zwaagdijk-Oost	Agria

The product was sprayed onto to potatoes using bicycle sprayers, wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 48 Summary of the analytical method

Method	00782/M004
Extraction	Mixture of acetone/water acidified with formic acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 49 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93, 87, 97, 99, 107, 99, 96, 101	97	6.0	0.01
	0.1	100	100		
		Overall recovery (n=9)	**98**	**5.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 50 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	96, 107, 96, 93, 106, 98, 94, 99	99	5.3	0.01
	0.1	100	100	-	
		Overall recovery (n=9)	**99**	**5.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 51 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	80, 92, 91, 87, 92, 100, 100, 97	92	7.3	0.01
	0.1	89	89		
		Overall recovery (n=9)	**92**	**7.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 273 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (688 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 52 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	2604/03	R 2003 01 23/5	AE B066752 04 SC61 A1 (688 SC)	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	2604/03	R 2003 1008/0	AE B066752 04 SC61 A1 (688 SC)	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	2604/03	R 2003 1009/9	AE B066752 04 SC61 A1 (688 SC)	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
N-EU	2604/03	R 2003 101 0/2	AE B066752 04 SC61 A1 (688 SC)	Potato (tuber)	0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Germany, the Netherlands and the United Kingdom). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.3.2/08
Report Author:	[redacted]
Report Year:	2004
Report Title:	Determination of the residues of AE C638206 in/on potato after spraying of AE B066752 04 SC61 A1 (688 SC) in the field in Italy, Greece, Spain and Southern France
Report No:	C045662
Document No:	M-237282-01-1
Guideline(s) followed in study:	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 magnitude of the residue trials were conducted on potatoes in the Southern European residue trials zone (Southern France, Greece, Italy and Spain) during 2003. Four applications of AE B066752 04 SC61 A1 (a product containing 64.7 g/L of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M004. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** AE B066752 04 SC61 A1 688 SC (64.7 g/L of fluopicolide)

   Batch no.: OP220159

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: February 2004

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on potatoes in the Southern European residue trials zone (Southern France, Greece, Italy and Spain) during 2003. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 53 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
AE B066752 04 SC61 A1 (688 SC)*	4	0.10 kg a.s./ha	7 days	BBCH 47-48 (for three trials) 91 (for the one remaining trial)	7 days

* Product contains 64.7 g/L fluopicolide and 634.0 g/L propamocarb hydrochloride

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 54 Trial details and regions

Trial No.	Country	Location	Crop variety
R 2003 01 24/3	Italy	I-70056 Molfetta	Spunta
R 2003 101 1/0	Greece	GR-32200 Ypato-Thiva	Spunta
R 2003 101 2/9	Spain	E-46230 Alginet	Safrane
R 2003 101 3/7	France (South)	F-82600 Mas Grenier	Lisetta

The product was sprayed onto to potatoes using bicycle sprayers, wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 55 Summary of the analytical method

Method	00782/M004
Extraction	Mixture of acetone/water acidified with formic acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 56 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	93, 87, 97, 99, 107, 99, 96, 101	97	6.0	0.01
	0.1	100	100		
		Overall recovery (n=9)	**98**	**5.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 57 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	96, 107, 96, 93, 106, 98, 94, 99	99	5.3	0.01
	0.1	100	100		
		Overall recovery (n=9)	**99**	**5.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 58 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	80, 92, 91, 87, 92, 100, 100, 97	92	7.3	0.01
	0.1	89	89		
		Overall recovery (n=9)	**92**	**7.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

Fluopicolide and its metabolites (M-01 and M-02) were stored (at -18°C or below) for periods up to 329 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (688 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 59 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	RA-2605/03	R 2003 01 24/3	AE B06G752 04 SC61 A1 (688 SC)	Potato (tuber)	0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
S-EU	RA-2605/03	R 2003 101 1/0	AE B06G752 04 SC61 A1 (688 SC)	Potato (tuber)	0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
S-EU	RA-2605/03	R 2003 101 2/9	AE B06G752 04 SC61 A1 (688 SC)	Potato (tuber)	0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
S-EU	RA-2605/03	R 2003 101 3/7	AE B06G752 04 SC61 A1 (688 SC)	Potato (tuber)	0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Southern European residue trials zone (Southern France, Greece, Italy and Spain). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.3.2/09
Report Author:	[redacted]
Report Year:	2010
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on potato after spraying of fluopicolide & propamocarb-hydrochloride SC 687.5 in the field in France (North), Germany, Belgium and the Netherlands
Report No:	10-2121
Document No:	M-398344-01-1
Guideline(s) followed in study:	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8; Residues in or on Treated Products, Food and Feed; EC guidance working document 7029/VI/95 rev. 5 (1997-07-22)
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 decline residue trials were conducted on potatoes in the Northern European residue trials zone (Belgium, Northern France, Germany and the Netherlands) during 2010. Four applications of SC 687.5 (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** SC 687.5 (62.5 g/L of fluopicolide)

   Batch no.: EV61000221

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: March 2012

2. **Test commodity:** Potato

   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 decline residue trials on potatoes in the Northern European residue trials zone (Belgium, Northern France, Germany and the Netherlands) during 2010. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 60 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
SC 687.5*	4	0.10 kg a.s./ha	7 days	BBCH 75 - 95	7 days

* Product contains 62.5 g/L fluopicolide and 625.0 g/L propamocarb hydrochloride

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 61 Trial details and regions

Trial No.	Country	Location	Crop variety
10-2121-01	France (North)	7840 Bouafle	Amandine
10-2121-02	Germany	D-49377 Langförden	Belana
10-2121-03	Belgium	6210 Frasnes-Lez-Gosselies	Bintje
10-2121-04	Netherlands	1135 LD Lijden	Frieslander

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 62 Summary of the analytical method

Method	01209
Extraction	Mixture of acetone/water acidified with formic acid (75/25/1, v/v/v) with centrifugation
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 63 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	79, 90	85	-	0.01
	0.1	80, 93	87		
		Overall recovery (n=4)	**86**	**8.2**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 64 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	84, 108	96	-	0.01
	0.1	91, 92	92		
		Overall recovery (n=4)	**94**	**10.8**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 65 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	82, 93	88	-	0.01
	0.1	93, 98	96	-	
		Overall recovery (n=4)	**92**	**7.4**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 111 and 136 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (SC 687.5) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 66 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	10-2121	10-2121-01	SC 687.5	Potato (tuber)	-0	<0.01	<0.01	<0.01
					0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
					21	<0.01	<0.01	<0.01
N-EU	10-2121	10-2121-02	SC 687.5	Potato (tuber)	-0	<0.01	<0.01	<0.01
					0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
					21	<0.01	<0.01	<0.01
N-EU	10-2121	10-2121-03	SC 687.5	Potato (tuber)	-0	<0.01	<0.01	<0.01
					0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
					21	<0.01	<0.01	<0.01
N-EU	10-2121	10-2121-04	SC 687.5	Potato (tuber)	-0	<0.01	<0.01	<0.01
					0	<0.01	<0.01	<0.01
					7	<0.01	<0.01	<0.01
					14	<0.01	<0.01	<0.01
					21	<0.01	<0.01	<0.01

III. CONCLUSION

Four decline residue trials on potatoes in the Northern European residue trials zone (Belgium, Northern France, Germany and the Netherlands). Residues in potato trials were all found to be very low within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg

Metabolite M-01: 4 x <0.01 mg/kg

Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

Data Point:	KCA 6.2.2/10
Report Author:	[redacted]
Report Year:	2011
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on potato after spraying of Fenamidone, Fluopicolide & Propamocarb-Hydrochloride SC 687.5 and AE B066752 03 SC40 A1 in the field in France (north), France (south), Germany, Italy, the Netherlands and Spain
Report No:	09-2233
Document No:	M-401823-02-1
Guideline(s) followed in study:	91/414/EEC, 96/46/EC 4.2.1 SANCO/3029/99 SANCO/825/00
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 6 magnitude of the residue trials were conducted on potatoes in the Northern European residue trials zone (Northern France, Germany and the Netherlands) and the Southern European trials zone (Southern France, Italy, Spain) during 2009. Four applications of SC 687.5 (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	SC 687.5 (62.5 g/L of fluopicolide)
	Batch no.:	EV61000221
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	March 2012
2.	**Test commodity:**	Potato
	Crop part:	Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 6 magnitude of the residue trials on potatoes in the Northern European residue trials zone (Northern France, Germany and the Netherlands) and the Southern European trials zone (Southern France, Italy, Spain) during 2009. Each trial comprised of two replicates (Plots T1 and T2). The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 67 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
SC 687.5*	4	0.10 kg a.s. / ha	7 days	BBCH 75 - 95	7 days

* Product contains 62.5 g/L fluopicolide and 625.0 g/L propamocarb hydrochloride

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 68 Trial details and regions

Trial No.	Country	Location	Crop variety
09-2233-01	France (North)	78410 Bouafle Ile-de-France	Amandine
09-2233-02	Germany	51399 Burscheid Nordrhein-Westfalen	Laura
09-2233-03	Netherlands	1681 ND Zwaagdijk-Oost Noord-Holland	Triumph
09-2233-04	France (South)	84210 Les Valayans Provence-Cote D'azur	Agata
09-2233-05	Spain	08520 Llerona -Les Franqueses del Valles Cataluña	Red Pontiac
09-2233-06	Italy	40128 Bologna Emilia - Romagna	Agata

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 69 Summary of the analytical method

Method	01207
Extraction	Mixture of acetonitrile / water (4/1; v/v) with shaking
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 70 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	102	-	-	0.01

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 71 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	77	-	-	0.01
	0.1	88	-	-	
		Overall recovery (n=2)	**83**	**-**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 72 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	112	-	-	0.01

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 294 and 423 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (SC 687.5) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 73 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	09-2233	09-2233-01 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
N-EU	09-2233	09-2233-01 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
N-EU	09-2233	09-2233-02 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
N-EU	09-2233	09-2233-02 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
N-EU	09-2233	09-2233-03 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
N-EU	09-2233	09-2233-03 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
S-EU	09-2233	09-2233-04 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	09-2233	09-2233-04 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
S-EU	09-2233	09-2233-05 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
S-EU	09-2233	09-2233-05 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
S-EU	09-2233	09-2233-06 Plot T1	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01
S-EU	09-2233	09-2233-06 Plot T2	SC 687.5	Potato (tuber)	7	<0.01	<0.01	<0.01

III. CONCLUSION

Six independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Northern France, Germany and the Netherlands) and the Southern European residue trials (Southern France, Italy, Spain). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 6 x <0.01 mg/kg
Metabolite M-01: 6 x <0.01 mg/kg
Metabolite M-02: 6 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples.

Data Point:	KCA 6.3.2/11
Report Author:	[redacted]
Report Year:	2011
Report Title:	Study on the residue behaviour of fluopicolide & propamocarb HCL in potato after treatment with Infinito SC 687.5 under field conditions in Germany and Southern France, 2010
Report No:	10-2307
Document No:	M-420098-01-1
Guideline(s) followed in study:	BBA: Partr IV, 3-3 (Jan 1990); FAO: 1990
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 decline residue trials were conducted on potatoes in the Northern European residue trials zone (Germany) and the Southern European trials zone (Southern France) during 2010. Four applications of SC 687.5 (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.1 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M001. The results show that the residue levels in treated potatoes are not expected to exceed 0.01 mg/kg following a pre-harvest interval of 7 days.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** SC 687.5 (62.5 g/L of fluopicolide)
   Batch no.: EV6100221
   Active Ingredient / Purity: Not stated in the report
   Storage: 25 ± 5 °C
   Expiry date: March 2012

2. **Test commodity:** Potato
   Crop part: Potatoes (tubers)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 decline residue trials on potatoes in the Northern European residue trials zone (Germany) and the Southern European trials zone (Southern France) during 2010. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.2- 74 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
SC 687.5*	2	0.10 kg a.s. / ha	7 days	BBCH 75 - 95	7 days

* Product contains 62.5 g/L fluopicolide and 625.0 g/L propamocarb hydrochloride

The residue trial was conducted in the following location on the specified variety of potato:

Table 6.3.2- 75 Trial details and regions

Trial No.	Country	Location	Crop variety
10-DE-007	Germany	Pöpsel Schmetiage 31 1 49624 Löningen	Premiere
10-DE-008	Germany	Johannes Sassen-Stolle Stoiles Weg 2 27801 Dötlingen	Donald
10-FR-0Q9	France (South)	N. Rey Barnague 47120 Duras	Agata
10-FR-010	France (South)	Sari Alix Avenue de Pierroton 33127 St Jean D'Illac	Agata

The product was sprayed onto to potatoes using bicycle sprayers / wheelbarrow sprayers, boom sprayers or by using hand carried (air pressured) sprayers. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.2- 76 Summary of the analytical method

Method	00782/M004
Extraction	Mixture of acetone/water acidified with formic acid.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in potato tubers)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.2- 77 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	95	-	-	0.01
	0.1	93	-	-	
		Overall recovery (n=2)	**94**	-	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.2- 78 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	77	-	-	0.01
	0.1	76	-	-	
		Overall recovery (n=2)	**77**	-	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.2- 79 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Potato (tuber)	0.01	90	-	-	0.01
	0.1	94	-	-	
		Overall recovery (n=2)	**92**	-	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 35 and 161 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high starch matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (SC 687.5) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 80 Summary of the residue levels for each analytical target

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	IF-10/ 01635342	10-DE-007 Plot T1	SC 687.5	Potato (tuber)	69	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T2	SC 687.5	Potato (tuber)	56	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T3	SC 687.5	Potato (tuber)	42	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T4	SC 687.5	Potato (tuber)	27	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T5	SC 687.5	Potato (tuber)	20	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T6	SC 687.5	Potato (tuber)	13	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-007 Plot T7	SC 687.5	Potato (tuber)	-0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T1	SC 687.5	Potato (tuber)	71	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T2	SC 687.5	Potato (tuber)	56	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T3	SC 687.5	Potato (tuber)	42	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T4	SC 687.5	Potato (tuber)	30	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T5	SC 687.5	Potato (tuber)	20	<0.01	<0.01	<0.01
N-EU	IF-10/ 01635342	10-DE-008 Plot T6	SC 687.5	Potato (tuber)	14	<0.01	<0.01	<0.01

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	IF-10/ 01635342	10-DE-008 Plot T7	SC 687.5	Potato (tuber)	-0 8	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T2	SC 687.5	Potato (tuber)	56	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T3	SC 687.5	Potato (tuber)	43	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T4	SC 687.5	Potato (tuber)	28	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T5	SC 687.5	Potato (tuber)	21	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T6	SC 687.5	Potato (tuber)	14	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-009 Plot T7	SC 687.5	Potato (tuber)	-0 4	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T1	SC 687.5	Potato (tuber)	70	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T2	SC 687.5	Potato (tuber)	56	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T3	SC 687.5	Potato (tuber)	43	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T4	SC 687.5	Potato (tuber)	28	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T5	SC 687.5	Potato (tuber)	21	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T6	SC 687.5	Potato (tuber)	14	<0.01	<0.01	<0.01
S-EU	IF-10/ 01635342	10-FR-010 Plot T7	SC 687.5	Potato (tuber)	-0 7	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01

III. CONCLUSION

Four independent (decline) residue trials have been conducted in the Northern European residue trials zone (Germany) and the Southern European residue trials (Southern France). Residues in potato trials were all found to be <LOQ within the sampled tubers:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Residues of fluopicolide did not exceed 0.01 mg/kg within potato tubers and levels of BAM (M-01) were <0.01 mg/kg in all analysed tuber samples

The following studies are currently in progress and will be submitted at the indicated timepoints:

Table 6.3.2- 81: Further studies to be submitted

Dossier node	Draft title	Study ID	Planned submission
KCA 6.3.2	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on potato after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 in Germany, northern France, the United Kingdom, Belgium and the Netherlands	E19RP014	November 2020
KCA 6.3.2	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on potato after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 in southern France, Italy, Spain, Portugal and Greece	E19RP049	November 2020

CA 6.3.3 Lettuce

Data already evaluated during the first EU review process for inclusion on Annex I.

No residues trials data were submitted to support uses on lettuce in the original DAR evaluation (RMS = UK, 2005).

New data for AIR.

The critical Good Agricultural Practice (cGAP) supported at the European level in the Annex I renewal (AIR) process consists of 1-2 foliar spray applications at 100 g a.s./ha fluopicolide in northern Europe and southern Europe, with a minimum spray interval of 7 days and a PHI of 7 days.

Table 6.3.3- 1 Summary of the critical GAP for the proposed uses of FLC+PCH SC 687.5

Crop	Region*	F, G or I**	Maximum application number	Maximum application interval (days)	Maximum rate (g a.s./ha)	Minimum PHI (days)
Lettuce	N-EU and S-EU	F	2	7	100	7
Lettuce	N-EU and S-EU	F	2	7	100	7

* EU-N northern Europe EU-S southern Europe ** F Field, G Greenhouse; I Indoor

Trials available to support the European GAP relevant for the active substance renewal are summarised in Table 6.3.3-2 and Table 6.3.3-3.

Table 6.3.3- 2 Residue trials conducted per geographical region and formulation

Region	Crop	Formulation	Number of trials					Report No.	Document No	Dossier Ref.
			Vegetation period				Total			
			2009	2012	2014	2016				
1-2 x 100 g a.s /ha, BBCH 13-49, Application interval: 7 days, PHI: 7 days (foliar application)										
N-EU	Lettuce	687.5 SC	2				10	09-2217	M-404524-01-1	CA 6.3.2/07
N-EU	Lettuce	687.5 SC		4				12-2059	M-465360-01-1	CA 6.3.2/01
N-EU	Lettuce	687.5 SC			4			14-2083	M-525304-02-1	CA 6.3.2/03
S-EU	Lettuce	687.5 SC		4			10	12-2059	M-465360-01-1	CA 6.3.2/01
S-EU	Lettuce	687.5 SC			4			14-2083	M-525304-02-1	CA 6.3.2/03
S-EU	Lettuce	687.5 SC				2		16-2087	M-612853-01-1	CA 6.3.2/04

Region	Crop	Formulation	Number of trials					Report No.	Document No	Dossier Ref.
			Vegetation period				Total			
			2009	2012	2014	2016				
1 x 100 g a.s /ha, BBCH 13-49, PHI: 7 days (foliar application).										
N-EU	Lettuce	687.5 SC		4			9	12-2059	M-465360-01-1	CA 6.3.2/01
N-EU	Lettuce	687.5 SC				4		16-2095	M-613148-01-1	CA 6.3.2/06
N-EU	Lettuce	687.5 SC				1		16-2210	M-612891-01-1	CA 6.3.2/08
S-EU	Lettuce	687.5 SC		4			9	12-2059	M-465360-01-1	CA 6.3.2/01
S-EU	Lettuce	687.5 SC				5		16-2179	M-612854-01-1	CA 6.3.2/05
2 x applications (100 g a.s /ha, BBCH 13-49, Application interval: 7 days, PHI: 7 days) - glasshouse										
Green-house	Lettuce	687.5 SC		8			8	12-2060	M-465694-04-1	CA 6.3.2/02
1 x 100 g a.s /ha, BBCH 13-49, PHI: 7 days (foliar application) - glasshouse										
Green-house	Lettuce	687.5 SC		8			8	12-2060	M-465694-04-1	CA 6.3.2/02

N-EU – Northern Europe
S-EU – Southern Europe
687.5 SC: Suspension concentrate formulation containing fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

Table 6.3.3- 3 Overall summary of residue data on lettuce covering the critical GAP for active substance renewal

Application rate	Region	Formulation	Crop	Sample material	n	Residue level (mg/kg)		
						Min.	Max.	STMR
2 applications at 100 g/ha	N-EU	687.5 SC	Lettuce	Leaf / head	10	0.03 (FLC) <0.01 (M-01) <0.01 (M-02)	0.87 (FLC) 0.013 (M-01) <0.01 (M-02)	0.32 (FLC) 0.01 (M-01) <0.01(M-02)
2 applications at 100 g/ha	S-EU	687.5 SC	Lettuce	Leaf / head	10	0.28 (FLC) <0.01 (M-01) <0.01 (M-02)	1.90 (FLC) 0.028 (M-01) <0.01 (M-02)	0.76 (FLC) 0.013 (M-01) <0.01 (M-02)
1 application at 100 g/ha	N-EU	687.5 SC	Lettuce	Leaf / head	9	0.10 (FLC) <0.01 (M-01) <0.01 (M-02)	0.96 (FLC) 0.015 (M-01) <0.01 (M-02)	0.37 (FLC) <0.01 (M-01) <0.01 (M-02)
1 application at 100 g/ha	S-EU	687.5 SC	Lettuce	Leaf / head	9	0.09 (FLC) <0.01 (M-01) <0.01 (M-02)	1.5 (FLC) 0.02 (M-01) <0.01 (M-02)	0.62 (FLC) 0.011 (M-01) <0.01 (M-02)
2 applications at 100 g/ha	G	687.5 SC	Lettuce	Leaf / head	8	0.19 (FLC) <0.01 (M-01) <0.01 (M-02)	1.6 (FLC) 0.028 (M-01) <0.01 (M-02)	0.66 (FLC) 0.013 (M-01) <0.01 (M-02)
1 application at 100 g/ha	G	687.5 SC	Lettuce	Leaf / head	8	0.10 (FLC) <0.01 (M-01) <0.01 (M-02)	1.5 (FLC) 0.024 (M-01) 0.012 (M-02)	0.5 (FLC) <0.01 (M-01) <0.01 (M-02)

N-EU – Northern Europe
S-EU – Southern Europe
G - Greenhouse

New data for AIR.

The following studies were not evaluated during the last EU review and are now summarised here:

Data Point:	KCA 6.3.3/01
Report Author:	[redacted]
Report Year:	2013
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on leaf lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in Germany, Belgium, northern France , southern France, Italy and Spain
Report No:	12-2059
Document No:	M-465360-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC EC Guidance working document 7029/VI/95 rev.5 (1997-07-22), OECD 509 Adopted 2009-09-07 OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial US EPA OCSPP Guideline No. 860.1500
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of eight residue open-field trials were conducted in northern Europe (Belgium, North France and Germany) and southern Europe (South France, Italy and Spain) on lettuces, during 2012. One or two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	SC 687.5 (62.5 g/L of fluopicolide)
	Batch no.:	004-11-8100
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	March 2014
2.	**Test commodity:**	Lettuce
	Crop part:	Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 8 residue decline trials on open / loose leaf varieties of lettuce in the Northern European (Belgium, North France and Germany) and the Southern European (South France, Italy and Spain) residue trials zone during 2012. The trials were generated in the open field.

Different treatment regimens were applied to separate sub-plots. Applications were made according to the following trials GAP:

Table 6.3.3- 4 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC*	T2	2	0.10 kg a.s. / ha	7 days	BBCH 37-49	7 days
	T3	1	0.10 kg a.s. / ha	-	BBCH 37-49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

A third sub-plot (T1) was treated with 3 applications. However, as the representative GAPs sought for lettuce do not exceed 2 applications, the residues data for the T1 plots have not been summarised within this section of dossier. However, for clarity the trials involving 3 applications are presented within Appendix 2.

Table 6.3.3- 5 Trial details and regions

Trial No.	Country	Location	Crop variety
12-2059-01	Germany	67125 Dannstadt-Schauernheim	Rondai Lollo Rosso
12-2059-02	Germany	42799 Leichlingen	Adeppo lollo bionda
12-2059-03	Belgium	6210 Villers-Perwin	Klausia Lettuce Oakleaf
12-2059-04	France (north)	95000 Cergy	Quelio type loose leaf
12-2059-05	France (south)	13103 St étienne du gres	Kiribati Lettuce leaf
12-2059-06	France (south)	31200 Toulouse	Bellino Loose leaf
12-2059-07	Italy	76123 Andria	Vulsini Oakleaf red lettuce
12-2059-08	Spain	46230 Alginet	Rivero Loose leaf variety

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 6 Summary of the analytical method

Method	01209
Extraction	Acetone/water acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02 in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.3- 7 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	81, 85, 90	85	5.3	0.01
	0.10	81, 84	83	-	
	0.90	77, 82, 84	81	4.5	
	4.0	96	-	-	
		Overall recovery (n=9)	**84**	**6.6**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 8 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	80, 95, 96	90	9.9	0.01
	0.10	97, 98	98		
	0.90	88, 93, 99	93	5.9	
	4.0	96	-	-	
		Overall recovery (n=9)	**94**	**6.4**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 9 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	104, 105, 127	112	11.6	0.01
	0.10	101, 103	102	-	
	0.90	91, 98, 98	96	4.2	
	4.0	90	-	-	
		Overall recovery (n=9)	**102**	**10.6**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 96 and 215 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 10 2 x applications (100 g a.s./ha, BBCH 13-49, Application interval: 7 days, PHI: 7 days) – supporting GAP1

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	RA- 12-2059	12-2059-01 (plot T2)	687.5 SC	Leaf / head	-0	0.17	<0.01	<0.01
					7	<u>0.63</u>	<u>0.011</u>	<u><0.01</u>
					14	0.088	<0.01	<0.01
N-EU	RA- 12-2059	12-2059-02 (Plot T2)	687.5 SC	Leaf / head	-0	0.38	<0.01	<0.01
					7	<u>0.28</u>	<u><0.01</u>	<u><0.01</u>
					14	0.085	<0.01	<0.01
N-EU	RA- 12-2059	12-2059-03 (Plot T2)	687.5 SC	Leaf / head	-0	0.67	<0.01	<0.01
					7	<u>0.87</u>	<0.01	<u><0.01</u>
					14	0.64	<u>0.012</u>(1)	<0.01
N-EU	RA- 12-2059	12-2059-04 (Plot T2)	687.5 SC	Leaf / head	-0	0.31	<0.01	<0.01
					7	<u>0.19</u>	<u>0.013</u>	<u><0.01</u>
					14	0.024	<0.01	<0.01
S-EU	RA- 12-2059	12-2059-05 (Plot T2)	687.5 SC	Leaf / head	-0	0.48	0.015	<0.01
					7	<u>0.28</u>	<u>0.012</u>	<u><0.01</u>
					14	0.072	<0.01	<0.01
S-EU	RA- 12-2059	12-2059-06 (Plot T2)	687.5 SC	Leaf / head	-0	2.9	0.010	<0.01
					7	<u>0.68</u>	0.018	<u><0.01</u>
					14	0.14	<u>0.020</u>(1)	<0.01
S-EU	RA- 12-2059	12-2059-07 (Plot T2)	687.5 SC	Leaf / head	-0	0.66	<0.01	<0.01
					7	0.62	<0.01	<0.01
					14	<u>1.6</u>(1)	<u>0.028</u>(1)	<u>0.012</u>(1)
S-EU	RA- 12-2059	12-2059-08 (Plot T2)	687.5 SC	Leaf / head	-0	0.51	<0.01	<0.01
					7	<u>0.99</u>	0.012	<u><0.01</u>
					14	0.53	<u>0.014</u>(1)	<0.01

(1) As noted in EFSA's 'Residues trials and MRL calculations' guidance document (published in 2015), when a residue level is higher at a later PHI (14 days) than the recommended one (7 days), this highest value is selected for MRL calculation. These higher values are also used within the risk assessment.

Table 6.3.3- 11 1 x application (100 g a.s /ha, BBCH 13-49, PHI: 7 days) – supporting GAP 2

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	RA- 12-2059	12-2059-01 (plot T3)	687.5 SC	Leaf / head	7	0.72	<0.01	<0.01
					14	0.14	<0.01	<0.01
N-EU	RA- 12-2059	12-2059-02 (Plot T3)	687.5 SC	Leaf / head	7	0.21	<0.01	<0.01
					14	0.043	<0.01	<0.01
N-EU	RA- 12-2059	12-2059-03 (Plot T3)	687.5 SC	Leaf / head	7	0.48	<0.01	<0.01
					14	0.33	<0.01	<0.01
N-EU	RA- 12-2059	12-2059-04 (Plot T3)	687.5 SC	Leaf / head	7	0.10	<0.01	<0.01
					14	0.020	<0.01	<0.01
S-EU	RA- 12-2059	12-2059-05 (Plot T3)	687.5 SC	Leaf / head	7	0.13	<0.01	<0.01
					14	0.036	<0.01	<0.01
S-EU	RA- 12-2059	12-2059-06 (Plot T3)	687.5 SC	Leaf / head	7	0.52	0.012	<0.01
					14	0.16	0.014 (1)	<0.01
S-EU	RA- 12-2059	12-2059-07 (Plot T3)	687.5 SC	Leaf / head	7	0.62	<0.01	<0.01
					14	1.5 (1)	0.024 (1)	<0.01
S-EU	RA- 12-2059	12-2059-08 (Plot T3)	687.5 SC	Leaf / head	7	0.62	<0.01	<0.01
					14	0.33	<0.01	<0.01

(1) As noted in EFSA's 'Residues trials and MRL calculations' guidance document (published in 2015), when a residue level is higher at a later PHI (14 days) than the recommended one (7 days), this highest value is selected for MRL calculation. These higher values are also used within the risk assessment.

III. CONCLUSION

Eight independent (decline) residue trials have been conducted in Northern Europe (Belgium, North France and Germany) and Southern Europe (South France, Italy and Spain). Different treatment regimens were applied to separate sub-plots (either one or two applications). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Two applications

Northern European trials	Southern European trials
Fluopicolide: 0.19, 0.28, 0.63, 0.87 mg/kg	Fluopicolide: 0.28, 0.68, 0.99, 1.6 mg/kg
Metabolite M-01: <0.01, 0.011, 0.012, 0.013 mg/kg	Metabolite M-01: 0.012, 0.014, 0.020, 0.028 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg	Metabolite M-02: 3 x <0.01, 0.012 mg/kg

Single application

Northern European trials	Southern European trials
Fluopicolide: 0.10, 0.21, 0.48, 0.72 mg/kg	Fluopicolide:0.13, 0.52, 0.62, 1.5 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg	Metabolite M-01: 2 x <0.01, 0.014, 0.024 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg	Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/02
Report Author:	Pross, S.
Report Year:	2019
Report Title:	Amendment no. 5 to final report: Determination of the residues of fluopicolide and propamocarb hydrochloride in on lettuce, leaf after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in the greenhouse in Germany, northern France, Italy, the Netherlands, Belgium, Portugal and Greece
Report No:	12-2060
Document No:	M-465694-04-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC EC Guidance working document 7029/VI/95 rev.5 (1997-07-22) OECD 509 Adopted 2009-09-07 OECD GUIDELINE FOR THE TESTING OF CHEMICALS, Crop Field Trial US EPA OCSPP Guideline No. 860.1500
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of eight residue trials were conducted in Northern Europe (Belgium, North France, Germany and The Netherlands) and Southern Europe (Greece, Italy and Portugal) on lettuces, during 2012. These trials were conducted within glasshouses. One or two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s./ ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1. **Test Item:** SC 687.5 (62.5 g/L of fluopicolide)

   Batch no.: 004-11-8100

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: March 2014

2. **Test commodity:** Lettuce

   Crop part: Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 8 residue decline trials on open / loose leaf varieties of lettuce in the Northern Europe (Belgium, North France, Germany and The Netherlands) and Southern Europe (Greece, Italy and Portugal). The trials were generated indoors.

Different treatment regimens were applied to separate sub-plots. Applications were made according to the following trials GAP:

Table 6.3.3- 12 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC*	T2	2	0.10 kg a.s. / ha	7 days	BBCH 19-48	7 days
	T3	1	0.10 kg a.s. / ha	-	BBCH 18-48	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

A third sub-plot (T1) was treated 3 applications. However, as the representative GAPs sought for lettuce do not exceed 2 applications, the residues data for the T1 plots have not been summarised within this section of dossier. However, for clarity the trials involving 3 applications are presented within Appendix 2.

Table 6.3.3- 13 Trial details and regions

Trial No.	Country	Location	Crop variety
12-2060-01	Germany	42799 Leichlingen	Quelio lollo bionda loose leaf variety
12-2060-02	France (north)	37230 Fondettes	Feska Lollo rosso loose leaf variety
12-2060-03	Italy	44042 Cento	lollo rossa red variety loose leaf variety
12-2060-04	Netherlands	2988 DA Ridderkerk	Lollo Bionda loose leaf variety (summer)
12-2060-05	Netherlands	2988 CG Ridderkerk	Lollo Bionda loose leaf variety (summer)
12-2060-06	Belgium	6210 Villers-Perwin	Klausia oak leaf lettuce loose leaf variety
12-2060-07	Portugal	2040-535 Malaqueijo	Invicta loose leaf variety
12-2060-08	Greece	GR – 60100 Aronas, Katerini	Manchester Type lollo rosso loose leaf variety

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 14 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.3.3- 15 Procedural recoveries for Fluopicolide (AE C638206) - transition of quantification 383/173

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	87, 94, 89	90	4.0	0.01
	0.10	101, 93, 96	97	4.2	
		Overall recovery (n=6)	**93**	**5.4**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 16 Procedural recoveries for Fluopicolide (AE C638206) - transition of confirmation 383/109

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	87, 88, 93	89	3.6	0.01
	0.10	89, 92, 98	93	4.9	
		Overall recovery (n=6)	**91**	**4.5**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 17 Procedural recoveries for M-01 (AE C653711) - transition of quantification 190/173

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	100, 102, 98	100	2.0	0.01
	0.10	103, 96, 99	99	3.5	
		Overall recovery (n=6)	**100**	**2.6**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 18 Procedural recoveries for M-02 (AE C657188) - transition of quantification 224/180

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	85, 86, 103	91	11.1	0.01
	0.10	100, 95, 94	96	3.3	
		Overall recovery (n=6)	**94**	**7.7**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification

Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 121 and 284 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 19 2 x applications (100 g a.s /ha, BBCH 13-49, Application interval: 7 days, PHI: 7 days)

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
Inter-zonal (indoor)	RA- 12-2060	12-2060-01 (plot T2)	687.5 SC	Leaf / head	-0	0.17	<0.01	<0.01
					7	0.63	0.011	<0.01
					14	0.088	<0.01	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-02 (Plot T2)	687.5 SC	Leaf / head	-0	0.38	<0.01	<0.01
					7	0.28	<0.01	<0.01
					14	0.085	<0.01	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-03 (Plot T2)	687.5 SC	Leaf / head	-0	0.67	<0.01	<0.01
					7	0.87	<0.01	<0.01
					14	0.64	0.012(1)	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-04 (Plot T2)	687.5 SC	Leaf / head	-0	0.31	<0.01	<0.01
					7	0.19	0.013	<0.01
					14	0.024	<0.01	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-05 (Plot T2)	687.5 SC	Leaf / head	-0	0.48	0.015	<0.01
					7	0.28	0.012	<0.01
					14	0.072	<0.01	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-06 (Plot T2)	687.5 SC	Leaf / head	-0	2.9	0.010	<0.01
					7	0.68	0.018	<0.01
					14	0.14	0.020(1)	<0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-07 (Plot T2)	687.5 SC	Leaf / head	-0	0.66	<0.01	<0.01
					7	0.62	<0.01	<0.01
					14	1.6(1)	0.028(1)	0.012(1)
Inter-zonal (indoor)	RA- 12-2060	12-2060-08 (Plot T2)	687.5 SC	Leaf / head	-0	0.51	<0.01	<0.01
					7	0.99	0.012	<0.01
					14	0.53	0.014(1)	<0.01

(1) As noted in EFSA's 'Residues trials and MRL calculations' guidance document (published in 2015), when a residue level is higher at a later PHI (14 days) than the recommended one (7 days), this highest value is selected for MRL calculation. These higher values are also used within the risk assessment.

Table 6.3.3- 20 1 x application (100 g a.s /ha, BBCH 13-49, PHI: 7 days)

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
Inter-zonal (indoor)	RA- 12-2060	12-2060-01 (plot T3)	687.5 SC	Leaf / head	7 14	0.72 0.14	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-02 (Plot T3)	687.5 SC	Leaf / head	7 14	0.21 0.043	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-03 (Plot T3)	687.5 SC	Leaf / head	7 14	0.48 0.33	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-04 (Plot T3)	687.5 SC	Leaf / head	7 14	0.10 0.020	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-05 (Plot T3)	687.5 SC	Leaf / head	7 14	0.13 0.036	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-06 (Plot T3)	687.5 SC	Leaf / head	7 14	0.52 0.16	0.012 0.014(1)	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-07 (Plot T3)	687.5 SC	Leaf / head	7 14	0.62 1.5(1)	<0.01 0.024(1)	<0.01 <0.01
Inter-zonal (indoor)	RA- 12-2060	12-2060-08 (Plot T3)	687.5 SC	Leaf / head	7 14	0.62 0.33	<0.01 <0.01	<0.01 <0.01

(1) As noted in EFSA's 'Residues trials and MRL calculations' guidance document (published in 2015), when a residue level is higher at a later PHI (14 days) than the recommended one (7 days), this highest value is selected for MRL calculation. These higher values are also used within the risk assessment.

III. CONCLUSION

Eight independent (decline) residue trials have been conducted in Northern Europe (Belgium, North France, Germany and The Netherlands) and Southern Europe (Greece, Italy and Portugal). These trials were conducted within glasshouses. Different treatment regimens were applied to separate sub-plots (either one or two applications). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Two applications

Inter-zonal (greenhouse) trials
Fluopicolide: 0.19, 2 x 0.28, 0.63, 0.68, 0.87, 0.99, 1.6 mg/kg
Metabolite M-01: <0.01, 0.011, 2 x 0.012, 0.013, 0.014, 0.020, 0.028 mg/kg
Metabolite M-02: 7 x <0.01, 0.012 mg/kg

Single application

Inter-zonal (greenhouse) trials
Fluopicolide: 0.10, 0.13, 0.21, 0.48, 0.52, 0.62, 0.72, 1.5 mg/kg
Metabolite M-01: 6 x <0.01, 0.014, 0.024 mg/kg
Metabolite M-02: 8 x <0.01 mg/kg

The GAP used within the residue field trials closely conforms with the recommended GAP for lettuce. These residue trials are considered to be acceptable to support the intended use on lettuce.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/03
Report Author:	[redacted]
Report Year:	2015
Report Title:	Amendment no.1 to study report no: 14-2083 - Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in Belgium, Germany, the Netherlands, northern France, Spain, Italy and Portugal
Report No:	14-2083
Document No:	M-525304-02-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market; OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009); US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 8 residue decline trials were conducted on open / loose leaf varieties of lettuce in the Northern European (Belgium, North France and Germany) and the Southern European (Italy, Portugal and Spain) residue trials zone during 2012. Two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test Item:	687.5 SC (62.5 g/L of fluopicolide)
	Batch no.:	EM4L011180
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	March 2014
2.	Test commodity:	Lettuce
	Crop part:	Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 8 residue decline trials on open, loose leaf varieties of lettuce in the Northern European (Belgium, North France and Germany) and the Southern European (Italy, Portugal and Spain) residue trials zone during 2012. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.3- 21 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	T2	2	0.10 kg a.s. / ha	7 days	BBCH 49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

A second sub-plot (T1) was treated with 3 applications. However, as the representative GAPs sought for lettuce do not exceed 2 applications, the residues data for the T1 plots have not been summarised within this section of dossier. However, for clarity the trials involving 3 applications are presented within Appendix 2.

Table 6.3.3- 22 Trial details and regions

Trial No.	Country	Location	Crop variety
14-2083-01	Belgium	6210 Villers-Perwin	Sansula, Oakleaf variety Loose leaf variety
14-2083-02	Germany	67125 Dannstadt-Schauernheim	Cavernet, Lollo Rosso Loose leaf variety
14-2083-03	Netherlands	1681 ND Zwaagdijk	Loka, Lollo Rossa Loose leaf variety
14-2083-04	France	37130 Ligmeres de Touraine	Kiribati Loose leaf variety
14-2083-05	Spain	46230 Alginet	Paladio Loose leaf variety
14-2083-06	Italy	95100 Cda Pigno; Catania	Nauplus - Canasta Loose leaf variety
14-2083-07	Italy	70044 Polignano a mare	Sirmai Red oak leaf lettuce Loose leaf variety
14-2083-08	Portugal	2590-409 Sapataria Casal Cochim	Kilomas Loose leaf variety

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02, were analysed within the residue trials samples according to the following method:

Table 6.3.3- 23 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 24 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	70(1), 81, 99, 92, 104, 111, 100	94	15.1	0.01
	0.10	84, 92, 89, 86, 90, 81	87	4.7	
	5.0	86	-	-	
	10	86	-	-	
		Overall recovery (n=15)			

RSD = Relative standard deviation, LOQ = Practical limit of quantification Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide
(1): value corrected by the level found in the used control sample (0.0037 mg/kg). Uncorrected value: 107%

Table 6.3.3- 25 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	89, 89, 89, 91, 93, 95, 107	93	6.9	0.01
	0.10	89, 92, 93, 94, 95	93	2.5	
	5.0	85	-	-	
		Overall recovery (n=13)	**92**	**5.7**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 26 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	74, 77, 82, 83, 84, 85, 98	83	9.1	0.01
	0.10	95, 96, 98, 100, 103	98	3.3	
	5.0	96	-	-	
		Overall recovery (n=13)	**90**	**10.6**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 90 and 308 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 27 2 x applications (100 g a.s./ha, BBCH 13-49, Application interval: 7 days, PHI: 7 days) – supporting GAP

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	14-2083	14-2083-01 Plot T2	687.5 SC	Leaf / head	-0	0.42	0.010	<0.01
					0	1.7	0.012	<0.01
					7	<u>0.73</u>	<u>0.012</u>	<u><0.01</u>
					14	0.24	0.011	<0.01
N-EU	14-2083	14-2083-02 Plot T2	687.5 SC	Leaf / head	-0	0.16	<0.01	<0.01
					0	1.5	<0.01	<0.01
					7	<u>0.19</u>	<u><0.01</u>	<u><0.01</u>
					14	0.020	<0.01	<0.01
N-EU	14-2083	14-2083-03 Plot T2	687.5 SC	Leaf / head	-0	1.3	0.028	<0.01
					0	3.6	0.030(1)	<0.01
					7	<u>0.36</u>	<u>0.010</u>	<u><0.01</u>
					14	0.048	<0.01	<0.01

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	14-2083	14-2083-04 Plot T2	687.5 SC	Leaf / head	-0	0.83	<0.01	<0.01
					0	2.4	<0.01	<0.01
					7	0.17	<0.01	<0.01
					14	<0.01	<0.01	<0.01
S-EU	14-2083	14-2083-05 Plot T2	687.5 SC	Leaf / head	-0	0.72	<0.01	<0.01
					0	2.1	<0.01	<0.01
					7	0.49	<0.01	<0.01
					14	0.21	<0.01	<0.01
S-EU	14-2083	14-2083-06 Plot T2	687.5 SC	Leaf / head	-0	0.56	<0.01	<0.01
					0	1.7	<0.01	<0.01
					7	0.76	<0.01	<0.01
					14	0.28	<0.01	<0.01
S-EU	14-2083	14-2083-07 Plot T2	687.5 SC	Leaf / head	-0	1.0	<0.01	<0.01
					0	4.6	<0.01	<0.01
					7	1.9	0.010	<0.01
					14	1.1	0.014	<0.01
S-EU	14-2083	14-2083-08 Plot T2	687.5 SC	Leaf / head	-0	0.63	<0.01	<0.01
					0	2.0	<0.01	<0.01
					7	0.50	<0.01	<0.01
					14	0.042	<0.01	<0.01

(1) Mean of two replicate values (0.033 and 0.028 mg/kg)

III. CONCLUSION

Eight independent (decline) residue trials have been conducted in Northern Europe (Belgium, North France and Germany) and Southern Europe (Italy, Portugal and Spain). Different treatment regimens were applied to separate sub-plots (either one or two applications). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Northern European trials
Fluopicolide: 0.17, 0.49, 0.36, 0.73 mg/kg
Metabolite M-01:2 x <0.01, 0.01, 0.012 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Southern European trials
Fluopicolide: 0.30, 0.49, 0.76, 1.9 mg/kg
Metabolite M-01: 3 x <0.01, 0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable.

Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/04
Report Author:	[redacted]
Report Year:	2018
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in southern France and Italy
Report No:	16-2087
Document No:	M-612853-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509, published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 2 residue decline trials were conducted on open / loose leaf varieties of lettuce in the Southern European (Southern France and Italy) residue trials zone during 2016. Two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 687.5 SC (62.5 g/L of fluopicolide)

   Batch no.: EVS8002080

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: January 2019

2. Test commodity: Lettuce

   Crop part: Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 2 residue decline trials on open / loose leaf varieties of lettuce in the Southern European (Southern France and Italy) residue trials zone during 2016. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.3- 28 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	T2	2	0.10 kg a.s. / ha	7 days	BBCH 37-49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

A second sub-plot (T1) was treated 3 applications. However, as the representative GAPs sought for lettuce do not exceed 2 applications, the residues data for the T1 plots have not been summarised within this section of dossier. However, for clarity the trials involving 3 applications are presented within Appendix 2.

The residues trials were conducted in the following locations on different varieties of open / loose leaf lettuces:

Table 6.3.3- 29 Trial details and regions

Trial No.	Country	Location	Crop variety
16-2087-01	France (South)	31200 Toulouse	Kiribati RZ (Oak leaf variety)
16-2087-02	Italy	95100 C.da Pigno, Catania	Ribai (Oak leaf variety)

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 30 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 31 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	91, 99, 106	99	7.6	0.01
	0.10	95, 97, 99, 110, 112	103	7.6	
	8.0	109, 111	110		
		Overall recovery (n=10)	**103**	**7.4**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 32 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	98, 99, 113	103	8.1	0.01
	0.10	98, 98, 101, 113, 117	105	8.5	
		Overall recovery (n=8)	**105**	**7.8**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 33 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	90	-	-	0.01
	0.10	93, 95	94	-	
		Overall recovery (n=3)	**93**	**2.7**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 105 and 149 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 34 Residue field trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	16-2087	16-2087-01 Plot T2	SC 687.5	Leaf / head	-0	1.5	0.014	<0.01
					0	3.4	0.015	<0.01
					7	<u>0.76</u>	<u>0.021</u>	<u><0.01</u>
					14	0.17	0.017	<0.01
S-EU	16-2087	16-2087-02 Plot T2	SC 687.5	Leaf / head	-0	1.3	0.012	<0.01
					0	4.0	0.015	<0.01
					7	<u>1.7</u>	<u>0.028</u>	<u><0.01</u>
					14	0.21	0.011	<0.01

III. CONCLUSION

Two independent (decline) residue trials have been conducted in Southern Europe (Southern France and Italy). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Southern European trials
Fluopicolide: 0.76, 1.7 mg/kg
Metabolite M-01: 0.021, 0.028 mg/kg
Metabolite M-02: 2 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant: Study acceptable Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/05
Report Author:	[redacted]
Report Year:	2018
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in southern France, Italy, Portugal and Greece
Report No:	16-2179
Document No:	M-612854-02-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 5 residue decline trials were conducted on open / loose leaf varieties of lettuce in the Southern European (Greece, South France, Italy and Portugal) residue trials zone during 2016. One application of 687.5 SC (a product containing 62.5 g/L of fluopicolide) was made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test Item:	687.5 SC (62.5 g/L of fluopicolide)
	Batch no.:	EV58002080
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	January 2019
2.	Test commodity:	Lettuce
	Crop part:	Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 5 residue decline trials on open / loose leaf varieties of lettuce in the Southern European (Greece, South France, Italy and Portugal) residue trials zone during 2016. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.3- 35 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC*	-	1	0.10 kg a.s. / ha		BBCH 49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residues trials were conducted in the following locations on different varieties of open / loose leaf lettuces:

Table 6.3.3- 36 Trials details and regions

Trial No.	Country	Location	Crop variety
16-2179-01	France (South)	13103 St Etienne du Gres	Kiribati (Oak leaf variety)
16-2179-02	Italy	85024 Lavello	Freestar (Oak leaf variety)
16-2179-03	Italy	93012 C.da Mignehi; Gela	Ribai (Oak leaf variety)
16-2179-04	Portugal	2590-409- Sapataria Sobral Monte Agraço	Radia (Oak leaf variety)
16-2179-05	Greece	GR - 601 00 Aronas, Katerini - Pieria	Exotine (EX DIP 9410) (Oak leaf variety)

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 37 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 38 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	81, 87, 88, 91, 94, 97, 102, 102, 103, 104	95	8.4	0.01
	0.10	79, 90, 94, 96, 98, 99, 101	94	8.0	
	10	81	-	-	
		Overall recovery (n=18)	**94**	**8.5**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 39 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	74, 82, 82, 87, 87, 89, 91, 92, 93, 93	87	7.0	0.01
	0.10	80, 88, 93, 93, 94, 95, 97	91	6.3	
	10	104			
		Overall recovery (n=18)	**90**	**7.8**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 40 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	71, 75, 77, 85, 86, 90, 91, 95, 99, 109	88	13.2	0.01
	0.10	81, 81, 81, 83, 86, 88, 90	84	4.4	
	10	94			
		Overall recovery (n=3)	**87**	**10.5**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 136 and 324 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 41 Residue field trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	16-2179	16-2179-01	SC 687.5	Leaf / head	0 7 14	2.2 <u>0.73</u> 0.15	<0.01 <u>0.014</u> <0.01	<0.01 <u><0.01</u> <0.01
S-EU	16-2179	16-2179-02	SC 687.5	Leaf / head	0 7 14	0.94 <u>0.099</u> 0.058	<0.01 <u><0.01</u> <0.01	<0.01 <u><0.01</u> <0.01
S-EU	16-2179	16-2179-03	SC 687.5	Leaf / head	0 7 14	2.5 <u>1.2</u> 0.50	<0.01 <u>0.011</u> 0.011	<0.01 <u><0.01</u> <0.01
S-EU	16-2179	16-2179-04	SC 687.5	Leaf / head	0 7 14	1.4 <u>0.092</u> 0.047	<0.01 <u><0.01</u> <0.01	0.016 <u>0.016</u> <0.01
S-EU	16-2179	16-2179-05	SC 687.5	Leaf / head	0 7 14	2.0 <u>1.2</u> 0.97	<0.01 <0.01 <u>0.011</u>	<0.01 <u><0.01</u> <0.01

III. CONCLUSION

Five independent (decline) residue trials have been conducted in Southern Europe (Greece, South France, Italy and Portugal). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Southern European trials
Fluopicolide: 0.092, 0.099, 0.73, 2 x 1.2 mg/kg
Metabolite M-01: 2 x <0.01, 2 x 0.011, 0.014 mg/kg
Metabolite M-02: 5 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/06
Report Author:	[redacted]
Report Year:	2018
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in northern France, Germany, the Netherlands and Belgium
Report No:	16-2095
Document No:	M-613148-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 4 residue decline trials were conducted on open / loose leaf varieties of lettuce in the Northern European (Belgium, Northern France, Germany and the Netherlands) residue trials zone during 2016. One application of 687.5 SC (a product containing 62.5 g/L of fluopicolide) was made at a target rate of 0.10 kg a.s. /ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 1209. Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test Item:	687.5 SC (62.5 g/L of fluopicolide)
	Batch no.:	EV58002080
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	January 2019
2.	Test commodity:	Lettuce
	Crop part:	Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 residue decline trials on open / loose leaf varieties of lettuce in the Northern European (Belgium, Northern France, Germany and the Netherlands) residue trials zone during 2016. The trials were generated in the open field.

Different treatment regimens were applied to separate sub-plots. Applications were made according to the following trials GAP:

Table 6.3.3- 42 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	-	1	0.10 kg a.s./ ha	-	BBCH 49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residues trials were conducted in the following locations on different varieties of open / loose leaf lettuces:

Table 6.3.3- 43 Trials details and regions

Trial No.	Country	Location	Crop variety
16-2095-01	France (North)	37130 Lignières de Touraine	Kiribati (Oak leaf variety)
16-2095-03	Germany	67125 Dannstadt-Schauernheim	Kisheri (Oak leaf variety)
16-2095-04	Netherlands	1756 CE Anna Paulowna	Mathix (red) (Oak leaf variety)
16-2095-5	Belgium	06221 Saint-Amand	Sansula (Oak leaf variety)

The product was applied onto lettuces using spray applicators. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 44 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02 in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 45 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	90, 101, 105, 107, 112	103	8.0	0.01
	0.10	100, 106, 112, 113, 114	109	5.4	
	1.0	101, 102	102		
	10	98, 98	98	-	
		Overall recovery (n=14)	**104**	**6.7**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 46 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	93, 95, 107, 112, 113	104	9.1	0.01
	0.10	99, 101, 110, 115, 116	108	7.3	
	1.0	105, 109	107	-	
		Overall recovery (n=12)	**106**	**7.3**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 47 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	94, 94, 96	95	1.2	0.01
	0.10	90, 97, 98	95	4.6	
	1.0	89, 94	92	-	
		Overall recovery (n=8)	**94**	**3.4**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 79 and 169 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.3- 48 Residues field trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	16-2095	16-2095-01	SC 687.5	Leaf / head	0 7 14	6.2 0.87 0.059	<0.01 0.012 <0.01	<0.01 <0.01 <0.01
N-EU	16-2095	16-2095-03	SC 687.5	Leaf / head	0 7 14	2.5 0.17 0.044	<0.01 0.015 0.013	<0.01 <0.01 <0.01
N-EU	16-2095	16-2095-04	SC 687.5	Leaf / head	0 7 14	4.8 0.96 0.25	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01
N-EU	16-2095	16-2095-05	SC 687.5	Leaf / head	0 7 14	3.1 0.37 0.14	<0.01 0.014 0.015 (1)	<0.01 <0.01 <0.01

(1) As noted in EFSA's 'Residues trials and MRL calculations' guidance document (published in 2015), when a residue level is higher at a later PHI (14 days) than the recommended one (7 days), this highest value is selected for MRL calculation. These higher values are also used within the risk assessment.

III. CONCLUSION

Four independent (decline) residue trials have been conducted in Northern Europe (Belgium, Northern France, Germany and the Netherlands). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Northern European trials
Fluopicolide: 0.17, 0.37, 0.87, 0.96 mg/kg
Metabolite M-01: <0.01, 0.012, 2 x 0.015 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:
Study acceptable
Positive residues were found for fluopicolide and BAM (M-01) in lettuces. No residues above the LOQ (0.01 mg/kg) were found for M-02.

Data Point:	KCA 6.3.3/07
Report Author:	[redacted]
Report Year:	2011
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spraying of Fluopicolide & Propamocarb-Hydrochloride SC 687.5 in the field in France (north) and Germany
Report No:	09-2217
Document No:	M-404524-01-1
Guideline(s) followed in study:	91/414/EEC 7029/VI/95
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of 2 residue decline trials were conducted on open / loose leaf varieties of lettuce in the Northern European (Northern France and Germany) residue trials zone during 2009. Two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209. Positive residues were found for fluopicolide in lettuces. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01) and M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1.	Test Item:	687.5 SC (62.5 g/L of fluopicolide)
	Batch no.:	EV61000221
	Active Ingredient / Purity:	Not stated in the report
	Storage:	Not stated in the report
	Expiry date:	March 2012
2.	Test commodity:	Lettuce
	Crop part:	Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 2 residue decline trials on open / loose leaf varieties of lettuce in the Northern European (Northern France and Germany) residue trials zone during 2009. The trials were generated in the open field.

Different treatment regimens were applied to separate sub-plots. Applications were made according to the following trials GAP:

Table 6.3.3- 49 Application details

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC*	T2	2	0.10 kg a.s./ ha	7 days	BBCH 37-49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residues trials were conducted in the following locations on different varieties of open / loose leaf lettuces:

Table 6.3.3- 50 Trials details and regions

Trial No.	Country	Location	Crop variety
09-2217-01	France (North)	80320 Puzeaux Picardie	Madras (Loose leaf)
09-2217-02	Germany	40764 Langenfeld-Reusrath Nordrhein-Westfalen	Argentinas (Loose leaf)

The product was applied onto lettuces using knapsack sprayers / spraying booms.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 51 Summary of the analytical method

Method	01209
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 52 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	97, 98	98	0.7	0.01
	0.10	94	-	-	
	8[1]	105	-	-	
		Overall recovery (n=4)	**99**	**4.4**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide
(1) For fluopicolide the highest field sample residue was 10 mg/kg. This sample was diluted together with the recovery at 8 mg/kg and re-injected in a later LC-MS/MS sequence. The method performance was demonstrated successfully at 8 mg/kg and therefore no additional recovery at 10 mg/kg was performed.

Table 6.3.3- 53 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	98	-	-	0.01
	0.10	98	-	-	
		Overall recovery (n=2)	**98**	**-**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 54 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	70	-	-	0.01
	0.10	70	-	-	
		Overall recovery (n=2)	**70**	-	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 435 and 470 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 55 Residues field trials

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	09-2217	09-2217-01	687.5 SC	Leaf / head	-0	0.97	0.01	<0.01
					0	10	0.02	<0.01
					3	0.07	0.05	<0.01
					7	0.03	<0.01	<0.01
					14	<0.01	<0.01	<0.01
					21	<0.01	<0.01	<0.01
N-EU	09-2217	09-2217-02	687.5 SC	Leaf / head	-0	0.52	<0.01	<0.01
					0	2.3	<0.01	<0.01
					3	1.2	<0.01	<0.01
					7	0.52	<0.01	<0.01
					14	0.08	<0.01	<0.01
					21	<0.01	<0.01	<0.01

III. CONCLUSION

Two independent (decline) residue trials have been conducted in Northern Europe (Belgium, North France and Germany). All trials used open leaf / loose leaf varieties of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Northern European trials
Fluopicolide: 0.03, 0.52 mg/kg
Metabolite M-01: 2 x <0.01 mg/kg
Metabolite M-02: 2 x <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

Positive residues were found for fluopicolide in lettuces. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01) and M-02.

Data Point:	KCA 6.3.3/08
Report Author:	[redacted]
Report Year:	2018
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on lettuce after spraying of fluopicolide & propamocarb-hydrochloride SC 687.5 in the United Kingdom
Report No:	16-2210
Document No:	M-612891-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509, published in September 2009) US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A single residue open-field trial was conducted in northern Europe (United Kingdom) on lettuces, during 2016. One application of 687.5 SC (a product containing 62.5 g/L of fluopicolide) was made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 01209/M001. Positive residues were found for fluopicolide in lettuces. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01) and M-02.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 687.5 SC (62.5 g/L of fluopicolide)
   Batch no.: EV58002080
   Active Ingredient / Purity: Not stated in the report
   Storage: Not stated in the report
   Expiry date: January 2019

2. Test commodity: Lettuce
   Crop part: Lettuce (head / leaves)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 1 residue decline trial on an open / loose leaf variety of lettuce in the Northern European (The United Kingdom) residue trials zone during 2016. The trials were generated in the open field.

Different treatment regimens were applied to separate sub-plots. Applications were made according to the following trials GAP:

Table 6.3.3- 56 Application detail

Applied product	Plot	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	-	1	0.10 kg a.s. / ha	-	BBCH 37-49	7 days

* Product contains fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residues trials were conducted in the following locations on different varieties of open / loose leaf lettuces:

Table 6.3.3- 57 Trials details and regions

Trial No.	Country	Location	Crop variety
16-2210-01	United Kingdom	IP31 2NG Pakenham, Bury St Edmunds	Kiribati (Oak Leaf Variety)

The product was applied onto lettuces using a knapsack sprayer / spraying boom.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.3- 58 Summary of the analytical method

Method	01209/M001
Extraction	Acetone/water, acidified with formic acid (75/25/1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in lettuce leaves)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.3- 59 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	101	-	-	0.01
	0.10	104	-	-	
	2.0	87	-	-	
		Overall recovery (n=3)	**97**	**9.3**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.3.3- 60 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	88	-	-	0.01
	0.10	93	-	-	
	2.0	93	-	-	
		Overall recovery (n=3)	**91**	**3.2**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Table 6.3.3- 61 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Lettuce, leaf / head	0.01	85	-	-	0.01
	0.10	86	-	-	
	2.0	88	-	-	
		Overall recovery (n=3)	**86**	**1.8**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification

Fortified with AE C657188, determined as AE C657188 and calculated as AE C657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 364 and 383 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.2- 62 Residue field trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	16-2210	16-2210-01	SC 687.5	Leaf / head	0	1.8	<0.01	<0.01
					6	1.0	<0.01	<0.01
					13	0.38	<0.01	<0.01

III. CONCLUSION

One independent (decline) residue trials has been conducted in Northern Europe (The United Kingdom). The trial used an open leaf / loose leaf variety of lettuce. Positive Residues of fluopicolide were observed within the lettuce leaves / heads:

Northern European trials
Fluopicolide: 0.1 mg/kg
Metabolite M-01: <0.01 mg/kg
Metabolite M-02: <0.01 mg/kg

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

Positive residues were found for fluopicolide in lettuces. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01) and M-02.

CA 6.3.4 Cucumber

No residues trials data were submitted to support uses on cucumber in the original DAR evaluation (RMS = UK, 2005).

The critical Good Agricultural Practice (cGAP) supported at the European level in the Annex I renewal (AIR) process consists of 3 foliar spray applications at 100 g a.s./ha fluopicolide in northern Europe and southern Europe, with a minimum spray interval of 7 days and a PHI of 1 day.

Table 6.3.4- 1 Summary of the critical GAP for the proposed uses of FLC+PCH SC 687.5

Crop	Region*	F, G or I**	Maximum application number	Maximum application interval (days)	Maximum rate (g a.s./ha)	Minimum PHI (days)
Cucumber	N-EU and S-EU	G	3	7	100	1

* EU-N northern Europe EU-S southern Europe ** F Field, G Greenhouse, I Indoor

Trials available to support the European GAP relevant for the active substance renewal are summarised in Table 6.3.4-2 and Table 6.3.4-3.

Table 6.3.4- 2 Residue trials conducted per geographical region and formulation

Region	Crop	Formulation	Number of trials			Report No.	Document No	Dossier Ref.
			Vegetation period		Total			
			2005	2007				
Greenhouse (N-EU and S-EU)	Cucumber	687.5 SC	7		7	RA-2162/05	M-281542-01-1	CA 6.3.3/01
Greenhouse (S-EU)	Cucumber	687.5 SC		1	1	RA-2632/07	M-307724-01-2	CA 6.3.3/02

N-EU – Northern Europe
S-EU – Southern Europe
687.5 SC: Suspension concentrate formulation containing fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

Table 6.3.4- 3 Overall summary of residue data on cucumber covering the critical GAP for active substance renewal

Application rate	Region	Formulation	Crop	Sample material	n	Residue level (mg/kg)		
						Min.	Max.	STMR
3 applications at 125 g/ha	N-EU S-EU	687.5 SC	Cucumber	Fruit	8	0.02 (FLC) <0.01 (M-01) <0.01 (M-02)	0.09 (FLC) <0.01 (M-01) <0.01 (M-02)	0.04 (FLC) <0.01 (M-01) <0.01 (M-02)

The following studies were not evaluated during the last EU review and have now been submitted for review.

New data for AIR.

Data Point:	KCA 6.3.4/01
Report Author:	[redacted]
Report Year:	2006
Report Title:	Determination of the residues of AE C638206 and propamocarb hydrochloride in/on cucumber after spraying of AE B066752 04 SC61 A1 (687.5 SC) in the field in the greenhouse in Italy, Spain, Greece, Germany and Portugal
Report No:	RA-2162/05
Document No:	M-281542-01-1
Guideline(s) followed in study:	Directive 91/414/EEC of July 15, 1991
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of eight residue open-field trials were conducted in northern Europe (Germany) and southern Europe (Greece, Italy, Portugal and Spain) on cucumbers, during 2005. Three applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.125 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M004. The results show that the residue levels in treated cucumbers are not expected to exceed 0.01 mg/kg for M-01 and M-02 following a pre-harvest interval of 1 day. Positive residues of fluopicolide were observed within the treated cucumbers.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 687.5 SC (62.5 g/L of fluopicolide)
   Batch no.: 08490/0020(0001)
   Active Ingredient / Purity: 99.6%
   Storage: Not stated in the report
   Expiry date: August 2006
2. Test commodity: Cucumber
   Crop part: Cucumber (fruit)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 8 magnitude of the residues trials on cucumber in the Northern European (Germany) and the Southern European (Greece, Italy, Portugal and Spain) residue trials zones during 2005. The trials were generated indoors (in greenhouses).

Applications were made according to the following trials GAP:

Table 6.3.4- 4 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	3	Approximately 0.125 kg a.s. / ha	7 days	BBCH 72-89	1 day

* fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residues trials were conducted in the following locations on different varieties of cucumber:

Table 6.3.4- 5 Trials details and regions

Trial No.	Country	Location	Crop variety
R 2005 0834/4	Italy	I-97017 Santa Croce Camerina, Sicilia	Solverde
R 2005 0861/1	Italy	I-70056 Molfetta, Bari, Puglia	Locale di Polignano
R 2005 0863/8	Spain	E-04738 Puebla de Vicar, Andalucia	Argos
R 2005 0864/6	Spain	E-11540 Sanlucar de Barrameda, Monte Algarda, Andalucia	Alanis F1 Hibrido
R 2005 0865/4	Greece	GR-57006 Vasilika, Macedonia	Z14
R 2005 0866/2	Germany	D-42799 Leichlingen, Nordrhein-Westfalen	Aramon
R 2005 0867/0	Germany	D-42799 Leichlingen, Nordrhein-Westfalen	Indira
R 2005 0868/9	Portugal	P-2560 Torres Vedras, Ribatejo e Oeste	Caman

The product was sprayed onto cucumbers using spraying booms or knapsack sprayers. Each type of sprayer was equipped with flat fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.4- 6 Summary of the analytical method

Method	00782/M004
Extraction	Acetone/water acidified with formic acid (75:25:1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in cucumber)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.4- 7 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	88*, 103*, 85*, 79	89	11.5	0.01
	0.10	101*, 103*, 100*, 97, 103	101	2.5	
	0.20	101	101		
		Overall recovery (n=10)	**96**	**9.1**	

RSD = Relative Standard Deviation,
LOQ = Practical Limit of Quantification
Final determination as: AE C638206, Residues calculated as: AE C638206
* - Recoveries performed before the analyses of the trial samples.

Table 6.3.4- 8 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	94*, 88*, 83*, 81	86	5.3	0.01
	0.10	88*, 87*, 84*, 94, 97	90	5.9	
	0.20	79	79	-	
		Overall recovery (n=10)	**87**	**6.5**	

RSD = Relative Standard Deviation,
LOQ = Practical Limit of Quantification
Final determination as: AE C638206-AE C657711, Residues calculated as: AE C653711
* - Recoveries performed before the analyses of the trial samples.

Table 6.3.4- 9 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	101*, 105*, 109*, 85	100	10.5	0.01
	0.10	83*, 88*, 84*, 90, 98	89	6.8	
	0.20	100	100	-	
		Overall recovery (n=10)	**94**	**6.5**	

RSD = Relative Standard Deviation,
LOQ = Practical Limit of Quantification
Final determination as: AE C638206-AE C657188, Residues calculated as: AE C638206-AE C657188
* - Recoveries performed before the analyses of the trial samples.

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 362 and 554 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.4- 10 Residue field trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
Inter-zonal (indoor)	RA-2162/05	R 2005 0834/4 (0834 -05)	687.5 SC	Fruit	0	0.04	<0.01	<0.01
					1	<u>0.04</u>	<u><0.01</u>	<u><0.01</u>
Inter-zonal (indoor)	RA-2162/05	R 2005 0861/1 (0861 -05)	687.5 SC	Fruit	0	0.03	<0.01	<0.01
					1	<u>0.02</u>	<u><0.01</u>	<u><0.01</u>
Inter-zonal (indoor)	RA-2162/05	R 2005 0863/8 (0863 -05)	687.5 SC	Fruit	0	0.06	<0.01	<0.01
					1	<u>0.04</u>	<u><0.01</u>	<u><0.01</u>
Inter-zonal (indoor)	RA-2162/05	R 2005 0864/6 (0864 -05)	687.5 SC	Fruit	0	0.04	<0.01	<0.01
					1	<u>0.03</u>	<u><0.01</u>	<u><0.01</u>
Inter-zonal (indoor)	RA-2162/05	R 2005 0865/4 (0865 -05)	687.5 SC	Fruit	0	0.12	<0.01	<0.01
					1	<u>0.09</u>	<u><0.01</u>	<u><0.01</u>
Inter-zonal (indoor)	RA-2162/05	R 2005 0866/2 (0866 -05)	687.5 SC	Fruit	0	0.05	<0.01	<0.01
					1	<u>0.03</u>	<u><0.01</u>	<u><0.01</u>

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
Inter-zonal (indoor)	RA-2162/05	R 2005 0867/0 (0867 -05)	687.5 SC	Fruit	0 1	0.03 0.02	<0.01 <0.01	<0.01 <0.01
Inter-zonal (indoor)	RA-2162/05	R 2005 0868/9 (0868 -05)	687.5 SC	Fruit	0 1	0.09 0.08	<0.01 <0.01	<0.01 <0.01

Trials R 2005 0866/2 (0866 -05) and R 2005 0867/0 (0867 -05) were both conducted at the same location (Germany, D-42799 Leichlingen, Nordrhein-Westfalen) and at similar timings during 2005. While different varieties were used, the EFSA guidance document on 'Residues trials and MRL calculations' does not considered this a sufficient difference to conclude that these should be considered as separate and distinct trials (based on the information on page 3 of the guidance document). These trials are considered to be replicates. The replicate with the highest residue level (R 2005 0866/2) has therefore been selected.

III. CONCLUSION

Seven independent (magnitude) residue trials have been conducted in the Northern and southern European residue trials zone (Germany, Greece, Italy, Portugal and Spain) on greenhouse grown cucumbers. An eighth trial was conducted, but this was concluded to be a replicate of the other trials conducted in Germany, so the residues results were not used in further residues calculation or the risk assessment. For the other seven independent trials, positive residues in the cucumber trials were for fluopicolide within the sampled fruit:

Fluopicolide: 0.02, 2 x 0.03, 2 x 0.04, 0.08, 0.09 mg/kg
Metabolite M-01: 7 x <0.01 mg/kg
Metabolite M-02: 7 x <0.01 mg/kg

While it is appreciated that the application rate for fluopicolide (125 g a.s. /ha) used in the trials is exaggerated when compared to the recommended critical GAP rate, the application rate is within the permitted ±25% limits of the recommended critical GAP for cucumbers (93.75 – 156.25 g a.s. /ha). It is therefore considered that these trials are appropriate to support the representative use for cucumbers.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:
Study acceptable.
Positive residues were found for fluopicolide in cucumbers. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01) and M-02.

Data Point:	KCA 6.3.4/02
Report Author:	[redacted]
Report Year:	2008
Report Title:	Determination of the residues of AE C638206 and Propamocarb hydrochloride in/on cucumber after spraying of AE B066752 04 SC61 A1 (687.5 SC) in the greenhouse in Italy
Report No:	RA-2632/07
Document No:	M-307724-01-2
Guideline(s) followed in study:	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A single residue open-field trials were conducted in southern Europe (Italy) on cucumbers, during 2007. One or two applications of 687.5 SC (a product containing 62.5 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M004. The results show that the residue levels in treated cucumbers are not expected to exceed 0.01 mg/kg for M-01 following a pre-harvest interval of 1 day. Positive residues of fluopicolide and M-02 were observed within the treated cucumbers.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 687.5 SC (62.5 g/L of fluopicolide)
   Batch no.: EV610000107
   Active Ingredient / Purity: Not stated in the report
   Storage: Not stated in the report
   Expiry date: January 2009

2. Test commodity: Cucumber
   Crop part: Cucumber (fruit)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted a single magnitude of the residues trial on cucumbers in the Southern European residue trials zone (Italy) during 2007. The trial was generated indoors (in a greenhouse)

Applications were made according to the following trials GAP:

Table 6.3.4- 11 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
687.5 SC *	3	Approximately 0.125 kg a.s./ha	7 days	BBCH 72-89	1 day

* fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)

The residue trial was conducted in the following location on the specified variety of cucumber:

Table 6.3.4- 12 Trials details and regions

Trial No.	Country	Location	Crop variety
R 2007 0333/3	Italy	I-70056 Molfetta, BA, Puglia)	Sarig

The product was sprayed onto cucumbers using a knapsack sprayer. Each type of sprayer was equipped with flat-fan nozzles which simulate the intended foliar application mode.

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method.

Table 6.3.3- 13 Summary of the analytical method

Method	00782/M004
Extraction	Acetone/water acidified with formic acid (75:25:1, v/v/v), with centrifugation.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in cucumber)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.4- 14 Procedural recoveries for Fluopicolide (AE C638206)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	94, 105	100	-	0.01
	0.10	98	98		
		Overall recovery (n=3)	**99**	**5.6**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
Final determination as: AE C638206, Residues calculated as: AE C638206

Table 6.3.4- 15 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	80, 99	90	-	0.01
	0.10	88	88	-	
		Overall recovery (n=3)	**89**	**10.7**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
Final determination as: AEC638206-AEC653711, Residues calculated as: AEC653711

Table 6.3.4- 16 Procedural recoveries for M-02 (AE C657188)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber fruit	0.01	86, 103	95	-	0.01
	0.10	103	103	-	
		Overall recovery (n=3)	**97**	**10.1**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
Final determination as: AEC638206-AEC657188, Residues calculated as: AEC657188

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 301 to 302 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and its metabolites (M-01 and M-02) when stored in high water matrices (at -18°C or below) for up to 30 months. These available data are sufficient to support the storage period between sampling and extraction.

Regarding the interval between extraction and analysis, the samples used for the procedural recovery determination were prepared at the same time as the field samples and they were analysed as part of the same analytical phase. Based on the acceptable procedural recoveries obtained, it can be concluded that the residues of fluopicolide and its metabolites (M-01 and M-02) were stable within the sample extract solutions.

II. RESULTS AND DISCUSSION

The residues field trial provided within the study report is summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (687.5 SC) also contained propamocarb hydrochloride, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.4- 17 Residue trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
Inter-zonal (indoor)	RA-2632/07	R 2007 0333/3 (0333 -07)	687.5 SC	Fruit	0 1	0.03 <u>0.02</u>	<0.01 <0.01	0.01 <u><0.01</u>

III. CONCLUSION

A single independent (magnitude) residue trial has been conducted in the Southern European residue trials zone (Italy) on greenhouse grown cucumbers. A positive residue value in the cucumber trial was detected for fluopicolide within the sampled fruit.

Fluopicolide: 0.02 mg/kg
Metabolite M-01: <0.01 mg/kg
Metabolite M-02: <0.01 mg/kg

While it is appreciated that the application rate for fluopicolide (125 g a.s. /ha) used in the trial is exaggerated when compared to the recommended critical GAP rate, the application rate is within the permitted ±25% limits of the recommended critical GAP for cucumbers (93.75 – 156.25 g a.s. /ha). It is therefore considered that these trials are appropriate to support the representative use for cucumbers.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

<u>Assessment and conclusion by applicant:</u>

Study acceptable

Positive residues were found for fluopicolide and M-02 in cucumbers. No residues above the LOQ (0.01 mg/kg) were found for BAM (M-01).

CA 6.3.5 Oilseed rape

No residues trials data were submitted to support uses on cucumber in the original DAR evaluation (RMS = UK, 2005).

The critical Good Agricultural Practice (cGAP) supported at the European level in the Annex I renewal (AIR) process consists of 3 foliar spray applications at 100 g a.s./ha fluopicolide in northern Europe and southern Europe, with a minimum spray interval of 7 days and a PHI of 1 day.

Table 6.3.5- 1 Summary of the critical GAP for the proposed uses of FLC+PXA FS 350

Crop	Region*	F, G or I**	Maximum application number	Maximum application interval (days)	Maximum rate (g a.s./ha)	Minimum PHI (days)
Oilseed rape	N-EU and S-EU	F	1	-	12	Not applicable for seed treatments

* EU-N northern Europe EU-S southern Europe ** F Field; G Greenhouse; I Indoor

Trials available to support the European GAP relevant for the active substance renewal are summarised in Table 6.3.5-2 and Table 6.3.5-3.

Table 6.3.5- 2 Residue trials conducted per geographical region and formulation

Region	Crop	Formulation	Number of trials		Report No.	Document No	Dossier Ref.
			Vegetation period 2008- 2009	Total			
Seed treatment (N-EU)	Oilseed rape	FS 510	4	6	08-2217	M-390353-01-1	CA 6.3.4/01
Seed treatment (N-EU)	Oilseed rape	FS 510	2		09-2225	M-396237-02-1	CA 6.3.4/02
Seed treatment (S-EU)	Oilseed rape	FS 510	4	4	08-2218	M-390357-01-1	CA 6.3.4/03

N-EU – Northern Europe
S-EU – Southern Europe
FS 510: Flowable concentrate for seed treatment formulation containing clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)

Table 6.3.5- 3 Overall summary of residue data on cucumber covering the critical GAP for active substance renewal

Application rate	Region	Formulation	Crop	Sample material	n	Residue level (mg/kg)		
						Min.	Max.	STMR
1 application at 9 g/ha	N-EU S-EU	FS 510	Oilseed rape	Seed	6	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)	<0.01 (FLC) <0.01 (M-01) <0.01 (M-02)

The following studies were not evaluated during the last EU review and are submitted for review:

New data for AIR.

Data Point:	KCA 6.3.5/01
Report Author:	[redacted]
Report Year:	2010
Report Title:	Determination of the residues of fluoxastriobin, clothianidin and fluopicolide in/on winter rape after seed treatment, of clothianidin & fluopicolide & fluoxastrobin FS 510 in the field in France (North), Germany and the Netherlands
Report No:	08-2217
Document No:	M-390353-01-1
Guideline(s) followed in study:	91/414/EEC of July 15, 1991 7029/VI/95 rev. 5 (1997-07-22)
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue open-field trials were conducted in Northern Europe (Northern France, Germany and The Netherlands) on winter oilseed rape during 2009. FS 510 (a product containing 120 g/L of fluopicolide) was applied as a seed treatment to oilseed rape seed before sowing. The target application rate was 1.5 g a.s./kg seed (equivalent to a nominal application rate of 9 g a.s./ha).

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M005. The results show that the residue levels in treated oilseed rape seed are not expected to exceed 0.01 mg/kg at commercial harvest.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 510 FS (120 g/L of fluopicolide)
   Batch no.: 2008-005058
   Active Ingredient / Purity: Not stated in the report
   Storage: Not stated in the report
   Expiry date: July 2010

2. Test commodity: Winter oilseed rape
   Crop part: Oilseed rape (seed)

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on seed treated oilseed rape in the Northern European residue trials zone (Northern France, Germany and The Netherlands) during 2008 / 2009. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.5- 4 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
FS 510*	Not applicable to seed treatments	9 g a.s. / ha (nominal)	Not applicable to seed treatments	BBCH 00	PHI is an inappropriate measure for seed treatments. Seed treated crops were harvested at BBCH 89

* Product contains clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)

The residue trial was conducted in the following location on the specified variety of oilseed rape:

Table 6.3.5- 5 Trials details and regions

Trial No.	Country	Location	Crop variety
08-2217-01	Germany	D-51399 Burscheid	Exocett
08-2217-02	The Netherlands	NL-9687 Nieuw Beerta	Exocett
08-2217-03	France (North)	F-37310 Chambourg sur Indre	Exocett
08-2217-04	Germany	D-53913 Swisttal-Miel	Exocett

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.5- 6 Summary of the analytical methods

Method	00782/M005
Extraction	Water (10 mL) and acetone (30 mL) adjusted to pH < 2 with sulfuric acid (2 mol/L) using a high-speed blender.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

The apparent residues in the control sample were below the LOQ. The mean of the concurrent recoveries was within the acceptable range of 70 - 110 % and the RSD level were all below 20 %.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries, except for AE C657188, green material, fortification level 0.01 mg/kg.

Table 6.3.5- 7 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	88, 97, 97	94	5.5	0.01
	0.10	85, 88, 89	87	2.4	
		Overall recovery (n=6)	**91**	**5.6**	
Winter rape – rest of plant	0.01	76, 79, 82	79	3.8	0.01
	0.10	83, 86, 87	85	2.4	
		Overall recovery (n=6)	**82**	**5.1**	
Winter rape – seed	0.01	91, 93, 96	93	2.7	0.01
	0.10	88, 90, 91	90	1.7	
		Overall recovery (n=6)	**92**	**3.0**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2217.

Table 6.3.5- 8 Procedural recoveries for AE C657188

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	88*, 94*, 116*	99	14.8	0.01
	0.10	106, 107, 110,	108	1.9	
		Overall recovery (n=6)	**104**	**10.1**	
Winter rape – rest of plant	0.01	80, 84, 93	86	7.8	0.01
	0.10	90, 91, 91	91	0.6	
		Overall recovery (n=6)	**88**	**5.7**	
Winter rape seed	0.01	84, 90, 91	91	8.3	0.01
	0.10	84, 86, 94	88	6.0	
		Overall recovery (n=6)	**90**	**6.8**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2217.
* background subtraction was performed: control sample 08-2217-03-0016E: 0.00457 mg/kg.

Table 6.3.5- 9 Procedural recoveries for AE C653711

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	84, 99, 100	94	9.5	0.01
	0.10	89, 91, 91	90	1.3	
		Overall recovery (n=6)	**92**	**6.6**	
Winter rape – rest of plant	0.01	75, 77, 80	77	3.3	0.01
	0.10	87, 88, 89	88	1.1	
		Overall recovery (n=6)	**83**	**7.4**	
Winter rape – seed	0.01	91, 93, 100	95	5.0	0.01
	0.10	93, 94, 96	94	1.6	
		Overall recovery (n=6)	**95**	**3.3**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2217.

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 165 and 503 days.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2013).

While the test product (FS 510) also contained clothianidin and fluoxastrobin, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.5- 10 Residues trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	08-2217	08-2217-01	FS 510	Seed	N/A – seed treatment	<0.01	<0.01	<0.01
N-EU	08-2217	08-2217-02	FS 510	Seed	N/A – seed treatment	<0.01	<0.01	<0.01
N-EU	08-2217	08-2217-03	FS 510	Green material Seed Rest of plant	N/A – seed treatment	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01
N-EU	08-2217	08-2217-04	FS 510	Green material Seed Rest of plant	N/A – seed treatment	0.01 <0.01 <0.01	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Northern France, Germany and The Netherlands). Residues in the oilseed rape trials were all found to be below the LOQ (<0.01 mg/kg) within the sampled seed:

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

While it is noted that the rate applied to the seeds (9 a.s. / ha) is lower than the maximum recommended rate (12 g a.s. /ha), the applied rate is within ±25% of the cGAP (9 - 15 g a.s. /ha). On this basis, the trials are considered to be acceptable to support the cGAP for both MRL setting and risk assessment purposes.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

No residues above the LOQ (0.01 mg/kg) were found for fluopicolide, BAM (M-01) or M-02 in seed treated oilseed rape at commercial harvest.

Data Point:	KCA 6.3.5/02
Report Author:	[redacted]
Report Year:	2010
Report Title:	Determination of the residues of fluoxastrobin, clothianidin and fluopicolide in/on winter rape after seed treatment, general of Clothianidin & Fluopicolide & Fluoxastrobin FS 510 in the field in France (South) and Spain
Report No:	08-2218
Document No:	M-390357-01-1
Guideline(s) followed in study:	91/414/EEC of July 15, 1991, 7029/VI/95 rev. 5 (1997-07-22)
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue open-field trials were conducted in Southern Europe (Southern France and Spain) on winter oilseed rape, during 2009. FS 510 (a product containing 120 g/L of fluopicolide) was applied as a seed treatment to oilseed rape seed before sowing. The target application rate was 1.8 g a.s./kg seed (equivalent to a nominal application rate of 10.8 g a.s./ha).

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M005. The results show that the residue levels in treated oilseed rape seed are not expected to exceed 0.01 mg/kg at commercial harvest.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Item: 510 FS (120 g/L of fluopicolide)

   Batch no.: 2008-005058

   Active Ingredient / Purity: Not stated in the report

   Storage: Not stated in the report

   Expiry date: July 2010

2. Test commodity:

   Crop parts: Winter oilseed rape

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 4 magnitude of the residue trials on seed treated oilseed rape in the Southern European residue trials zone (Southern France and Spain) during 2008 / 2009. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.5- 11 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
FS 510*	Not applicable to seed treatments	9.6 – 10.8 g a.s. ha	Not applicable to seed treatments	BBCH 00	PHI is an inappropriate measure for seed treatments. Seed treated crops were harvested at BBCH 89

* Product contains clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)

The residue trial was conducted in the following location on the specified variety of oilseed rape:

Table 6.3.5- 12 Trials details and regions

Trial No.	Country	Location	Crop variety
08-2218-01	Spain	E-17185 Vilobi d'Onyar	Exocett
08-2218-02	France (South)	F-31620 Villmeuve les Bouloc	Exocett
08-2218-03	Spain	E-41310 Brenes Sevilla	Exocett
08-2218-04	France (South)	F-69480 Amberieux	Exocett

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.5- 13 Summary of the analytical method

Method	00782/M005
Extraction	Water (10 mL) and acetone (30 mL) adjusted to pH < 2 with sulfuric acid (2 mol/L) using a high-speed blender.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The average recoveries were within the acceptable range of 70 – 110 %.

Table 6.3.5- 14 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	92			
	0.10	96	-	-	0.01
		Overall recovery (n=2)	**94**	-	
Winter rape – rest of plant	0.01	92	-	-	
	0.10	85	-	-	0.01
		Overall recovery (n=2)	**89**	-	
Winter rape – seed	0.01	95	-	-	
	0.10	92	-	-	0.01
		Overall recovery (n=2)	**94**	-	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2218.

Table 6.3.5- 15 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	88	-	-	
	0.10	89	-	-	0.01
		Overall recovery (n=2)	**89**	-	
Winter rape – rest of plant	0.01	84	-	-	
	0.10	85	-	-	0.01
		Overall recovery (n=2)	**85**	-	
Winter rape – seed	0.01	81	-	-	
	0.10	78	-	-	0.01
		Overall recovery (n=2)	**80**	-	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2218.

Table 6.3.5- 16 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	94	-	-	0.01
	0.10	100	-	-	
		Overall recovery (n=2)	**97**		
Winter rape – rest of plant	0.01	91	-	-	0.01
	0.10	88	-	-	
		Overall recovery (n=2)	**90**		
Winter rape – seed	0.01	95	-	-	0.01
	0.10	100	-	-	
		Overall recovery (n=2)	**98**	**-**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2218.

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 203 and 497 days.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2013).

While the test product (FS 510) also contained clothianidin and fluoxastrobin, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.5- 17 Residue trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
S-EU	08-2218	08-2218-01	FS 510	Seed	N/A – seed treatment	<0.01	<0.01	<0.01
S-EU	08-2218	08-2218-02	FS 510	Seed	N/A – seed treatment	<0.01	<0.01	<0.01
S-EU	08-2218	08-2218-03	FS 510	Green material	N/A – seed treatment	<0.01	<0.01	<0.01
				Seed		<0.01	<0.01	<0.01
				Rest of plant		0.01	<0.01	<0.01
S-EU	08-2218	08-2218-04	FS 510	Green material	N/A – seed treatment	0.02	<0.01	<0.01
				Seed		<0.01	<0.01	<0.01
				Rest of plant		<0.01	<0.01	<0.01

III. CONCLUSION

Four independent (magnitude) residue trials have been conducted in the Southern European residue trials zone (Southern France and Spain). Residues in the oilseed rape trials were all found to be below the LOQ (<0.01 mg/kg) within the sampled seed.

Fluopicolide: 4 x <0.01 mg/kg
Metabolite M-01: 4 x <0.01 mg/kg
Metabolite M-02: 4 x <0.01 mg/kg

While it is noted that the rate applied to the seeds (9 a.s. / ha) is lower than the maximum recommended rate (12 g a.s. /ha), the applied rate is within ±25% of the cGAP (9 - 15 g a.s. /ha). On this basis, the trials are considered to be acceptable to support the cGAP for both MRL setting and risk assessment purposes.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Study acceptable

No residues above the LOQ (0.01 mg/kg) were found for fluopicolide, BAM (M-01) or M-02 in seed treated oilseed rape at commercial harvest.

Data Point:	KCA 6.3.5/03
Report Author:	[redacted]
Report Year:	2010
Report Title:	Determination of the residues of fluoxastrobin, clothianidin and fluopicolide in/on summer rape after seed treatment, general of Clothianidin & Fluopicolide & Fluoxastrobin FS 510 in the field in Germany and Poland
Report No:	09-2225
Document No:	M-396237-02-1
Guideline(s) followed in study:	91/414/EEC, 7029/VI/95
Deviations from current test guideline:	none
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of two residue open-field trials were conducted in Northern Europe (Germany and Poland) on winter oilseed rape, during 2009. FS 510 (a product containing 120 g/L of fluopicolide) was applied as a seed treatment to oilseed rape seed before sowing. The target application rate was 1.5 g a.s./kg seed (equivalent to a nominal application rate of 9 g a.s./ha).

Residue levels (fluopicolide, M-01 and M-02) within the treated tubers were quantified using analytical method 00782/M005. The results show that the residue levels in treated oilseed rape seed are not expected to exceed 0.01 mg/kg at commercial harvest.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test item: 510 FS (120 g/L of fluopicolide)
   Batch no.: 2008-005058
   Active Ingredient / Purity: Not stated in the report
   Storage: Not stated in the report
   Expiry date: July 2010
2. Test commodity:
   Crop part: Winter oilseed rape

B. STUDY DESIGN AND METHODS

1. Test Procedure

Bayer CropScience conducted 2 magnitude of the residue trials on seed treated oilseed rape in the Northern European residue trials zone (Germany and Poland) during 2009. The trials were generated in the open field.

Applications were made according to the following trials GAP:

Table 6.3.5- 18 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	PHI (days)
FS 510*	Not applicable to seed treatments	9 g a.s. / ha	Not applicable to seed treatments	BBCH 00	PHI is an inappropriate measure for seed treatments. Seed treated crops were harvested at BBCH 89

* Product contains clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)

The residue trial was conducted in the following location on the specified variety of oilseed rape:

Table 6.3.5- 19 Trials details and regions

Trial No.	Country	Location	Crop variety
09-2225-01	Germany	21739 Dollern Lower Saxony	Senator
09-2225-02	Poland	64-560 Ostrorog Wielkopolska	Senator

2. Description of Analytical Procedures

Residues of fluopicolide and its metabolites, M-01 and M-02 were, analysed within the residue trials samples according to the following method:

Table 6.3.5- 20 Summary of the analytical method

Method	00782/M005
Extraction	Water (10 mL) and acetone (30 mL) adjusted to pH < 2 with sulfuric acid (2 mol/L) using a high-speed blender.
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01 and M-02, in all of the tested matrices: seed, green material, rest of plant)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis (at least one recovery for ten study samples). Control samples from the study were fortified and used as the recovery samples. Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

The mean of the concurrent recoveries was for all matrices and for all fortification levels, within the acceptable range of 70 – 110% except in rape, summer seed for fluopicolide (LOQ: 67% and overall recovery: 68%). Nevertheless, all the analytical results are considered as valid since they are close to guideline requirements.

Table 6.3.5- 21 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	102, 102	102	-	0.01
	0.10	79	79	-	
		Overall recovery (n=3)	**94**	**14.1**	
Winter rape – seed	0.01	61, 73	67	-	0.01
	0.10	70	70	-	
		Overall recovery (n=3)	**68**	**9.2**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as fluopicolide equivalent.

Table 6.3.5- 22 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	78, 85	82	-	0.01
	0.10	83	83	-	
		Overall recovery (n=3)	**82**	**4.4**	
Winter rape – seed	0.01	87, 104	96	-	0.01
	0.10	77	77	-	
		Overall recovery (n=3)	**89**	**15.3**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
FL and LOQ calculated and expressed as AE C653711 equivalent.

Table 6.3.5- 23 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Winter rape – green material	0.01	90, 91	91	-	0.01
	0.10	76	76	-	
		Overall recovery (n=3)	**86**	**9.8**	
Winter rape – seed	0.01	78, 80	79	-	0.01
	0.10	82	82	-	
		Overall recovery (n=3)	**80**	**2.5**	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
These recoveries were performed during the conduct of the study 08-2218.

3. Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and its metabolites (M-01 and M-02) ranged between 322 and 475 days.

II. RESULTS AND DISCUSSION

The residues field trials provided within the study report are summarised within the following table. Trials which are considered to be appropriate to support the intended GAP have been underlined. The trials have been selected according to the advice provided within EFSA's 'Residues trials and MRL calculations' guidance document (September 2015).

While the test product (FS 510) also contained clothianidin and fluoxastrobin, only residues values for fluopicolide and its metabolites have been presented, as these are the only components which are relevant to the fluopicolide renewal. While neither the enforcement nor risk assessment definitions contain Metabolite M-02, the residue values for this component has been included within the table for completeness (as this component was analysed within the analytical phase of the study).

Full results set are presented in the form of Tier II summary tables in Appendix 2.

Table 6.3.4- 24 Residue trials results

EU Zone	Study No.	Trial No.	Formulation Code	Matrix	Sampling (DALA)	Residues (mg/kg)		
						FLC	M-01	M-02
N-EU	09-2225	09-2225-01	FS 510	Green material	N/A – seed treatment	<0.01	<0.01	<0.01
				Seed		<u><0.01</u>	<u><0.01</u>	<u><0.01</u>
N-EU	09-2225	09-2225-02	FS 510	Green material	N/A – seed treatment	<0.01	<0.01	<0.01
				Seed		<u><0.01</u>	<u><0.01</u>	<u><0.01</u>

III. CONCLUSION

Two independent (magnitude) residue trials have been conducted in the Northern European residue trials zone (Germany and Poland). Residues in the oilseed rape trials were all found to be below the LOQ (<0.01 mg/kg) within the sampled seed:

Fluopicolide: 2 x <0.01 mg/kg

Metabolite M-01: 2 x <0.01 mg/kg

Metabolite M-02: 2 x <0.01 mg/kg

While it is noted that the rate applied to the seeds (9 a.s. / ha) is lower than the maximum recommended rate (12 g a.s. /ha), the applied rate is within ±25% of the cGAP (9 - 15 g a.s. /ha). On this basis, the trials are considered to be acceptable to support the cGAP for both MRL setting and risk assessment purposes.

Residues trials were conducted at application rates and timings comparable to the representative GAP. The trials conform to the requirements outlined within OECD Test No. 509 (for the field trials phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

<u>Assessment and conclusion by applicant:</u>

Study acceptable

No residues above the LOQ (0.01 mg/kg) were found for fluopicolide, BAM (M-01) or M-02 in seed treated oilseed rape at commercial harvest.

CA 6.4 Feeding studies

Fluopicolide is sought for use on potatoes and oilseed rape with parts of these crops being fed to livestock as culled potatoes, the processed by-products of potatoes and rape seed meal (refer to CA 6.3.1).

Fluopicolide and M-01 are observed to persist within soil (refer to CA 6.6) and can be observed within succeeding crop fractions. It is therefore necessary to consider the combined residue intakes from both primary crops and succeeding crops, within the livestock dietary burden calculation.

The maximum dietary burdens were therefore calculated for different groups of livestock as described in the OECD Guidance Document on Residues in Livestock (ENV/JM/MONO(2013) dated of 4th September 2013). The input values for all relevant commodities are summarized in Table 6.4 - 1 for fluopicolide and Table 6.4 - 2 for metabolite M-01.

Table 6.4- 1 Inputs for animal burden calculations (Fluopicolide)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Alfalfa forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Barley straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Beet / mangel fodder leaves	0.09	Extrapolation from carrot leaves (rotational crop study: early plant-back)	1.9	Extrapolation from carrot leaves (rotational crop study: early plant-back)
Sugar beet tops	0.09	Extrapolation from carrot leaves (rotational crop study: early plant-back)	1.9	Extrapolation from carrot leaves (rotational crop study: early plant-back)
Cabbage heads	0.01	Cabbage (rotational crop study: early plant-back)	0.01	Cabbage (rotational crop study: early plant-back)
Clover forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Corn stover	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Cowpea forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Grass forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Kale leaves (forage)	0.05	Extrapolation from lettuce (rotational crop study: early plant-back)	0.10	Extrapolation from lettuce (rotational crop study: early plant-back)
Lespedeza forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Millet straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Oat straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Rye straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Sorghum straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Trefoil forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)
Triticale straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Turnip top / leaves	0.09	Extrapolation from carrot leaves (rotational crop study: early plant-back)	1.9	Extrapolation from carrot leaves (rotational crop study: early plant-back)
Vetch forage	0.115	Extrapolation from barley green material (rotational crop study: early plant-back)	1.02	Extrapolation from barley green material (rotational crop study: early plant-back)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Wheat straw	0.38	Extrapolation from barley straw (rotational crop study: early plant-back)	1.50	Extrapolation from barley straw (rotational crop study: early plant-back)
Root and tubers (carrots, cassava, potato, swede and turnip)	0.11	Extrapolation from carrot roots (rotational crop study: early plant-back)	0.134	Extrapolation from carrot roots (rotational crop study: early plant-back)
Corn grain	<0.01	Maize (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Cereal grains (excluding corn)	0.93	Extrapolation from barley grain (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Pea seed	<0.01	Dry pea (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Sugar beet dried pulp	0.11	Extrapolation from carrot roots (rotational crop study: early plant-back) – Default PF	-	Not applicable to processed fractions.
Oilseed meal (flax, rape, sunflower, safflower)	0.03	Extrapolation from oilseed rape (rotational crop study: early plant-back) – Default PF	-	Not applicable to processed fractions.

Table 6.4-2 Inputs for animal burden calculations (M-01)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Alfalfa forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Barley straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Beet / mangel fodder leaves	0.19	Extrapolation from carrot leaves (rotational crop study: late plant-back)	2.04	Extrapolation from carrot leaves (rotational crop study: late plant-back)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Sugar beet tops	0.19	Extrapolation from carrot leaves (rotational crop study: late plant-back)	2.04	Extrapolation from carrot leaves (rotational crop study: late plant-back)
Cabbage heads	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Clover forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Corn stover	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Cowpea forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Grass forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Kale leaves (forage)	0.08	Extrapolation from lettuce (rotational crop study: mid plant-back)	0.26	Extrapolation from lettuce (rotational crop study: mid plant-back)
Lespedeza forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Millet straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Oat straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Rye straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Sorghum straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Trefoil forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Triticale straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Turnip top / leaves	0.19	Extrapolation from carrot leaves (rotational crop study: late plant-back)	2.04	Extrapolation from carrot leaves (rotational crop study: late plant-back)
Vetch forage	0.09	Extrapolation from corn green material (rotational crop study: mid plant-back)	0.35	Extrapolation from corn green material (rotational crop study: mid plant-back)
Wheat straw	0.09	Extrapolation from barley straw (rotational crop study: early plant-back)	1.02	Extrapolation from barley straw (rotational crop study: early plant-back)
Root and tubers (carrots, cassava, potato, swede and turnip)	0.02	Extrapolation from carrot roots (rotational crop study: mid plant-back)	0.07	Extrapolation from carrot roots (rotational crop study: mid plant-back)
Corn grain	0.01	Maize (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Cereal grains (excluding corn)	0.02	Extrapolation from barley grain (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Pea seed	0.01	Dry pea (rotational crop study: early plant-back)	-	Not applicable (not a post-harvest use)
Sugar beet dried pulp	0.02	Extrapolation from carrot roots (rotational crop study: mid plant-back) – Default PF	-	Not applicable to processed fractions.
Oilseed meal (flax, rape, sunflower, safflower)	0.09	Extrapolation from oilseed rape (rotational crop study: mid plant-back) – Default PF	-	Not applicable to processed fractions.

The results of the calculations are reported in Table 6.4 - 3 for fluopicolide and Table 6.4 - 4 for metabolite M-01 (BAM).

Table 6.4- 3 Results of the dietary burden calculation for fluopicolide- OECD methodology

Livestock category	Maximum dietary burden (mg/kg bw/day)	Max dietary burden (mg/kg DM)	Highest contributing commodity	Trigger exceeded? (≥0.004 mg/kg bw/day)
Cattle (all diets)	0.311	9.51	Potato process waste	Yes
Cattle (dairy only)	0.311	8.08	Potato process waste	Yes
Sheep (all diets)	0.326	9.78	Potato process waste	Yes
Sheep (ewe only)	0.326	9.78	Potato process waste	Yes
Swine (all diets)	0.116	5.04	Potato process waste	Yes
Poultry (all diets)	0.092	1.30	Potato dried pulp	Yes
Poultry (layer only)	0.086	1.26	Potato dried pulp	Yes

Table 6.4- 4 Results of the dietary burden calculation for M-01- OECD methodology

Livestock category	Maximum dietary burden (mg/kg bw/day)	Max dietary burden (mg/kg DM)	Highest contributing commodity	Trigger exceeded? (≥0.004 mg/kg bw/day)
Cattle (all diets)	0.175	5.62	Beet, mangel	Yes
Cattle (dairy only)	0.175	4.55	Beet, mangel	Yes
Sheep (all diets)	0.124	3.58	Turnip	Yes
Sheep (ewe only)	0.119	3.58	Turnip	Yes
Swine (all diets)	0.069	2.99	Beet, mangel	Yes
Poultry (all diets)	0.045	0.66	Beet, mangel	Yes
Poultry (layer only)	0.045	0.66	Beet sugar	Yes

The results of the livestock dietary burden calculations show that need for poultry and cattle feeding studies has been triggered for both fluopicolide and BAM.

CA 6.4.1 Poultry

The following studies are currently on-going and will be submitted at the following time-points:

Dossier node	Draft title	Study ID	Planned submission
KCA 6.4.1	Laboratory Study: Fluopicolide: Feeding Study with Laying Hens	2020-FLC-01	2nd Quarter 2021
KCA 6.4.1	Laboratory Study: BAM: Feeding Study with Laying Hens	2020-BAM-01	2nd Quarter 2021

CA 6.4.2 Ruminants

Data Point:	KCA 6.4.2/01
Report Author:	[redacted]
Report Year:	2004
Report Title:	Residues of AE C638206 and major metabolites in milk and edible cattle tissues following 28 days dosing of technical product to lactating cows; 2002. Final report.
Report No:	02-105
Document No:	M-219457-01-2
Guideline(s) followed in study:	EU (=EEC): 7031/VI/95 rev. 4; USEPA (=EPA): OPPTS 860.1480
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

The study will be superseded by the on-going livestock feeding studies (once they have been completed). This study does not consider the two prominent metabolites found within livestock tissues / products: M-06 and M-07 (which will be quantified as part of the new dairy cattle feeding study).

The following studies are currently on-going and will be submitted at the following time-points:

Dossier node	Draft title	Study ID	Planned submission
KCA 6.4.2	Laboratory Study: Fluopicolide: Feeding Study with Dairy Cows	2020-FLC-02	2nd Quarter 2021
KCA 6.4.2	Laboratory Study: BAM: Feeding Study with Dairy Cows	2020-BAM-02	2nd Quarter 2021

CA 6.4.3 Pigs

The available animal metabolism studies (for poultry, ruminants and rats) show that fluopicolide appears to undergo hydroxylation and conjugation to sulphate or glucuronic acid, oxidative N-dealkylation and conjugation to glutathione followed by the subsequent biotransformation of the glutathione in all three species.

It is therefore not necessary to generate a further set of livestock feeding studies for pigs exposed to fluopicolide and M-01 through the diet.

CA 6.4.4 Fish

A fish feeding study is not required. Currently no test method or guidance document is available. As a consequence waiving of this particular data requirement is considered acceptable according to the "Guidance document for applicants on preparing dossiers for the approval of a chemical new active substance and the renewal of the chemical active substance according to regulation (EU) No. 283/2013 and regulation (EU) No. 284/2013" (SANCO/10181/2013-rev.2 of 2-May-2013).

Based on the available information, there is a low probability for the intake of fluopicolide as well as its biotransformation. Residues of fluopicolide in fish are considered to be of no concern and no accumulation in the food chain is to be expected. Please refer to section CA 6.2.5 of this document, for further details.

In addition to the above consideration, a supplementary dietary burden for aquaculture (farmed fish) has been undertaken within the remainder of this section.

The commercial processing of the target uses (potatoes and oilseed rape) typically result in the by-products potato protein and rape seed meal, which are commonly used as feed items for farmed fish. As described within section CA 6.6.2, some of the metabolites of fluopicolide are persistent within soil and may be taken up by the roots of developing succeeding crops and translocate to the edible portions.

In order to provide an approximation of the dietary burden in aquaculture diets, a fish dietary burden was calculated using the Fish Dietary Burden Calculator of Fraunhofer Institute in Schmallenberg, Germany in accordance to EU working document (SANCO/11187/2013 rev. 3 of 31 January 2013) for trout and carp feed. Details for this calculation are included within Appendix 1 of this document. A calculation of the dietary burden for fish has been undertaken in Appendix 1 of this document.

The results show that high fluopicolide intakes are expected for fish (>0.1 mg/kg) based on the residues expected with the treated and succeeding crops: 0.726 mg/kg for the common carp and 0.483 mg/kg for rainbow trout. For M-01, low exposures for fish through the diet are expected: 0.089 mg/kg for the common carp and 0.068 mg/kg for rainbow trout.

The output of the dietary burden calculator is shown in Appendix 1 of this document. While relatively high intakes for fluopicolide within the fish diet are expected, the physical chemical properties (partition coefficients) and the bioaccumulation study for this substance show that it is unlikely to persist at significant levels within fish tissues (refer to section CA 6.2.5).

Overall, residues of the active substances fluopicolide in fish are considered to be of no concern and no accumulation in the food chain is to be expected.

CA 6.5 Effects of processing

The hydrolysis studies (covering the representative processing scenarios of baking, brewing, and boiling) are available to demonstrate that fluopicolide and M-01 remain stable under the tested conditions.

Processing studies for grape fractions have been previously reviewed at the EU level (DAR, 2016). These studies were previously considered to be acceptable and have again been summarised within this dossier for completeness (though grapes are not a representative renewal use).

As the residue of fluopicolide were observed to exceed 0.1 mg/kg in lettuce, a processing study for leafy crops (conducted on spinach) was undertaken to derive processing factors for the washed and cooked product. The following processing factors were derived for reach residue component for cooked (steamed) spinach leaves: FLC - 0.69; M-01 - 0.89; M-02 - 1.43.

CA 6.5.1 Nature of the residue

Data on the nature of the residue in processing was submitted for the first inclusion of fluopicolide into Annex I of Council Directive 91/414/EEC (DAR, UK, 2005) to cover the stability of fluopicolide when subjected to high temperature hydrolysis. A new study has been conducted to demonstrate the stability of metabolite M-01 under similar high temperature hydrolysis conditions, as such a study was not previously generated or submitted. It is considered that this new study is for M-01 is necessary, as M-01 is a component of the plant residue definition for pre-registration / risk assessment purposes.

Summary of the nature of residues of [2,6-^{14}C-pyridyl]-Fluopicolide and [phenyl-UL-^{14}C]-BAM in processed commodities – high temperature hydrolysis

Test System	Experimental conditions	Endpoint	Reference
New data			
[2,6-^{14}C-pyridyl]-Fluopicolide Buffered at pH 4, pH 5 and pH 6	Pasteurisation Baking, Brewing, Boiling Sterilisation	Fluopicolide is predominantly stable	KCA 6.5.1/01 M-205032-01-1 [redacted] 2001
[phenyl-UL-^{14}C]-BAM (M-01) Buffered at pH 4, pH 5 and pH 6	Pasteurisation Baking, Brewing, Boiling Sterilisation	M-01 is predominantly stable	KCA 6.5.1/02 M-685570-02-1 [redacted] 2020

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.5.1/01
Report Author:	[redacted]
Report Year:	2001
Report Title:	Simulated processing (14C)-AE C638206
Report No:	C013665
Document No:	M-205032-01-1
Guideline(s) followed in study:	EU (=EEC): 7035/VI/95, REV5, APPENDIX E, 91/414/EEC
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

The hydrolytic degradation of [2,6-^{14}C-pyridyl]-Fluopicolide at elevated temperatures was investigated at 1.0 mg/L in buffer solutions. The test systems were incubated under three representative sets of hydrolysis conditions; 90°C and pH 4 for 20 minutes simulating pasteurization, 100°C and pH 5 for 60 minutes simulating baking, brewing and boiling, and 120°C and pH 6 for 20 minutes simulating sterilisation.

At time zero (test start) and after 20 or 60 minutes incubation, the samples were taken and analysed by HPLC. Selected samples were additionally submitted to TLC analysis. The temperatures were maintained constant throughout the incubation period and no significant variation of the pH values were observed.

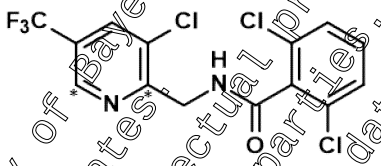
The mean recoveries of radioactivity were 99.3 ±1.9% (pH 4), 102.7 ±2.3% (pH 5) and 100.1 ±3.0 (pH 6).

Fluopicolide was found to be predominantly stable and virtually resistant to hydrolysis under all test conditions.

I. Materials and methods

A. Materials

1. Test Material:

IUPAC Name	2,6-dichloro-N-[(3-chloro-5-trifluoromethyl-2-pyridyl) methyl]benzamide
Common name	Fluopicolide
Empirical formula	$C_{14}H_8Cl_3F_3N_2O$
CAS Number	239110-15-7
Molar mass	383.59
Chemical structure	 * position of the radiolabel
Radiolabelled test material	[2,6-14C-pyridyl]-Fluopicolide
Batch number	GAR2019/1 (RCC No. 113085/A)
Specific radioactivity	5.88 MBq/mg
Radiochemical purity	> 99% (determined by HPLC)
Stability of test compound	Shown to be stable under the conditions of the test
Application vehicle	Acetone

B. Study Design

1. In-life dates:

30 March 2001 - 02 July 2001

2. Test System

The study was performed in citrate buffered drinking water at pH 4, pH 5 and pH 6.

Experimental design

Parameter			Description
Test concentration (Nominal)			1.0 mg/L
Number of replicates			Single sample
Preparation of test medium	Volume of treatment solution per vessel		5 mL
	Test medium		Buffered drinking water
Test material application	Co-solvent		Acetone, final concentration approx. 0.5% (v/v)
	Volume of test solution		100 µL of stock solution into 9.9 mL buffer at each pH
	Application method		An aliquot of the application solution (100 µL) was pipetted into 9.9 mL of buffered drinking water (pH 4, pH 5 or pH 6) under stirring.
Test apparatus			Glass vials with a septum and crimp top
Traps for CO_2 and organic volatiles			None
Is there any indication of the test material absorbing to the walls of the test apparatus			No
Experimental conditions	Pasteurisation	Temperature	90°C ± 5.0°C in an oil bath
		pH	4
		Duration of the test	20 minutes
	Baking, Brewing, Boiling	Temperature	100°C ± 5.0°C under reflux conditions
		pH	5
		Duration of the test	60 minutes
	Sterilisation	Temperature	120°C ± 5.0°C in an autoclave
		pH	6
		Duration of the test	20 minutes

Sampling

Parameter	Details
Sampling intervals for the parent/transformation products	Zero time and at test termination
Sampling procedure	Entire vessel
Measurements at sampling: pH measurement	Zero time and at test termination, at room temperature
Sample storage before analysis	All analyses were performed on the day of sampling
Other observations	None

The processes were stopped by cooling the samples to ambient temperature as rapidly as possible.

Description of analytical procedures

The pH values were measured at zero time and again at termination after cooling to ambient temperature and were all found to be within the acceptable limits at pH 4, pH 5 and pH 6 (± 0.1).

Aqueous samples were radioassayed using LSC and analysed by HPLC (co-chromatography with unlabeled compounds) to determine the levels of parent and significant degradates in each sample.

II. Results and Discussion

A. Mass balance:

The mean recovery of applied radioactivity was in the range of 94.9 - 98.6%.

B. Findings:

Following hydrolysis the solutions were assayed to determine the level of applied radioactivity remaining as AE C638206 and whether any breakdown products were observed.

The distribution of [^{14}C] AE C638206 in the respective buffer solutions is shown below.

Substrate	Temperature (˚C)	Incubation time (min.)	Simulation of	Mean % of applied radioactivity determined as AE C638206
pH 4 buffer	90	20	pasteurisation	98.9
pH 5 buffer	100	60	baking, brewing or boiling	103.8
pH 6 buffer	120	20	sterilisation	100.4

III. Conclusions

Since >98% of [2,6-14C-pyridyl]-Fluopicolide was accounted for as unchanged parent material, fluopicolide was confirmed as the only relevant target for determination in studies designed to investigate the effect on residue by processing. Analytical methods used in such studies still determined the residue levels of the defined plant metabolites AE C653711 and AE C657188 since they are found in the raw plant commodities, but not in significant amounts.

Assessment and conclusion by applicant:

Fluopicolide was found to be predominantly stable and resistant to hydrolysis under conditions representative for pasteurisation, baking, brewing, boiling and sterilisation.

New data for AIR:

Data Point:	KCA 6.5.1/02
Report Author:	[redacted]
Report Year:	2020
Report Title:	Amendment no. 01: [14C]-BAM: High temperature (processing) hydrolysis (OECD 507)
Report No:	VC/19/036
Document No:	M-685570-02-1
Guideline(s) followed in study:	OECD Test Guideline No. 507 (Oct. 2007) Regulation (EU) No. 283/2013 Regulation (EC) No. 1107/2009
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

The hydrolytic degradation of [phenyl-UL-^{14}C]-BAM at elevated temperatures was investigated at 1.0 mg/L in buffer solutions. The test systems were incubated under three representative sets of hydrolysis conditions; 90°C and pH 4 for 20 minutes simulating pasteurization, 100°C and pH 5 for 60 minutes simulating baking, brewing and boiling, and 120°C and pH 6 for 20 minutes simulating sterilisation.

At time zero (test start) and after 20 or 60 minutes incubation, the samples were taken and analysed by HPLC. Selected samples were additionally submitted to TLC analysis. The temperatures were maintained constant throughout the incubation period and no significant variation of the pH values were observed.

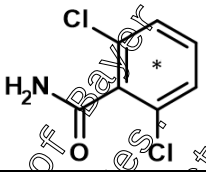
The mean recoveries of radioactivity in the test samples were 98.7 (pH 4), 98.4% (pH 5) and 98.6 (pH 6). No other individual component was detected at levels >1.0% (0.010 mg/L) in any experiment. The equivalent recoveries for the ambient control samples accounted for 103.2%, 101.6% and 100.8% for pH 4, pH 5 and pH 6 experiments respectively.

M-01 was found to be predominantly stable and virtually resistant to hydrolysis under all test conditions.

I. Materials and methods

A. Materials

1. Test Material:

IUPAC Name	2,6-dichlorobenzamide
Common name	BAM (M-01)
Empirical formula	$C7H_5Cl_2NO$
CAS Number	2008-58-4
Molar mass	190.03
Chemical structure	 * position of the radiolabel
Radiolabelled test material	[phenyl-UL-^{14}C]-BAM
Batch number	KML-10697
Specific radioactivity	3.91 MBq/mg
Radiochemical purity	97.8 % (HPLC) (data from certificate of analysis) 97.5 % (HPLC) (data from certificate of analysis) 98.5% (HPLC) (data from in-house testing)
Stability of test compound	Shown to be stable under the conditions of the test
Application vehicle	Acetone

B. Study Design

1. In-life dates:

03 May 2019 - 31 May 2019

2. Test System

The study was performed in citrate buffered drinking water at pH 4, pH 5 and pH 6.

Experimental design

Parameter			Description
Test concentration (Nominal)			1.0 mg/L
Number of replicates			Duplicate samples
Preparation of test medium	Volume of treatment solution per vessel		40 mL
	Test medium		Buffered ultrapure water
Test material application	Co-solvent		Acetone
	Volume of test solution		0.06 mL of treatment solution into 40 mL buffer at each pH
	Application method		An aliquot of the application solution (0.06 mL) was pipetted into 40 mL of buffered ultrapure water (pH 4, pH 5 or pH 6) under stirring.
Test apparatus			Glass tubes with glass stoppers held in place using screwable over caps
Traps for CO_2 and organic volatiles			None
Is there any indication of the test material absorbing to the walls of the test apparatus			No
Experimental conditions	Pasteurisation	Temperature	90°C ± 5.0°C using a dry-block heater
		pH	4
		Duration of the test	20 minutes
	Baking, Brewing, Boiling	Temperature	100°C ± 5.0°C using a dry-block heater
		pH	5
		Duration of the test	60 minutes
	Sterilisation	Temperature	120°C ± 5.0°C in an autoclave
		pH	6
		Duration of the test	20 minutes

Sampling

Parameter	Details
Sampling intervals for the parent/transformation products	Zero time and at test termination
Sampling procedure	Entire vessel
Measurements at sampling: pH measurement	Zero time and at test termination, at room temperature
Sample storage before analysis	All analyses were performed on the day of sampling
Other observations	None

The processes were stopped by cooling the samples to ambient temperature as rapidly as possible.

Description of analytical procedures

The pH values were measured at zero time and again at termination after cooling to ambient temperature and were all found to be within the acceptable limits at pH 4, pH 5 and pH 6 (± 0.1).

Aqueous samples were radioassayed using LSC and analysed by HPLC (co-chromatography with unlabeled compounds) to determine the levels of parent and significant degradates in each sample.

II. Results and Discussion

A. Mass balance:

For each test, a material balance was established by comparing the total radioactivity in the test solution after hydrolysis to that originally dosed (from dose check samples). Based on the results of LSC treatment checks, the concentration of the total radioactivity applied for each process was determined to be:

• pH 4 = 1.0 mg/L

• pH 5 = 0.9 mg/L

• pH 6 = 1.0 mg/L

The mean radioactive recoveries from duplicate processed samples accounted for 103.2%, 99.8% and 99.8% for the pasteurisation (90 °C at pH 4), baking, brewing, boiling (100°C at pH 5) and sterilisation experiments (120 °C at pH 6) respectively. The equivalent recoveries for the ambient control samples accounted for 103.2%, 101.6% and 100.8% for pH 4, pH 5 and pH 6 experiments respectively.

B. Findings:

Following hydrolysis the solutions were assayed to determine the level of applied radioactivity remaining as AE C638206 and whether any breakdown products were observed.

The distribution of [phenyl-UL-^{14}C]-BAM in the respective buffer solutions is shown below.

	Processing conditions					
	pH 4 / 90 °C; 20 minutes		**pH 5 / 100 °C; 60 minutes**		**pH 6 / 120 °C; 20 minutes**	
Hydrolysis product	**AR [%] (mean)**	**mg/L (mean)**	**AR [%] (mean)**	**mg/L (mean)**	**AR [%] (mean)**	**mg/L (mean)**
M-01	98.7	1.002	98.4	0.933	98.6	1.004
Other minor products	1.3	0.013	1.7	0.016	1.5	0.015
Sum of identified	**98.7**	**1.002**	**98.4**	0.933	**98.6**	**1.004**
Sum of characterised	1.3	0.013	1.7	0.016	1.5	0.015
Accountability	**100.0**	**1.015**	**100.0**	**0.948**	**100.0**	**1.018**

III. Conclusions

Metabolite M-01 was found to be stable under processing conditions representative of pasteurisation, boiling/baking/brewing and sterilisation. Since no degradation was evident, no degradation pathway was proposed.

Assessment and conclusion by applicant:

Metabolite M-01 was found to be predominantly stable and resistant to hydrolysis under conditions representative for pasteurisation, baking, brewing, boiling and sterilisation.

CA 6.5.2 Distribution of the residue in inedible peel and pulp

An evaluation of the distribution of residues between inedible peel/pulp is not relevant, as the residue levels for potatoes and cucumbers did not exceed 0.1 mg/kg in the residues field trial studies for fluopicolide or M-01. Furthermore, the additional representative commodities, oilseed rape and lettuce, are not separated in this way. So, there is no need to investigate the distribution of residues between peel/pulp.

CA 6.5.3 Magnitude of residues in processed commodities

Data on the magnitude of residues in processed commodities was submitted for the first inclusion of fluopicolide into Annex I of Council Directive 91/414/EEC (DAR, UK, 2005). These studies covered the common household / industrial processes for grapes (which was a representative use for fluopicolide at the Annex I evaluation). While grapes are no longer a representative use at the fluopicolide renewal, these studies have been included within this section for completeness.

A new residues processing studies for spinach (representative of leafy crops) has been generated to support the representative use on lettuce. This study has also been summarised within this section.

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.5.3/01
Report Author:	[redacted]
Report Year:	2003
Report Title:	Determination of the residues in processed fractions derived from red grapes following three treatments under field conditions in Southern Europe 2000 AE C638206 Code: AE C638206 00 SE10 A3
Report No:	C035551
Document No:	M-218649-01-1
Guideline(s) followed in study:	EU (=EEC) 7035/VI/95 rev.5 - 22/07/97, OPPTS 860.5200
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

Treated and untreated specimens of red grape varieties from three field trials with AE C638206 00 SE10 A3 in Southern Europe were processed in a pilot plant in order to produce processed fractions of wine (such as pomace, must, yeast young wine and mature wine). The field trials were conducted in Spain (Sevilla), Greece (Thessaloniki) and Southern France (Aquitaine). The same amount of AE C638206 00 SE10 A3 was applied to each trial (nominal 1.33 L/ha, for each of the three applications).

The processing phase was conducted in accordance with the requirements outlined within the working document 7035/VI/95 rev.5. All grape specimens were processed in the same manner to fulfil the requirements of both the balance study type and the follow-up study.

Residue transfer factors were calculated. The residue transfer indicates that not more than 14% of the original residues of fluopicolide and less than 24% of fluopicolide and its metabolites remain in the wine fraction while the majority of the analytes were removed within the pomace fraction.

I. Materials and methods

A. Materials

1. Test Material:

AE C638206 00 SE10 A3 as formulated SE product (95 g/L) for field phase.

Fluopicolide, M-01 and M-02 (parent and defined plant metabolites) as analytical reference standards.

Red grape varieties were used in the field and processing phases.

B. Study Design

1. In-life dates:

11 July 2000 – 24 February 2003

2. Test System

Field phase

Treated and untreated specimens of red grape varieties from three field trials with AE C638206 00 SE10 A3 in Southern Europe were processed in a pilot plant in order to produce processed fractions of wine (such as pomace, must, yeast young wine and mature wine). The field trials were conducted in Spain (Sevilla), Greece (Thessaloniki) and Southern France (Aquitaine). The same amount of AE C638206 00 SE10 A3 was applied to each trial (nominal 1.33 L/ha for each of the three applications).

Experimental design

The sampled grapes were destemmed and crushed. The mash was heated to approximately 70°C and them cooled down to ambient temperature. On the following day the must was separated from the skins and the seeds using a press. The further processing comprised the fermentation, post-fermentation treatment, such as clarification with first and second racking, filtering and bottling and finally maturation. The collected fractions were placed into a freezer after collection and labelling.

The following specimens were collected during the processing phase:

Must:	After pressing (juice separation).
Pomace:	After pressing.
Yeast:	Suspension that remained after the first racking – yeast cells were separated by centrifuge.
Young wine:	After aging for 6 weeks after the second racking.
Mature wine:	Storage after bottling for approximately four further months

The specimens were stored deep-frozen until analysis.

Description of analytical procedures

Analytical method used: Agredoc Number C024784 (IF-101/05424) with minor modifications.

Grapes were sampled from vines at three sites in Southern Europe following application of the formulated SE product at the proposed GAP. Sufficient quantity was taken to enable processing at a pilot plant into fractions of pomace, must, yeast, young wine and mature wine. These fractions and the RAC samples were analysed for fluopicolide and its metabolites M-01 and M-02 using an analytical method with LC/MS/MS determination.

II. Results and Discussion

Following the field trial phase, the following residue level were found within the sampled grapes:

Country, year (trial ref)	Rate (kg as/ha)	Fraction analysed	Residue level (mg/kg)		
			Fluopicolide	M-01	M-02
EU South Spain, 2000 (00S041R)	3 x 0.133	RAC	0.32	0.02	0.07
		must	0.12	0.02	0.08
		pomace	2.1	0.03	0.07
		yeast	1.2	0.01	0.04
		young wine	0.08	0.01	0.07
		mature wine	0.09	0.01	0.07
EU South Greece, 2000 (00RF021/2)	3 x 0.133	RAC	0.35	0.03	0.03
		must	0.20	0.03	0.03
		pomace	2.2	0.05	0.04
		yeast	3.1	0.04	0.05
		young wine	0.11	0.03	0.03
		mature wine	0.11	0.03	0.03
EU South France, 2000 (00 F VI FR P04)	3 x 0.133	RAC	0.40	0.02	0.02
		must	0.15	0.02	0.02
		pomace	2.0	0.03	0.03
		yeast	2.4	0.02	0.03
		young wine	0.15	0.02	0.02
		mature wine	0.15	0.02	0.02

The residue transfer factors for each fraction are presented in the table on the next page. This is calculated by dividing the residue found in a fraction, e.g. mature wine, by the residue in the grapes used to make the wine (RAC).

The residue transfer in absolute terms was used to establish a mass balance in each of the three trials. The mass balance values ranged from 87 to 137 % across the three trials in terms of fluopicolide residue values. Within the bounds of experimental error associated with wine processing studies these mass balance figures are considered good enough to show that mass balance was achieved.

Country, year (trial ref)	Fraction	Residue transfer factor AE C638206
EU South Spain, 2000 (00S041R)	RAC	-
	must	0.38
	pomace	6.6
	yeast	3.8
	young wine	0.25
	mature wine	0.28
EU South Greece, 2000 (00RF021/2)	RAC	-
	must	0.57
	pomace	6.3
	yeast	8.9
	young wine	0.31
	mature wine	0.31
EU South France, 2000 (00 F VI FR P04)	RAC	-
	must	0.38
	pomace	5.0
	yeast	6.0
	young wine	0.38
	mature wine	0.38

III. Conclusions

Following commercially representative processing of wine grapes, treated with AE C638206, into mature wine, residues of fluopicolide and its metabolites were found in all fractions. Fluopicolide residues in mature wine ranged from 0.09 to 0.15 mg/kg.

The transfer factors of fluopicolide residues (parent only) from RAC into mature wine ranged from 0.28 to 0.38 (mean value of 0.32).

Achieved mass balance figures ranged from 87 to 137%. This data is considered to be good for processes representative of commercial wine processing.

Assessment and conclusion by applicant:

Average transfer factors were established based on the results of the study for the following red grape wine fractions:

Must	0.44
Pomace	6.0
Yeast	6.2
Young Wine	0.31
Mature Wine	0.32

Data Point:	KCA 6.5.3/02
Report Author:	[redacted]
Report Year:	2003
Report Title:	Determination of the residues in processed fractions derived from white grapes following four treatments under field conditions in Northern Europe 2000 Code: AE C638206 00 SE10 A3
Report No:	C037343
Document No:	M-242674-01-1
Guideline(s) followed in study:	BBA: Part IV 3-2.4; EU (=EEC): 7035/VI/95 rev.5
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

Treated and untreated specimens of red grape varieties from three field trials with AE C638206 00 SE10 A3 in Northern Europe were processed in a pilot plant in order to produce processed fractions of wine (such as pomace, must, yeast young wine and mature wine). The field trials were conducted in Northern France (Maine-et-Loire) and Germany (Hesse and Rhineland-Palatinate). The same amount of AE C638206 00 SE10 A3 was applied to each trial (nominal 1.33 L/ha, for each of the three applications).

The processing phase was conducted in accordance with the requirements outlined within the working document 7035/VI/95 rev.5. All grape specimens were processed in the same manner to fulfil the requirements of both the balance study type and the follow-up study.

Residue transfer factors were calculated. The residue transfer indicates that not more than 30 % of the original residues of fluopicolide and of fluopicolide and its metabolites remain in the wine fraction while the majority of the analytes were removed within the pomace fraction.

I. Materials and methods

A. Materials

1. Test Material:

AE C638206 00 SE10 A3 as formulated SE product (95 g/L) for field phase.

Fluopicolide, M-01 and M-02 (parent and defined plant metabolites) as analytical reference standards.

Red grape varieties were used in the field and processing phases.

B. Study Design

1. In-life dates:

19 July 2000 – 25 February 2003

2. Test System

Field phase

Treated and untreated specimens of red grape varieties from three field trials with AE C638206 00 SE10 A3 in Northern Europe were processed in a pilot plant in order to produce processed fractions of wine (such as pomace, must, yeast young wine and mature wine). The field trials were conducted in Northern France (Maine-et Loire) and Germany (Hesse and Rhineland-Palatinate). The same amount of AE C638206 00 SE10 A3 was applied to each trial (nominal 1.33 L/ha, for each of the three applications).

Experimental design

The sampled grapes were destemmed and crushed. The mash was heated to approximately 70°C and them cooled down to ambient temperature. On the following day the must was separated from the skins and the seeds using a press. The further processing comprised the fermentation, post-fermentation treatment, such as clarification with first and second racking, filtering and bottling and finally maturation. The collected fractions were placed into a freezer after collection and labelling.

The following specimens were collected during the processing phase:

Must:	After pressing (juice separation)
Pomace:	After pressing
Yeast:	Suspension that remained after the first racking – yeast cells were separated by centrifuge.
Young wine:	After aging for 6 weeks after the second racking.
Mature wine:	Storage after bottling for approximately four further months

The specimens were stored deep-frozen until analysis.

Description of analytical procedures

Analytical method used: Agredoc Number C024784 (IF-101/05424) with minor modifications.

Grapes were sampled from vines at three sites in Southern Europe following application of the formulated SE product at the proposed GAP. Sufficient quantity was taken to enable processing at a pilot plant into fractions of pomace, must, yeast, young wine and mature wine. These fractions and the RAC samples were analysed for AE C638206 and its metabolites AE C653710 and AE C657188 using an analytical method with LC/MS/MS determination.

II. Results and Discussion

Following the field trial phase, the following residue level were found within the sampled grapes:

Country, year (trial ref)	Rate (kg as/ha)	Fraction analysed	Residue level (mg/kg)		
			Fluopicolide	M-01	M-02
EU North France, 2000 (BKA/683/00/RES 1)	4 x 0.133	RAC	0.62	<0.02	0.02
		pomace	1.1	0.01	0.03
		must (np)	0.27	<0.01	0.01
		yeast (np)	4.2	0.01	0.03
		young wine (np)	0.28	0.01	<0.01
		mature wine (np)	0.25	<0.01	<0.01
		must (p)	0.18	<0.01	<0.01
		yeast (p)	2.5	0.01	0.01
		young wine (p)	0.15	<0.01	<0.01
		mature wine (p)	0.15	0.01	<0.01
EU North Germany, 2000 (AT-00/021-1)	4 x 0.133	RAC	0.61	0.01	0.02
		pomace	1.4	0.01	0.02
		must (np)	0.29	<0.01	<0.01
		yeast (np)	3.7	<0.01	0.02
		young wine (np)	0.25	<0.01	<0.01
		mature wine (np)	0.26	<0.01	<0.01
		must (p)	0.19	<0.01	<0.01
		yeast (p)	2.1	<0.01	<0.01
		young wine (p)	0.14	<0.01	<0.01
		mature wine (p)	0.14	<0.01	<0.01
EU North Germany, 2000 (AT-00/021-2)	4 x 0.133	RAC	0.51	0.01	0.01
		pomace	0.80	0.01	0.03
		must (np)	0.33	<0.01	0.01
		yeast (np)	4.8	0.02	0.06
		young wine (np)	0.32	<0.01	<0.01
		mature wine (np)	0.31	<0.01	<0.01
		must (p)	0.20	<0.01	0.01
		yeast (p)	3.2	0.01	0.02
		young wine (p)	0.13	<0.01	0.01
		mature wine (p)	0.22	<0.01	0.01

The residue transfer factors for each fraction are presented in the table on the next page. This is calculated by dividing the residue found in a fraction, e.g. mature wine, by the residue in the grapes used to make the wine (RAC).

The residue transfer in absolute terms was used to establish a mass balance in each of the three trials. The mass balance values ranged from 66 to 86 % across the three trials in terms of fluopicolide residue values. Within the bounds of experimental error associated with wine processing studies these mass balance figures are considered good enough to show that mass balance was achieved.

Country, year (trial ref)	Fraction	Residue transfer factor AE C638206
EU North France, 2000 (BKA/683/00/RES 1)	RAC	-
	pomace	1.8
	must (np)	0.44
	yeast (np)	6.8
	young wine (np)	0.45
	mature wine (np)	0.40
	must (p)	0.29
	yeast (p)	3.7
	young wine (p)	0.24
	mature wine (p)	0.24
EU North Germany, 2000 (AT-00/021-1)	RAC	-
	pomace	2.3
	must (np)	0.48
	yeast (np)	6.1
	young wine (np)	0.41
	mature wine (np)	0.43
	must (p)	0.31
	yeast (p)	3.4
	young wine (p)	0.23
	mature wine (p)	0.23
EU North Germany, 2000 (AT-00/021-2)	RAC	-
	pomace	1.6
	must (np)	0.65
	yeast (np)	9.4
	young wine (np)	0.63
	mature wine (np)	0.61
	must (p)	0.39
	yeast (p)	6.3
	young wine (p)	0.25
	mature wine (p)	0.43

(p) = pasteurized
(np) = not pasteurised

III. Conclusions

Following commercially representative processing of wine grapes treated with fluopicolide, into mature wine, residues of fluopicolide were found in all fractions. The metabolites M-01 and M-02 were found in some fractions but not at significant levels. fluopicolide residues in mature wine ranged from 0.14 to 0.31 mg/kg.

The transfer factors of fluopicolide residues (parent only) from RAC into mature wine (both non-pasteurised and pasteurised) ranged from 0.23 to 0.61 (mean value of 0.39).

Achieved mass balance figures ranged from 66 to 86%. This is considered to be good data for processes representative of commercial wine processing.

Assessment and conclusion by applicant:

Average transfer factors were established based on the results of the study for the following red grape wine fractions:

pomace	1.9
must (np)	0.52
yeast (np)	7.4
young wine (np)	0.50
mature wine (np)	0.48
must (p)	0.33
yeast (p)	4.5
young wine (p)	0.24
mature wine (p)	0.3

New data for AIR:

Data Point:	KCA 6.5.3/03
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide and propamocarb hydrochloride in/on spinach and the processed fractions (leaf, cooked and leaf, stored) after spraying of fluopicolide & propamocarb-hydrochloride SC 687.5 in the field in Germany, the Netherlands and Belgium
Report No:	E19PR001
Document No:	M-685591-01-1
Guideline(s) followed in study:	Regulation (EC) No. 1107/2009, (Oct. 2009) OECD Test Guideline No. 509, (Sept. 2009) OECD Test Guideline No. 508, (Oct. 2008) OECD Guidance Document No. 96, (Jul. 2008) US EPA OCSPP 860.1520, (Aug. 1996) US EPA OCSPP 860.1500, (Aug. 1996)
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

The study comprised three supervised residues trials with spinach in Germany, The Netherlands and Belgium, during the 2019 season. At each trial site there was an untreated plot in addition to treated plots. The treated and untreated plots were cultivated in a similar manner. Three spray applications were made to each treatment plot using the product SC 687.5, with a nominal target application of 0.5 kg fluopicolide /ha (an exaggerated rate).

The processing phase was conducted in accordance with the requirements outlined within the OECD test guideline 508. The study simulated the processing conditions for spinach leaves which are washed and then steam-cooked.

Residue transfer factors were calculated for the washed / steam-cooked leaves. The average processing factor were 0.69, 0.89 and 1.43 (for fluopicolide, M-01 and M-02, respectively).

I. MATERIALS AND METHODS

A – MATERIALS

1. **Test Material**
   - **Description:** Fluopicolide & Propamocarb hydrochloride SC 687.5
   - **Lot/Batch no.:** Suspension concentrate
   - **Active substance content:** EM4L023437
     Fluopicolide: 62.5 g/L (nominal)
     Propamocarb hydrochloride: 625 g/L (nominal)
   - **Expiry date:** 26-03-2021

2. Test Commodity

Crop:	Spinach
Variety:	
Botanical name:	Polydane F1, PV 1435, Santa Cruz
Crop part(s) or processed commodity:	leaves
Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

Field phase

Treated and untreated specimens of spinach varieties from three field trials with SC 687.5 in northern Europe were processed (sorted, washed and steam-cooked). The field trials were conducted in Germany, The Netherlands and Belgium. The same amount of SC 687.5 was applied (as a foliar treatment) to each trial:

Table 6.5- 1 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment
SC 687.5	3	0.5 kg a.s. / ha	7-9 days	BBCH 13 - 17

* Product contains 62.5 g/L of fluopicolide

The residue trial was conducted in the following location on the specified variety of spinach:

Table 6.5- 2 Trial details and regions

Trial No.	Country	Location	Crop variety
E19PR001-01	Germany	42799 Leichlingen	Polydane F1
E19PR001-02	Netherlands	1619 PH Andijk	PV 1435
E19PR001-03	Belgium	5030 Gembloux	Santa Cruz

At each trial site there was an untreated plot in addition to treated plots. The treated and untreated plots were cultivated in a similar manner.

Experimental design

Samples were collected from the trials sites in the manner as would be expected to obtain representative samples. The samples were taken, prepared in the field (or at a field station), transported and stored according to OECD guideline 509. Samples were stored deep frozen at ≤ - 18 °C.

The following procedures were applied to the collected field samples:

Sorting

The processing started with the weighing of the fresh bulk field sample of spinach leaves for processing (approx. 5 kg each). During the sorting step, rotten leaves were removed. A portion of these samples were stored and designated as "Leaf, stored" (approx. 0.5 kg from each site).

Washing

An aliquot of the remaining field sample of fresh spinach was washed with cold tap water in a ratio of 3 kg of water to 1 kg of spinach leaves. After washing, the leaves were dried using a salad spinner.

Cooking (steaming)

The washed spinach leaves were cooked in hot water steam. Cold tap water was filled into a large cooking pot and heated to boil (the ratio of water to leave was approx. 1:1, kg/kg). The leaves were cooked in portions using a sieve with a lid over the steam (for approx. 7 minutes). After steaming, the "Leaf, cooked" was taken as a sample.

After processing, the samples were stored at ≤ - 18 °C until the analytical phase.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01 and M-02 were analysed within the samples according to the following method:

Table 6.5- 3 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1:1 v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09 in spinach leaves

Full analytical details for this method, and conclusions on its acceptability, are presented within document MCA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Spinach leaves, stored	0.01	102, 105, 106, 108, 111	106	3.2	0.01
	0.10	92, 92, 93, 93, 94	93	0.9	
	1.0	86	-	-	
	2.0	92, 95, 98	95	3.2	
		Overall recovery (n=14)	98	7.6	
Spinach leaves cooked	0.01	102, 102, 103, 104, 114	105	4.9	0.01
	0.10	90, 96, 99, 100, 102	97	4.8	
	1.0	93	-	-	
	2.0	91, 92, 96	93	2.8	
		Overall recovery (n=14)	99	6.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Spinach leaves, stored	0.01	100, 102, 103, 105, 110	104	3.7	0.01
	0.10	97, 103, 105, 107, 110	104	4.7	
	1.0	94	-	-	
	2.0	95, 101, 102	99	3.8	
		Overall recovery (n=10)	102	4.8	
Spinach leaves cooked	0.01	90, 93, 94, 99, 101, 103, 104, 108	99	6.3	0.01
	0.10	91, 92, 94, 96, 97	94	2.7	
	1.0	95	-	-	
	2.0	102, 105, 107	105	2.4	
		Overall recovery (n=10)	98	5.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Spinach leaves, stored	0.01	100, 102, 103, 105, 110	104	3.7	0.01
	0.10	97, 103, 105, 107, 110	104	4.7	
	1.0	94	-	-	
	2.0	95, 101, 102	99	3.8	
		Overall recovery (n=10)	102	4.8	
Spinach leaves cooked	0.01	90, 93, 94, 99, 101, 103, 104, 108	99	6.3	0.01
	0.10	91, 92, 94, 96, 97	94	2.7	
	1.0	95	-	-	
	2.0	102, 105, 107	105	2.4	
		Overall recovery (n=10)	98	5.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01 and M-02 residues was 42 – 291 days in spinach leaves.

II. Results and Discussion

No residues were found in the samples obtained from the control plots (< 0.01 mg/kg in all cases).

Following the field trial phase, the following residue level were found within the sampled spinach plants:

Table 6.5- 4 Residue trials results for fluopicolide treated spinach

Trial No. Country	Sample	Growth stage [BBCH]	DALT	Residues [mg/kg]		
				Fluopicolide	M-01	M-02
E19PR001-01 Germany	Leaves	49	14	1.8	0.069	0.16
	Leaf, stored (RAC)**	49	14	1.6	0.077	0.01
		49	14	2.4	0.089	0.012
		49	14	1.6	0.078	0.013
		Mean*		**1.87**	**0.081**	**0.012**
	Leaf, cooked	49	14	1.1	0.061	0.016
E19PR001-02 Netherlands	Leaves	49	14	1.8	0.13	0.18
	Leaf, stored (RAC)**	49	14	1.6	0.14	0.17
		49	14	1.5	0.13	0.16
		49	14	1.5	0.13	0.16
		Mean*		**1.5**	**0.13**	**0.16**
	Leaf, cooked	49	13	1.2	0.14	0.031
E19PR001-03 Belgium	Leaves	49	13	2.2	0.17	0.22
	Leaf, stored (RAC)**	49	13	0.84	0.12	0.028
		49	13	0.76	0.13	0.024
		49	13	0.79	0.12	0.026
		Mean*		**0.80**	**0.12**	**0.026**
	Leaf, cooked	49	13	0.55	0.10	0.028

DALT: Days after last treatment (for processed commodities it refers to the DALT of the corresponding field sample)

RAC: Raw agricultural commodity

* For the calculations of the processing factor the average of the rounded individual RAC samples was taken. The average values are marked in bold.

** "Leaf , stored" are samples of fresh leaves which were taken from the bulk processing sample and deep-frozen at - - 18 °C at the time the processing began. The residues measured in these samples serve as the basis for the calculation of the processing factors.

The residue transfer factors for each fraction are presented in the following table. This is calculated by dividing the residue found in a fraction, e.g. "leaf, cooked", by the residue in the "Leaf, stored" (RAC).

Table 6.5- 5 Processing factors for washed / cooked spinach leaves

Trial No. Country	Fraction	Residue transfer factor		
		Fluopicolide	M-01	M-02
E19PR001-01 Germany	Spinach leaves, cooked	0.59	0.75	1.3
E19PR001-02 Netherlands	Spinach leaves, cooked	0.80	1.1	1.9
E19PR001-03 Belgium	Spinach leaves, cooked	0.69	0.83	1.1

III. Conclusions

Following the steam-cooking of spinach leaves, treated with fluopicolide, residues of fluopicolide and its metabolites were found in almost all of the samples obtained from the 3 test sites.

The transfer factors of fluopicolide from RAC to cooked leaves ranged from 0.59 to 0.80 (mean value of 0.69).

The transfer factors of metabolite M-01 from RAC to cooked leaves ranged from 0.75 to 1.1 (mean value of 0.89).

The transfer factors of metabolite M-01 from RAC to cooked leaves ranged from 1.1 to 1.9 (mean value of 1.43).

Assessment and conclusion by applicant:

The study is acceptable.

Average processing factors were established based on the results of the study for the processing of the RAC to cooked (steamed) spinach leaves:

FLC: 0.69

M-01 0.89

M-02 1.43

CA 6.6 Residues in rotational crops

A confined rotational crop study using [U-^{14}C-phenyl]-Fluopicolide and [2,6-^{14}C-pyridyl]-Fluopicolide was presented within the DAR for the first inclusion of fluopicolide. The metabolism within succeeding crops was found to be similar, but more extensive as in primary crops. In lettuce, radish tops and radish roots fluopicolide, M-01 and M-02 were identified as main components of the radioactive residues. Additionally, M-05 and M-09 were found in some of the matrices. The main components of radioactive residues in wheat grain, forage and straw were fluopicolide, M-01, M-02, M-04 and M-05. Low concentrations of M-06, M-08 and M-09 were identified in some of the samples. Further details of the results are summarized within the following tables.

Table 6.6- 1 Distribution of fluopicolide and its metabolites in rotational crops in % or the total radioactivity (parent equivalent in mg/kg) – phenyl label

Component	Wheat forage	Wheat grain	Wheat straw	Lettuce	Radish tops	Radish roots
Crop planted in soil for 29 days						
Fluopicolide	36.6 (1.81)	27.3 (0.04)	23.1 (3.13)	11.1 (0.11)	24.5 (1.64)	47.9 (0.07)
M-04	32.7 (1.62)	-	13.6 (1.84)	-	-	-
M-01	6.3 (0.31)	3.6 (<0.01)	3.4 (0.46)	81.2 (0.82)	65.3 (4.38)	43.2 (0.06)
M-06	<1.0 (<0.05)	13.1 (0.02)	-	-	-	-
Crop planted in soil for 133 days						
Fluopicolide	23.3 (0.05)	7.0 (<0.01)	15.5 (0.13)	26.6 (0.03)	15.1 (0.04)	28.2 (<0.01)
M-04	28.9 (0.07)	23.5 (<0.01)	14.6 (0.12)	-	-	-
M-01	5.1 (0.01)	19.0 (<0.01)	25.5 (0.22)	60.9 (0.07)	77.3 (0.19)	54.9 (0.01)
M-06	-	-	-	-	-	-
Crop planted in soil for 365 days						
Fluopicolide	4.8 (0.04)	7.3 (<0.01)	7.2 (0.17)	2.1 (0.01)	3.8 (0.08)	24.2 (<0.01)
M-04	59.3 (0.51)	24.5 (0.01)	28.0 (0.66)	-	-	-
M-01	14.8 (0.13)	17.9 (0.01)	15.1 (0.12)	87.0 (0.53)	87.5 (1.76)	60.9 (0.02)
M-06	-	-	-	-	-	-

Table 6.6- 2 Distribution of fluopicolide and its metabolites in rotational crops in % or the total radioactivity (parent equivalent in mg/kg) – pyridinyl label

Component	Wheat forage	Wheat grain	Wheat straw	Lettuce	Radish tops	Radish roots
Crop planted in soil for 29 days						
Fluopicolide	33.7 (1.45)	1.8 (0.05)	34.9 (2.46)	35.8 (0.11)	51.1 (1.07)	41.1
M-08	-	-	-	-	-	-
M-05	3.8 (0.16)	13.1 (0.34)	7.7 (0.54)	13.0 (0.04)	3.3 (0.07)	9.6 (0.01)
M-02	43.0 (1.84)	69.6 (1.81)	7.0 (0.49)	17.4 (0.05)	10.4 (0.22)	33.5 (0.04)
M-09	-	-	-	5.6 (0.02)	4.8 (0.10)	-
M-06	1.4 (0.06)	-	-	-	-	-
Crop planted in soil for 133 days						
Fluopicolide	26.2 (0.04)	3.2 (<0.01)	25.7 (0.09)	79.9 (0.03)	72.2 (0.17)	54.9 (0.04)
M-08	-	-	9.4 (0.03)	-	-	-
M-05	41.0 (0.06)	66.6 (0.06)	1.2 (<0.01)	-	-	2.9 (<0.01)
M-02	5.4 (<0.01)	10.9 (0.01)	2.1 (<0.01)	-	-	9.6 (<0.01)
M-09	10.5 (0.02)	-	21.5 (0.08)	-	-	19.1 (<0.01)
M-06	-	-	-	-	-	-
Crop planted in soil for 365 days						
Fluopicolide	27.8 (0.07)	2.9 (<0.01)	27.5 (0.28)	41.5 (0.02)	25.2 (0.11)	55.8 (0.02)
M-08	6.3 (0.02)	-	4.8 (0.05)	9 (<0.01)	-	9.5 (<0.01)
M-05	18.3 (0.05)	64.9 (0.11)	14.2 (0.14)	7.8 (<0.01)	5.1 (0.02)	5.3 (<0.01)
M-02	8.2 (0.02)	14.2 (0.03)	4.1 (0.04)	11.8 (<0.04)	27.1 (0.11)	10.0 (<0.01)
M-09	9.9 (0.02)	-	-	3.7 (<0.01)	6.0 (0.03)	-
M-06	-	-	-	-	-	-

Based on the available data presented within in the available rotational crop studies, the potential for fluopicolide residue uptake in succeeding crops cannot be avoided. A plateau concentration level of 800 g a.s. ha has been calculated for fluopicolide, based on a DT50 of 650 days. Taking into account these considerations, the impact of proposing a minimum plant-back interval of 30 DAT (option 1), 120 DAT (option 2) or 365 DAT (option 3) has been investigated.

These new studies conducted according to the advice provided within the OECD "Draft Guidance Document on Residues in Rotational Crops". While the guidance remains in draft form, the principles outlined within the guidance have been previously used by EFSA for MRL setting purposes. As such, data has been generated on crops representative of each of the "super groups", to allow for a wider extrapolation of the residue results to cover all commodities which may be grown in rotation.

These studies are summarised within section CA 6.6.2 of this document.

For all commodities where a representative GAP has been supported at the renewal, a rough estimate to assess whether or not the possible uptake of fluopicolide residues would exceed the MRL derived from primary crop treatment (comparison made on the highest residue values) was performed. If the uptake of residues from rotational crops exceeds the MRL derived from primary treatment, a proposal has been made by the applicant to raise the MRL based on the rotational crops data. In the opposite case, if the uptake of residues is inferior to the MRL derived from primary crop treatment, the applicant maintains to keep the MRL proposal derived from the primary treatment. For all crops that may be grown in rotation but for which GAPs are not sought as part of the renewal, the need for an MRL proposal was estimated on the basis of the results of the rotational crops data. It is noted that, when deriving an MRL proposal from rotational crops data, the OECD calculation method was used, as done for the primary crops.

This methodology was applied to all plant commodities for which MRLs are applied, using the tested crops in the rotational crop studies as surrogates, where appropriate for all the plant back intervals where data are available (30 DAT – option 1, 120 DAT – option 2 and 365 DAT – option 3) an examination of the appropriate values for each commodity was made. The results of this process are included within Table 6.6-3 (option 1), Table 6.6-4 (for option 2), and Table 6.6-5 (for option 3). The worst-case values from each of the proposed plant-back interval scenarios were used within the consumer risk assessment for fluopicolide (refer to section CA 6.9 of this document), in the livestock dietary burden assessment for fluopicolide (refer to section CA 6.4 of this document) and used to support the applicant's MRL proposals for fluopicolide refer to section CA 6.7.2 of this document.

While the residue definition for monitoring (crops) is defined as 'fluopicolide' only, metabolite M-01 (BAM) forms the second component of the residue definition for risk assessment within plant commodities (refer to section CA 6.7.1 of this document for further discussion). For this reason, it is necessary to undertake a similar process to identify the critical STMR and HR values, by comparison of the primary and rotational crop data (as described for fluopicolide). The results of this comparison are included within Table 6.6-6 (for option 1), Table 6.6-7 (for option 2), and Table 6.6-8 (for the option 3). The worst-case values from each of the proposed plant-back interval scenarios were collated and tabulated within Table CA 6.9; these values were used within the consumer risk assessment for M-01 (refer to section CA 6.4 of this document) and in the livestock dietary burden assessment for M-01 (refer to section CA 6.7.2 of this document).

Table 6.6- 3 Comparison of residues in primary crops with those present within succeeding crops following an early plant-back scenario.

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Potatoes †	<0.01	0.013	0.02	Carrot	0.105	0.134	Yes	0.105	0.134	0.3
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Other root and tuber vegetables	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Spice (roots and rhizome)	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Sugar beet	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Other sugar plants	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Witloof	No primary crop data			Carrot §	0.105	0.134	Not applicable	0.105	0.134	0.3
Garlic /shallot	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Onions	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Spring onions	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Other bulb vegetables	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
All stem vegetables (except leek)	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Leek	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Sugar cane	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2
Other sugar plants	No primary crop data			Leek	0.039	0.110	Not applicable	0.039	0.110	0.2

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Cereals	No primary crop data			Barley (grain)	0.093	0.134	Not applicable	0.093	0.134	0.3
Maize	No primary crop data			Maize (kernels)	0.01	0.01	Not applicable	0.01	0.01	0.01*
Lettuce ‡	0.58	1.9	3	Lettuce §	0.057	0.102	No	0.58	1.9	3
Other salad plants	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Spinach and similar leaves	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Spices (seeds)	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Spices (flower stigma)	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Herbs	No primary crop data			Lettuce §	0.057	0.102	Not applicable	0.057	0.102	0.2
Cucumber	0.035	0.09	0.15	Cucumber	0.029	0.043	No	0.035	0.09	0.15
Cucurbits with edible peel	No primary crop data			Cucumber	0.029	0.043	Not applicable	0.029	0.043	0.09
Cucurbits with inedible peel	No primary crop data			Cucumber	0.029	0.043	Not applicable	0.029	0.043	0.09
Strawberries	No primary crop data			Strawberries	0.034	0.039	Not applicable	0.034	0.039	0.09
Sweet corn	No primary crop data			Strawberries	0.034	0.039	Not applicable	0.034	0.039	0.09
Other fruiting vegetables	No primary crop data			Strawberries	0.034	0.039	Not applicable	0.034	0.039	0.09
Oilseed rape	0.01	0.01	0.01*	Oilseed rape	0.027	0.053	Yes	0.027	0.053	0.15
Oilseeds	No primary crop data			Oilseed rape	0.027	0.053	Not applicable	0.027	0.053	0.15

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Pulses	No primary crop data			Peas (dried)	<0.01	0.01	Not applicable	<0.01	0.01	0.02
Legumes	No primary crop data			Peas (in pods)	<0.01	0.01	Not applicable	<0.01	0.01	0.01*
Flowering brassica	No primary crop data			Cauliflower	<0.01	0.01	Not applicable	<0.01	0.01	0.02
Head brassica	No primary crop data			Head cabbage	<0.01	0.01	Not applicable	<0.01	0.01	0.03

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2 x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1, where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

Table 6.6- 4 Comparison of residues in primary crops with those present within succeeding crops following an mid-season plant-back scenario.

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Potatoes †	<0.01	0.013	0.02	Carrot §	0.06	0.07	Yes	0.06	0.07	0.2
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Other root and tuber vegetables	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Spice (roots and rhizome)	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Sugar beet	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Other sugar plants	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Witloof	No primary crop data			Carrot §	0.06	0.07	Not applicable	0.06	0.07	0.2
Garlic /shallot	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Onions	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Spring onions	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Other bulb vegetables	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
All stem vegetables (except leek)	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Leek	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Sugar cane	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15
Other sugar plants	No primary crop data			Leek	0.042	0.066	Not applicable	0.042	0.066	0.15

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Cereals	No primary crop data			Barley (grain)	0.04	0.077	Not applicable	0.04	0.077	0.15
Maize	No primary crop data			Maize (kernels)	0.01	0.01	Not applicable	0.01	0.01	0.01*
Lettuce ‡	0.58	1.9	3	Lettuce §	0.041	0.068	No	0.58	1.9	3
Other salad plants	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Spinach and similar leaves	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Spices (seeds)	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Spices (flower stigma)	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Herbs	No primary crop data			Lettuce §	0.041	0.068	Not applicable	0.041	0.068	0.15
Cucumber	0.035	0.09	0.15	Cucumber	0.019	0.04	No	0.035	0.09	0.15
Cucurbits with edible peel	No primary crop data			Cucumber	0.019	0.04	Not applicable	0.019	0.04	0.07
Cucurbits with inedible peel	No primary crop data			Cucumber	0.019	0.04	Not applicable	0.019	0.04	0.07
Strawberries	No primary crop data			Strawberries	0.02	0.028	Not applicable	0.02	0.028	0.05
Sweet corn	No primary crop data			Strawberries	0.02	0.028	Not applicable	0.02	0.028	0.05
Other fruiting vegetables	No primary crop data			Strawberries	0.02	0.028	Not applicable	0.02	0.028	0.05
Oilseed rape	0.01	0.01	0.01*	Oilseed rape	0.022	0.029	Yes	0.022	0.029	0.07
Oilseeds	No primary crop data			Oilseed rape	0.022	0.029	Not applicable	0.022	0.029	0.07

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Pulses	No primary crop data			Peas (dried)	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Legumes	No primary crop data			Peas (in pods)	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Flowering brassica	No primary crop data			Cauliflower	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Head brassica	No primary crop data			Head cabbage	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2 x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1, where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

Table 6.6- 5 Comparison of residues in primary crops with those present within succeeding crops following a typical annual plant-back scenario.

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Potatoes †	<0.01	0.013	0.02	Carrot §	0.033	0.06	Yes	0.033	0.06	0.15
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Other root and tuber vegetables	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Spice (roots and rhizome)	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Sugar beet	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Other sugar plants	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Witloof	No primary crop data			Carrot §	0.033	0.06	Not applicable	0.033	0.06	0.15
Garlic /shallot	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Onions	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Spring onions	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Other bulb vegetables	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
All stem vegetables (except leek)	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Leek	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Sugar cane	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15
Other sugar plants	No primary crop data			Leek	0.027	0.077	Not applicable	0.027	0.077	0.15

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Cereals	No primary crop data			Barley (grain)	0.027	0.06	Not applicable	0.027	0.06	0.15
Maize	No primary crop data			Maize (kernels)	0.01	0.01	Not applicable	0.01	0.01	0.01*
Lettuce ‡	0.58	1.9	3	Lettuce §	0.022	0.041	No	0.58	1.9	3
Other salad plants	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Spinach and similar leaves	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Spices (seeds)	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Spices (flower stigma)	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Herbs	No primary crop data			Lettuce §	0.022	0.041	Not applicable	0.022	0.041	0.08
Cucumber	0.035	0.09	0.15	Cucumber	0.01	0.025	No	0.035	0.09	0.15
Cucurbits with edible peel	No primary crop data			Cucumber	0.01	0.025	Not applicable	0.01	0.025	0.04
Cucurbits with inedible peel	No primary crop data			Cucumber	0.01	0.025	Not applicable	0.01	0.025	0.04
Strawberries	No primary crop data			Strawberries	0.018	0.021	Not applicable	0.018	0.021	0.06
Sweet corn	No primary crop data			Strawberries	0.018	0.021	Not applicable	0.018	0.021	0.06
Other fruiting vegetables	No primary crop data			Strawberries	0.018	0.021	Not applicable	0.018	0.021	0.06
Oilseed rape	0.01	0.01	0.01*	Oilseed rape	-	-	-	-	-	-
Oilseeds	No primary crop data			Oilseed rape	-	-	Not applicable	-	-	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Fluopicolide – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Pulses	No primary crop data			Peas (dried)	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Legumes	No primary crop data			Peas (in pods)	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Flowering brassica	No primary crop data			Cauliflower	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*
Head brassica	No primary crop data			Head cabbage	<0.01	<0.01	Not applicable	<0.01	<0.01	0.01*

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2 x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1, where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

Table 6.6- 6 Comparison of residues in primary crops with those present within succeeding crops following an early plant-back scenario

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Potatoes †	<0.01	<0.01	-	Carrot §	0.022	0.031	Yes	0.022	0.031	-
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Other root and tuber vegetables	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Spice (roots and rhizome)	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Sugar beet	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Other sugar plants	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Witloof	No primary crop data			Carrot §	0.022	0.031	Not applicable	0.022	0.031	-
Garlic /shallot	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Onions	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Spring onions	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Other bulb vegetables	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
All stem vegetables (except leek)	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Leek	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Sugar cane	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-
Other sugar plants	No primary crop data			Leek	0.01	0.022	Not applicable	0.01	0.022	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Cereals	No primary crop data			Barley (grain)	0.021	0.08	Not applicable	0.021	0.08	-
Maize	No primary crop data			Maize (kernels)	0.01	0.02	Not applicable	0.01	0.02	-
Lettuce ‡	0.011	0.028	-	Lettuce §	0.054	0.187	Yes	0.054	0.187	-
Other salad plants	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Spinach and similar leaves	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Spices (seeds)	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Spices (flower stigma)	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Herbs	No primary crop data			Lettuce §	0.054	0.187	Not applicable	0.054	0.187	-
Cucumber	<0.01	<0.01	-	Cucumber	0.019	0.03	Yes	0.019	0.03	-
Cucurbits with edible peel	No primary crop data			Cucumber	0.019	0.03	Not applicable	0.019	0.03	-
Cucurbits with inedible peel	No primary crop data			Cucumber	0.019	0.03	Not applicable	0.019	0.03	-
Strawberries	No primary crop data			Strawberries	0.02	0.07	Not applicable	0.02	0.07	-
Sweet corn	No primary crop data			Strawberries	0.02	0.07	Not applicable	0.02	0.07	-
Other fruiting vegetables	No primary crop data			Strawberries	0.02	0.07	Not applicable	0.02	0.07	-
Oilseed rape	<0.01	<0.01	-	Oilseed rape	0.08	0.25	Yes	0.08	0.25	-
Oilseeds	No primary crop data			Oilseed rape	0.08	0.25	Not applicable	0.08	0.25	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 1: Comparison of the primary crop data with data for succeeding crops planted ca. 25-30 days after application (representative of crop failure scenario)										
Pulses	No primary crop data			Peas (dried)	0.01	0.02	Not applicable	0.01	0.02	-
Legumes	No primary crop data			Peas (in pods)	0.03	0.07	Not applicable	0.03	0.07	-
Flowering brassica	No primary crop data			Cauliflower	<0.01	<0.01	Not applicable	<0.01	<0.01	-
Head brassica	No primary crop data			Head cabbage	0.01	0.01	Not applicable	0.01	0.01	-

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2 x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1, where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

Table 6.6- 7 Comparison of residues in primary crops with those present within succeeding crops following a mid-season plant-back scenario.

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Potatoes †	<0.01	<0.01	-	Carrot §	0.019	0.061	Yes	0.019	0.061	-
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Other root and tuber vegetables	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Spice (roots and rhizome)	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Sugar beet	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Other sugar plants	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Witloof	No primary crop data			Carrot §	0.019	0.061	Not applicable	0.019	0.061	-
Garlic /shallot	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Onions	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Spring onions	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Other bulb vegetables	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
All stem vegetables (except leek)	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Leek	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Sugar cane	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-
Other sugar plants	No primary crop data			Leek	0.013	0.068	Not applicable	0.013	0.068	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Cereals	No primary crop data			Barley (grain)	0.018	0.027	Not applicable	0.018	0.027	-
Maize	No primary crop data			Maize (kernels)	0.01	0.01	Not applicable	0.01	0.01	-
Lettuce ‡	0.011	0.028	-	Lettuce §	0.082	0.255	Yes	0.082	0.255	-
Other salad plants	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Spinach and similar leaves	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Spices (seeds)	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Spices (flower stigma)	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Herbs	No primary crop data			Lettuce §	0.082	0.255	Not applicable	0.082	0.255	-
Cucumber	<0.01	<0.01	-	Cucumber	0.024	0.082	Yes	0.024	0.082	-
Cucurbits with edible peel	No primary crop data			Cucumber	0.024	0.082	Not applicable	0.024	0.082	-
Cucurbits with inedible peel	No primary crop data			Cucumber	0.024	0.082	Not applicable	0.024	0.082	-
Strawberries	No primary crop data			Strawberries	0.03	0.044	Not applicable	0.03	0.044	-
Sweet corn	No primary crop data			Strawberries	0.03	0.044	Not applicable	0.03	0.044	-
Other fruiting vegetables	No primary crop data			Strawberries	0.03	0.044	Not applicable	0.03	0.044	-
Oilseed rape	<0.01	<0.01	-	Oilseed rape	0.09	0.19	Yes	0.09	0.19	-
Oilseeds	No primary crop data			Oilseed rape	0.09	0.19	Not applicable	0.09	0.19	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 2: Comparison of the primary crop data with data for succeeding crops planted ca. 120-180 days after application (representative of two crops planted in one year)										
Pulses	No primary crop data			Peas (dried)	<0.01	0.01	Not applicable	<0.01	0.01	-
Legumes	No primary crop data			Peas (in pods)	0.04	0.07	Not applicable	0.04	0.07	-
Flowering brassica	No primary crop data			Cauliflower	0.01	0.03	Not applicable	0.01	0.03	-
Head brassica	No primary crop data			Head cabbage	0.01	0.02	Not applicable	0.01	0.02	-

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2 x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1, where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

Table 6.6- 8 Comparison of residues in primary crops with those present within succeeding crops following a typical annual plant-back scenario.

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Potatoes †	<0.01	<0.01	-	Carrot §	0.02	0.039	Yes	0.02	0.039	-
Tropical root and tuber vegetables	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Other root and tuber vegetables	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Spice (roots and rhizome)	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Sugar beet	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Other sugar plants	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Herbal infusion (dried roots)	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Witloof	No primary crop data			Carrot §	0.02	0.039	Not applicable	0.02	0.039	-
Garlic /shallot	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Onions	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Spring onions	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Other bulb vegetables	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
All stem vegetables (except leek)	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Leek	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Sugar cane	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-
Other sugar plants	No primary crop data			Leek	0.01	0.1	Not applicable	0.01	0.1	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Cereals	No primary crop data			Barley (grain)	<0.01	0.014	Not applicable	<0.01	0.014	-
Maize	No primary crop data			Maize (kernels)	<0.01	<0.01	Not applicable	<0.01	<0.01	-
Lettuce ‡	0.011	0.028	-	Lettuce §	0.137	0.187	Yes	0.137	0.187	
Other salad plants	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Spinach and similar leaves	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Herbal infusion (dried flowers)	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Herbal infusion (dried leaves)	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Spices (seeds)	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Spices (flower stigma)	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Herbs	No primary crop data			Lettuce §	0.137	0.187	Not applicable	0.137	0.187	-
Cucumber	<0.01	<0.01		Cucumber	0.03	0.037	Yes	0.03	0.037	-
Cucurbits with edible peel	No primary crop data			Cucumber	0.03	0.037	Not applicable	0.03	0.037	-
Cucurbits with inedible peel	No primary crop data			Cucumber	0.03	0.037	Not applicable	0.03	0.037	-
Strawberries	No primary crop data			Strawberries	0.03	0.045	Not applicable	0.03	0.045	-
Sweet corn	No primary crop data			Strawberries	0.03	0.045	Not applicable	0.03	0.045	-
Other fruiting vegetables	No primary crop data			Strawberries	0.03	0.045	Not applicable	0.03	0.045	-
Oilseed rape	<0.01	<0.01		Oilseed rape	-	-	-	-	-	-
Oilseeds	No primary crop data			Oilseed rape	-	-	Not applicable	-	-	-

Commodity	Primary crop data (mg/kg)			Rotational crop data (mg/kg)			HR rotation > HR primary	Final proposal (mg/kg)		
	STMR	HR	MRL	Surrogate crop (study ref.)	STMR	HR		STMR	HR	MRL
Metabolite M-01 (BAM) – Option 3: Comparison of the primary crop data with data for succeeding crops planted ca. 300-365 days after application (representative of a typical annual crop)										
Pulses	No primary crop data			Peas (dried)	<0.01	<0.01	Not applicable	<0.01	<0.01	-
Legumes	No primary crop data			Peas (in pods)	0.04	0.11	Not applicable	0.04	0.11	-
Flowering brassica	No primary crop data			Cauliflower	0.01	0.03	Not applicable	0.01	0.03	-
Head brassica	No primary crop data			Head cabbage	0.01	<0.01	Not applicable	0.01	0.01	-

† Potatoes – based on the GAP leading to the highest residue levels: 3 x 100 g FLC / ha (per crop)

‡ Lettuce – based on the GAP leading to the highest residue levels: 2x 100 g FLC / ha (per crop)

§ Data originate from the study M-623459-02-1 where a nominal rate of 0.7 kg FLC/ha was applied to / incorporated into bare soil before sowing / transplanting the following crops. In the time since this study was completed, further calculations have been made. The DT_{50} for fluopicolide in soil of 650 days results in a plateau concentration of 0.8 kg FLC/ha. The plateau concentration combined with the annual application rate of FLC is 0.4 kg FLC/ha (for potatoes) and leads to a final application rate of 1.2 kg FLC/ha – this target application rate was used in all the other rotational crop studies referred to in this table. Consequently, the proportionality principle has been applied to data generated in M-623459-02-1 by a scaling factor of 1.7 (derived from the ratio of the rates: 1.2 / 0.7).

◊ Combined data for barley from separate sources: M-623459-02-1 and M-679637-01-1

CA 6.6.1 Metabolism in rotational crops

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.6.1/01
Report Author:	[redacted]
Report Year:	2003
Report Title:	Uptake of [14C]-AE C638206 residues in soil by rotational crops under confined conditions
Report No:	B004552
Document No:	M-240707-03-1
Guideline(s) followed in study:	EU (=EEC): 91/414; EC 7524/VI95 Rev. 2; USEPA (=EPA): OPPTS 860.1850
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

On characterisation of the extractable radioactivity three major component were identified in the crops at harvest in the 29-day study as parent fluopicolide and its metabolites M-01 (phenyl label metabolite only) and M-02 (pyridinyl label metabolite only).

For lettuce the three components accounted for 92% (phenyl study) and 50% (pyridinyl study) of the total radioactivity in the crop at harvest. Several other metabolites were identified in the 29-day studies, plus several unknowns which individually were present at levels of less than 0.05 mg/kg. In the 133-day study (representing the usual rotation), again the three components accounted for the majority of the identified radioactivity (88% phenyl study; 53% pyridinyl study) at harvest.

For radish tops the three components accounted for 90% (phenyl study) and 62% (pyridinyl study) of the total radioactivity in the crop at harvest. Several other metabolite were identified in the 29 day studies, plus several unknowns which individually were present at levels of at or less than 0.11 mg/kg, with the exception of an unknown present at a level of 0.14 mg/kg which was postulated to be a conjugate (e.g. glucose) of the parent. In the 133-day study (representing the usual rotation), again the three components accounted for the majority of the identified radioactivity (92% phenyl study; 72% pyridinyl study) at harvest.

For radish root (tops not normally consumed) the three components accounted for 91% (phenyl study) and 75% (pyridinyl study) of the total radioactivity in the crop at harvest. One other metabolite was identified in the 29-day studies, plus several unknowns which individually were present at levels of less than 0.02 mg/kg. In the 133-day study (representing the usual rotation), again the three components accounted for the majority of the identified radioactivity (83% phenyl study; 65% pyridinyl study) at harvest.

For wheat grain the three components accounted for 31% (phenyl study) and 72% (pyridinyl study) of the total radioactivity in the crop at harvest. Several other metabolites were identified in the 29-day studies, plus several unknowns which individually were present at levels of at or less than 0.05 mg/kg, with the exception of M-05 (0.34 mg/kg). In the 133-day study (representing the usual rotation), fluopicolide and its metabolite M-01 were again the major components present in the phenyl study accounting for 26% of the radioactivity at harvest. However, in the pyridinyl label study fluopicolide and its metabolites M-02 only accounted for 14% of the total radioactivity at harvest, while M-05

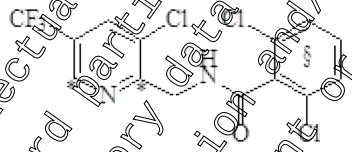
accounting for 67% (0.06 mg/kg). For wheat straw the three components accounted for 26% (phenyl study) and 42% (pyridinyl study) of the total radioactivity in the crop at harvest. Two other metabolites were identified in the 29 day studies M-04 and M-05, accounting for 14 and 8% of the total radioactivity in the crop at harvest respectively, plus several unknowns which individually were present at levels of at or less than 0.6 mg/kg, the majority of which were postulated to be conjugates (e.g. glucose) of the parent. In the 133-day study (representing the usual rotation), again the three components accounted for the majority of the identified radioactivity (41% phenyl study; 28% pyridinyl study) at harvest.

I. Materials and Methods

A. Materials

1. Test Material:

Chemical structure



Label positions:
§ = [U-^{14}C-phenyl]-Fluopicolide
* = [2,6-^{14}C-pyridyl]-Fluopicolide

Radiolabelled test material	[2,6^{14}C-pyridyl] or [U-^{14}C-phenyl] labelled Fluopicolide
Specific radioactivity	[U-^{14}C-phenyl]-Fluopicolide = 159 µCi/mg [2,6-^{14}C-pyridyl]-Fluopicolide = 144 µCi/mg
Batch Number	[U-^{14}C-phenyl]-Fluopicolide = 902AE-1 [2,6-^{14}C-pyridyl]-Fluopicolide = 903AE-1
Radiochemical purity	>99% for both radiolabelled test items

2. Soil: Experimental plots were filled with a sandy loam soil. The soil characteristics are listed below.

Table 6.6.1- 1 Physico-chemical characteristics of the soil used in the confined crop rotation study

Characteristic	Units	Lab ID 530
Origin	State, Country	North Carolina, USA
Location	City or Township	Pikeville
Particle Size Analysis, USDA		
Total Sand	(0.05 - 2.0 mm)	76.9%
Silt	(0.002 - 0.05 mm)	13.5%
Clay	(<0.002 mm)	9.6%
Textural Class	USDA	Sandy Loam
pH	Water (1:1)	6.2
	0.01 M $CaCl_2$ (1:1)	5.7
Organic Matter	%	0.81
Cation Exchange Capacity	meq/100g	1.87
Water Holding Capacity	% at Saturation	17.27
	% at 1/3 bar	7.12
	% at 15 bar	1.53
Bulk Density (disturbed)	g/cm^3	1.55

3. Plants:

29 days after treatment (30 April 1999) two test plots and the control plot were planted with crops. Each plot was divided into thirds and each third allocated to one of the three crops. The rotational crops were lettuce var. Black-seeded Simpson (leafy vegetable), spring wheat var. Butte 86 (cereal) and radishes var. Cherry Belle (root crop).

At 133 days after treatment, on the 27 October and 28 October 1999 for the [2,6-^{14}C-pyridyl]-labelled and [U-^{14}C-phenyl]-labelled plots respectively, the remaining two test plots and the control plot were planted with crops as before. Winter wheat var. Coker 9803 was planted in the 133 day plot due to the different season.

Finally the 29 day study plots were replanted for the 1 year sowings. On the 31 March 2000, 365 days after treatment the test plots were replanted with lettuce var. Black-seeded Simpson (leafy vegetable), spring wheat var. Butte 86 (cereal) and radishes var. Cherry Belle (root crop).

B. Study Design

1. Experimental conditions:

Test plots were contained in tanks, 83.8 cm by 152.4 cm, constructed of aluminized steel. The depth in one-third of the tank was 61 cm, while the remaining two-thirds were 30.5 cm deep. The deeper section was planted with wheat. The tanks were buried to within about 5 cm of the rim and filled with sandy loam soil. Two plots were used for each radiolabelled treatment, with one designated for the 29 day and 365 day ageing periods and one for the 133 day ageing period. A fifth plot remained uncreated to provide control crops. The test site was located at Aventis CropScience Research Farm in Pikeville, North Carolina, USA.

[2,6-^{14}C-pyridyl]- or [U-^{14}C-phenyl] labelled fluopicolide (AE C638206) was applied to plots of bare soil at an application rate equivalent to 400 g /ha. The radiochemical purity was > 99% for both radiolabelled test items. The initial specific activity of the [2,6-^{14}C-pyridyl] and [U-^{14}C-phenyl] labelled fluopicolide (AE C638206) was 144 and 159 µCi/mg, respectively. The radiolabelled treatment solutions were formulated separately. Radiolabelled and non-labelled fluopicolide (AE C638206) were milled together with blank formulation to prepare a 20SC (suspension concentrate) formulation equivalent to that planned for commercialisation. Prior to application, 0.05% (v/v) Crodamol PC® was added as an adjuvant to the formulation. The final specific activity of the test item applied to the plots was *ca*. 40 µCi/mg. The target application rate was 400 g as/ha and the actual application rates achieved are summarised below. Formulated test material was applied evenly to each plot by hand held sprayer.

Table 6.6.1- 2 Fluopicolide (AE C638206) Application Details

Description	Plot Number	Radiolabel	Final specific activity (µCi/mg)	AE C638206 applied (mg)	Application rate (g as/ha)
29 / 365 day	4B	U-^{14}C-phenyl	39.6	51.2	400
133 day	4C	U-^{14}C-phenyl	41.5	51.3	401
29 / 365 day	8B	2,6-^{14}C-pyridyl	39.9	51.3	401
133 day	8C	2,6-^{14}C-pyridyl	40.1	51.7	404

Both combined 29 and 365 day plots were treated on the 1 April 1999. The 133 day plot treated with [2,6-^{14}C-pyridyl]-labelled fluopicolide (AE C638206) was treated on the 17 June 1999 and the plot treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) on the 18 June 1999.

29 days after treatment (30 April 1999) two test plots and the control plot were planted with crops. Each plot was divided into thirds and each third allocated to one of the three crops. The rotational crops were

lettuce var. Black-seeded Simpson (leafy vegetable), spring wheat var. Butte 86 (cereal) and radishes var. Cherry Belle (root crop).

At 133 days after treatment, on the 27 October and 28 October 1999 for the [2,6^{14}C-pyridyl]-labelled and [U-^{14}C-phenyl]-labelled plots respectively, the remaining two test plots and the control plot were planted with crops as before. Winter wheat var. Coker 9803 was planted in the 133-day plot due to the different season.

Finally, the 29 day study plots were replanted for the 1 year sowings. On the 31 March 2000, 365 days after treatment the test plots were replanted with lettuce var. Black-seeded Simpson (leafy vegetable), spring wheat var. Butte 86 (cereal) and radishes var. Cherry Belle (root crop).

2. Sampling:

Raw Agricultural Commodities (RAC) sampled for this study included immature wheat, mature wheat straw (including hulls) and wheat grain, mature radish tops and roots, and mature lettuce. Immature wheat was taken at a stage corresponding to forage. Triplicate samples of lettuce and radishes were taken from the treated plots. Due to the limited amount of crop available, single samples of treated wheat were taken. Control crops were taken as single samples.

In addition, soil cores from critical timepoints (treatment, planting and harvest) were also taken and analysed.

C. Analytical Procedures

TRR values of raw agricultural commodities and soil samples were quantified by combustion. Samples with a TRR ≥ 0.01 mg eq./kg were extracted for further analysis.

1. Extraction:

When necessary, harvested crops were dried briefly in air and then stored frozen at -15 ºC. Crop samples were chopped in a flail chopper, if necessary, and ground in a disc mill with sufficient dry ice to keep the sample thoroughly frozen during homogenisation. Ground samples were returned to the freezer to allow the dry ice to sublime and for storage until analysis. Total radioactive residues in plant samples were determined by combustion of aliquots of the ground samples followed by liquid scintillation counting (LSC).

Radioactive residues were detected in all treated crops and were consequently subjected to extraction procedures to allow metabolite characterisation/identification. Sub-samples of selected samples were extracted three times with acetonitrile and acetonitrile/water (1:1) at ambient temperature. All crops from the first planting and where necessary, wheat RACs from the later plantings were further extracted with acetonitrile/water (4:1) in a Soxhlet apparatus for 16 hours. The acetonitrile extract and the acetonitrile/water extracts were combined and concentrated. In cases where a precipitate occurred upon concentration, the sample was centrifuged and decanted. The solid was typically suspended in methanol/water (1:1), then centrifuged and decanted again. The supernatants were combined and concentrated. Recoveries throughout the sample processing were generally good.

Extracted fibre samples containing significant (>0.05 ppm) residues were subjected to acid hydrolysis. An aliquot of fibre was combined with 1 N hydrochloric acid and heated at approximately 50°C for 24 hours. Extracted fibres which still contained significant radioactivity were subjected to further hydrolysis. An aliquot was combined with 2 N sodium hydroxide and heated to reflux for two hours. The extracts were filtered and the filtrates were partitioned with ethyl acetate at acidic, neutral and basic pH. The radioactive content of extracts and concentrated extracts was determined by direct LSC and that of post-extraction residues by combustion followed by LSC.

2. Identification and characterisation:

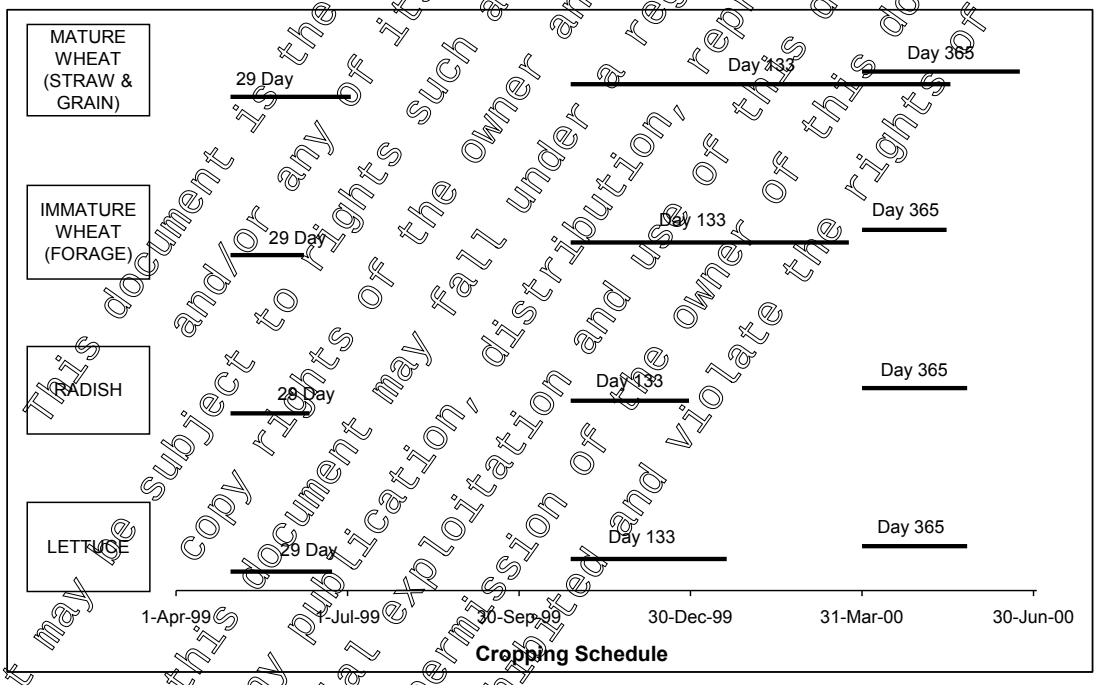
Initial characterisation of plant extracts was performed by thin layer chromatography (TLC) and included analysis to establish storage stability of samples.

High performance liquid chromatography (HPLC) was used for the quantitation and identification of metabolites for which standards were available. Confirmation of metabolite identification was carried out using liquid chromatography-mass spectrometry (LC-MS). To further characterise and quantify unidentified components, aliquots of 29 Day wheat forage and straw were transferred to the cooperating Bayer CropScience laboratories in Germany where they were analysed by HPLC and LC-MS.

II. Results and Discussion

Total residues declined with longer soil ageing. Mean residues in 29-day RAC's ranged from 0.09 ppm (radish root) to 13.56 ppm (wheat straw), but residues declined greatly in the 133-day and 365-day ageing periods. The 133-day crop residues ranged from 0.02 ppm (radish root) to 0.84 (wheat straw). The 365-day crop residues were observed to increase slightly, ranging from 0.02 ppm (radish root) to 2.37 ppm (wheat straw). This is a result of seasonal variation. The 133-day plots were planted in October and developed through the winter. In contrast, the 365 Day plots were planted in March and developed through the summer when the plants would be more metabolically active (see figure below).

Figure 6.6.1- 1 Growing Period of Crops from Planting to Harvest



The 133-day plot (phenyl label) was flooded by the rain of Hurricane Floyd on 16 September 1999 (91 days after treatment). Planting was delayed until the soil was sufficiently dry. It was not considered to influence the crop residues.

Total radioactive residues (TRR) in raw agricultural commodities grown in treated soil plots are given in the following table. The levels of radioactivity in control crops were negligible.

Table 6.6.1- 3 Total radioactive residues (mg/kg AE C638206 equivalents) in crops (mean values)

Phenyl Label			
Crop	Total Radioactive Residue (mg/kg AE C638206 equivalents)		
	29 Day	133 Day	365 Day
Lettuce	1.01	0.10	0.53
Radish Tops	6.40	0.23	1.75
Radish Roots	0.13	0.02	0.03
Immature Wheat	4.95	0.22	0.86
Wheat Grain	0.16	0.02	0.05
Wheat Straw	13.56	0.84	2.37
Pyridyl Label			
Crop	Total Radioactive Residue (mg/kg AE C638206 equivalents)		
	29 Day	133 Day	365 Day
Lettuce	0.27	0.03	0.05
Radish Tops	1.96	0.23	0.40
Radish Roots	0.09	0.02	0.02
Immature Wheat	4.29	0.16	0.24
Wheat Grain	2.60	0.10	0.18
Wheat Straw	7.05	0.35	1.01

The distribution of radioactivity following extraction of crop samples is given in the following table. Residues in all RACs were characterised as extractable with acetonitrile, extractable by acetonitrile/water (1:1), with acetonitrile/water Soxhlet, or non-extractable. The percent of extractable residues was generally consistent in each RAC across the ageing periods. In most RACs, the large majority of radioactivity was recovered in the acetonitrile extract. The exceptions were wheat grain and straw, where a significant percentage was found in the more polar extracts, and which had a higher percentage of non-extractable residue.

Table 6.6.1- 4 Distribution of total radioactive residues (% TRR and mg/kg AE C638206 equivalents) in RACs following extraction

a) Phenyl label

Plot (Day)	Crop Part	Total Radioactive Residue *	Extractable		Non-Extractable Residue	
		mg/kg	%TRR	mg/kg	%TRR	mg/kg
29	Lettuce	1.013	98.1	0.994	1.9	0.019
	Radish Tops	6.705	98.4	6.659	0.7	0.046
	Radish Roots	0.143	97.4	0.139	2.6	0.004
	Wheat Forage	4.949	95.4	4.723	4.6	0.226
	Wheat Grain	0.158	79.9	0.137	13.5	0.021
	Wheat Straw	13.560	71.4	9.680	28.6	3.881
133	Lettuce	0.115	96.5	0.111	3.5	0.004
	Radish Tops	0.240	98.3	0.237	1.7	0.004
	Radish Roots	0.023	96.8	0.023	3.2	0.001
	Wheat Forage	0.225	92.3	0.210	6.7	0.015
	Wheat Grain	0.020	65.3	0.013	35.8	0.007
	Wheat Straw	0.843	84.6	0.713	15.4	0.130
365	Lettuce	0.619	97.0	0.600	3.0	0.019
	Radish Tops	2.006	98.8	1.981	1.2	0.024
	Radish Roots	0.036	96.2	0.034	3.9	0.001
	Wheat Forage	0.865	92.7	0.803	7.3	0.063
	Wheat Grain	0.054	65.7	0.035	34.3	0.019
	Wheat Straw	2.373	64.8	1.538	35.2	0.835

b) Pyridyl label

Plot (Day)	Crop Part	Total Radioactive Residue *	Extractable		Non-Extractable Residue	
		mg/kg	%TRR	mg/kg	%TRR	mg/kg
29	Lettuce	0.302	95.2	0.288	4.8	0.015
	Radish Tops	2.097	98.8	2.072	1.2	0.025
	Radish Roots	0.116	97.5	0.113	2.5	0.003
	Wheat Forage	4.288	97.5	4.183	2.5	0.105
	Wheat Grain	2.600	93.3	2.426	6.7	0.175
	Wheat Straw	7.054	93.8	6.616	6.2	0.438
133	Lettuce	0.034	96.8	0.033	3.2	0.001
	Radish Tops	0.237	99.0	0.235	1	0.002
	Radish Roots	0.025	95.1	0.024	4.9	0.001
	Wheat Forage	0.156	97.2	0.151	2.8	0.004
	Wheat Grain	0.096	94.0	0.090	6	0.006
	Wheat Straw	0.348	93.5	0.324	6.5	0.023
365	Lettuce	0.058	89.6	0.051	10.4	0.006
	Radish Tops	0.419	96.5	0.405	3.5	0.015
	Radish Roots	0.032	95.0	0.030	5	0.002
	Wheat Forage	0.243	93.7	0.228	6.3	0.015
	Wheat Grain	0.178	94.2	0.168	5.8	0.010
	Wheat Straw	1.009	87.3	0.880	12.7	0.128

%TRR = % of total radioactive residue *TRR for individual samples subject to extraction

Non-extractable residue (NER) was less than 10% or less than 0.05 mg/kg in most RACs with exception of some wheat forage and straw. Non-extractable residue greater than 10% and greater than 0.05 mg/kg were subjected to extraction with 1 N hydrochloric acid followed by 2 N sodium hydroxide. Radioactive residue which remained non-extractable after sequential treatment with acid and base was less than 0.05 mg/kg, except in 29-day wheat straw (phenyl) where 0.310 mg/kg represented only 2.4% of the total radioactive residue.

Filtrates from the acid or base hydrolysis, where they exceeded 0.05 mg/kg, were partitioned into organic and aqueous fractions.

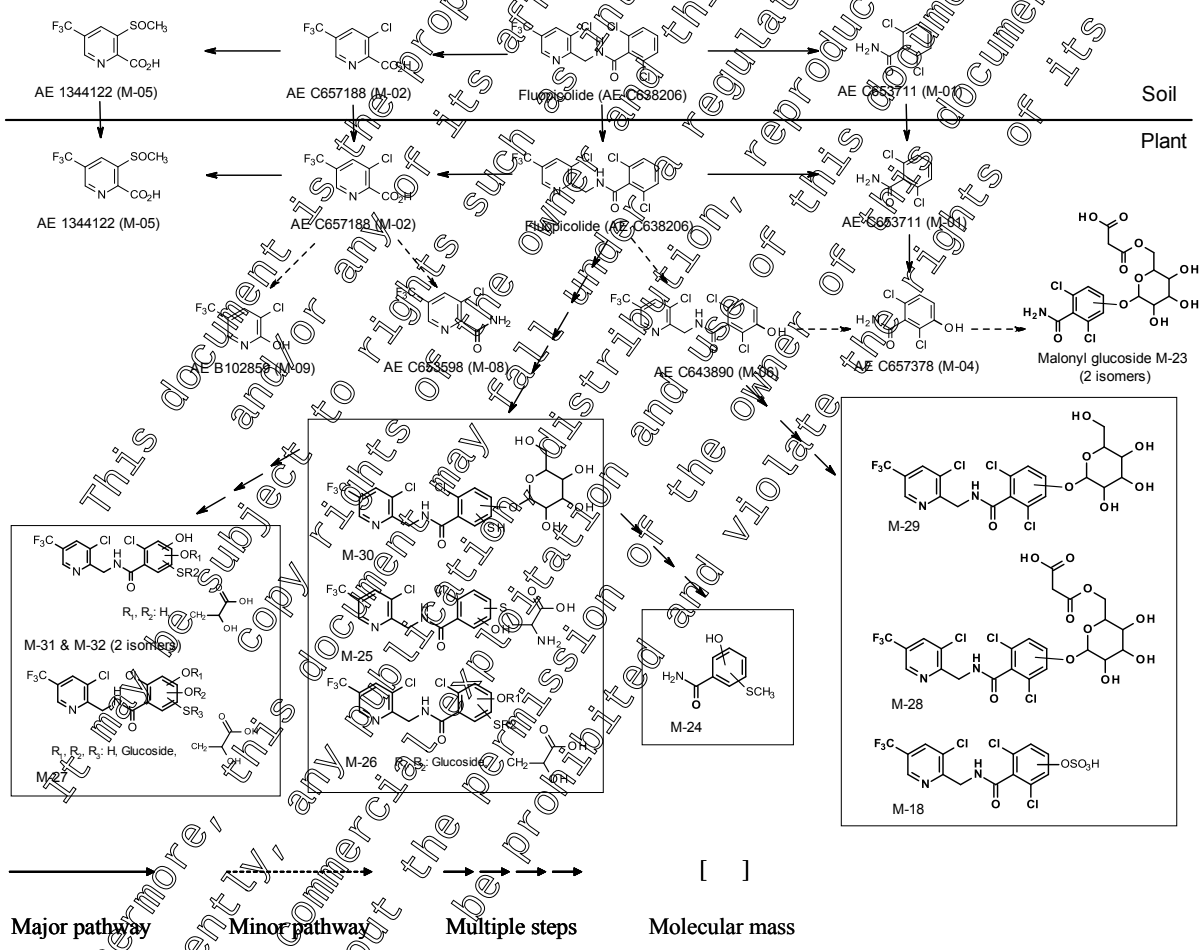
Storage Stability:

TLC analysis confirmed no significant changes in the sample composition of samples harvested following the 29-day planting for up to 1018-days storage at -15 ºC. Quantification of the residue components was established within this time, although analysis to enable characterisation and identification of residue continued past these timepoints. The principal metabolites identified in phenyl-labelled and pyridyl-labelled experiments were found at each planting period. Thus, the storage stability established with samples harvested after the 29-day planting also covered the storage period of the RACs harvested after the 133 and 365-day plantings.

Characterisation and Identification of Residues:

The characterisation and identification of residues in lettuce, radish and wheat is summarised in the following sections. An overview of the metabolic route of fluopicolide (AE C638206) in rotational crops is given in the following figure.

Figure 6.6.1- 2 The Proposed Metabolic Pathway for AE C638206 in Confined Rotational Crops



It was not possible to define the position of substituents in the phenyl ring by mass spectroscopy. Co-chromatography with reference standards confirmed the hydroxyl groups in M-06 (AE C643890) and M-04 (AE C657378) as being in the 3 position and therefore the most probable position of the conjugates in the structures marked (*) is also in the 3 position.

Fluopicolide (AE C638206) and its metabolites M-01 (AE C653711; from the phenyl ring) and M-02 (AE C657188; from the pyridyl ring) were detected in all crops. M-01 (AE C653711) and M-02 (AE C657188) were not thought to be formed in plants directly but formed part of the crop residue by plant uptake from soil. M-02 (AE C657188) is known to be rapidly metabolised to M-05 (AE 1344122) in soil. No metabolites other than M-01 (AE C653711) have been detected in soil arising from the phenyl ring. The soil metabolite M-03 (AE 0608000) was not detected in rotational crops as it is rapidly hydrolysed even in acidic soils in which it is most stable. The metabolite was observed at low levels in an aerobic soil laboratory study conducted with the parent in Pikeville soil. Although M-03 (AE 0608000) was not identified in soil analysis conducted as part of the confined crop rotation study, it would be expected to have formed in the soil.

fluopicolide (AE C638206) taken up by rotational crops was further metabolised to form hydroxylated or thiolated (addition of –SH) versions of the parent, and then formed a variety of conjugates with glucose, malonic acid, glyceric acid or amino acids. Occasionally very low concentrations of the free hydroxylated parent fluopicolide (AE C638206) were observed in wheat. These plant detoxification mechanisms were most significant in wheat forage and straw. All the derivatisation observed was associated with the phenyl ring of the parent structure. Some derivatisation and conjugation was observed in lettuce and radish (tops only) crops developing through the summer months where very minor amounts were detected in lettuce and radish crops in the [2,6-^{14}C-pyridyl]-labelled experiment while the equivalent concentration in the [U-^{14}C-phenyl]-labelled experiment represented such low percentages of the TRR that they were not resolved from background radioactivity.

The pyridyl ring metabolites M-02 (AE C657188), M-05 (AE 1344122), M-08 (AE C653598) and M-09 (AE B102859) were observed in rotational crops. M-02 (AE C657188) and M-05 (AE 1344122) are known to be formed in soil and may have been taken up from the soil directly. In lettuce and radish M-02 (AE C657188) was usually the most abundant pyridyl ring metabolite. In wheat forage and grain the percentage of M-02 (AEC657188) declined after the 29-day planting with the percentage of M-05 (AE 1344122) detected increasing at both the 133- and 365-day plantings (although the concentrations were lower with time).

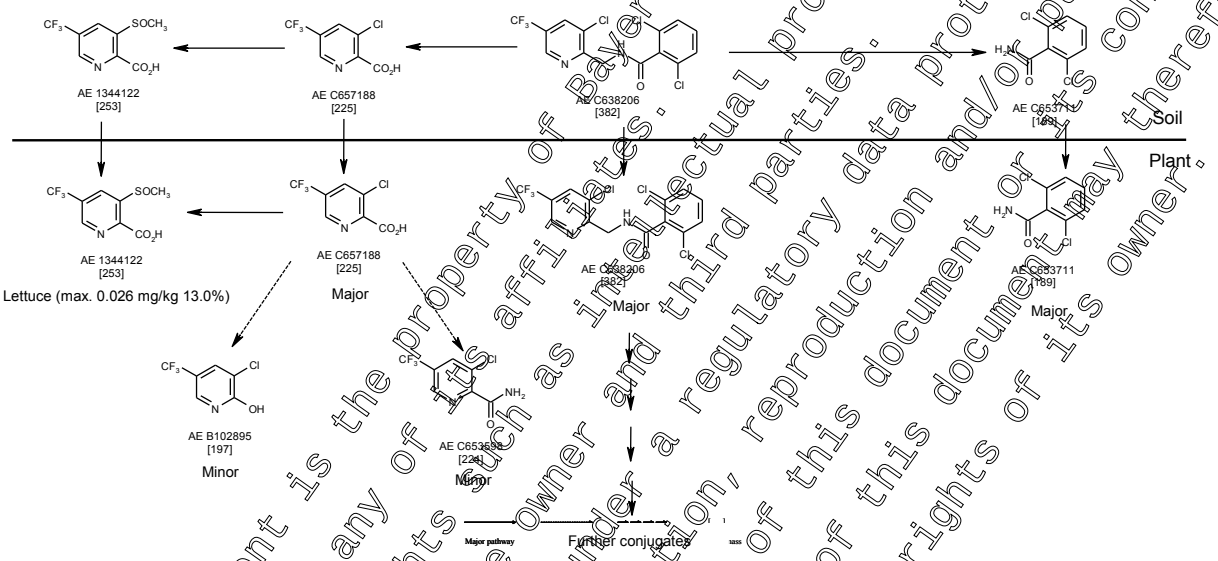
M-01 (AE C653711) taken up by wheat grown as a rotational crop was further metabolised to form M-04 (AE C657378; free hydroxylated AE C653711). Further derivatives of the phenyl ring were observed in wheat forage including glucose-malonoic acid conjugates of M-04 (AE C657378). M-01 (AE C653711) was detected in all rotational crops but further metabolism of this metabolite to M-04 (AE C657378) or conjugates of M-04 (AE C657378)was only observed in wheat.

The concentrations (in mg/kg) of parent, derivatives and conjugates of hydroxylated or thiolated (addition of –SH) versions of the parent and the small amounts of M-06 (AE C643890; free hydroxylated parent) in individual RACs were similar at each harvest in the [U-^{14}C-phenyl]-labelled and [2,6^{14}C-pyridyl]-labelled experiments. This was not true for metabolites formed from the individual pyridyl or phenyl rings and thus the total radioactive residues in individual RACs at each harvest in the [U-^{14}C-phenyl]-labelled and [2,6^{14}C-pyridyl]-labelled experiments were different. The metabolites arising from the phenyl ring, M-01 (AE C653711) and M-04 (AE C657378; hydroxylated AE C653711) formed a larger proportion of the TRR with time (although the concentrations were lower with time) in the individual RACs compared to metabolites arising from the pyridyl ring. M-02 (AE C657188) and M-05 (AE 1344122) are much more rapidly metabolised in soil than M-01 (AE C653711) and higher concentrations of the phenyl ring metabolites would be expected in rotational crops based on the different stabilities of the ring structures in soil. An exception to this was observed in wheat grain where the concentrations in the [2,6^{14}C-pyridyl]-labelled experiment were higher as M-02 (AE C657188) and M-05 (AE 1344122) were, as expected from the known phloem mobility of aromatic carboxylic acids, transported to grain.

Lettuce:

Lettuce, representative of leafy vegetable crops, was considered as a potential RAC for human consumption. The residues of fluopicolide (AE C638206) and its metabolites detected in lettuce were greatest in crops harvested after the 29-day planting and dropped significantly in those harvested after the 133 and 365-day plantings. The proposed metabolic route of fluopicolide (AE C638206) in lettuce is given in the following figure.

Figure 6.6.1- 3 The Proposed Metabolic Pathway for AE C638206 in Lettuce Grown as a Confined Rotational Crop



[U-^{14}C-phenyl]-Labelled Experiment:

Following application of [U-^{14}C-phenyl]-labelled AE C638206 to soil, the total radioactive residues in lettuce were 1.013, 0.115 and 0.619 mg/kg parent equivalents from the 29, 133 and 365 day plantings, respectively.

Fluopicolide (AE C638206) and its metabolite M-01 (AE C653711) were identified at each harvest. AE C638206 was detected at 11.1% (0.112 mg/kg), 26.6% (0.031 mg/kg) and 2.1% (0.013 mg/kg) of the TRR and AE C653711 at 81.2% (0.407 mg/kg), 60.9% (0.035 mg/kg) and 87.0% (0.267 mg/kg) for the 29, 133 and 365 day plantings, respectively. Some seasonal variation in the uptake of M-01 (AE C653711) was observed. In the 133-day plot, planted with lettuce in October and harvested in January, the levels of M-01 (AE C653711) observed were lower than those detected after the 365-day planting, planted in spring and harvested in May. The rate of formation of M-01 (AE C653711) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures. Fluopicolide (AE C638206) and M-01 (AE C653711) accounted for 87.5 to 92.3% of the TRR in lettuce grown as a rotational crop. No other metabolites exceeded 2.4% of the TRR or 0.015 mg/kg parent equivalents.

[2,6^{14}C-pyridyl]-Labelled Experiment:

Following application of [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206) to soil, the total radioactive residues in lettuce were 0.302, 0.034 and 0.058 mg/kg parent equivalents from the 29, 133 and 365 day plantings, respectively which were lower than the radioactive residues detected in the [U-^{14}C-phenyl]-labelled experiment.

The concentrations of fluopicolide (AE C638206) were comparable in both radiolabelled experiments, with parent detected in lettuce grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206) at 35.8% (0.108 mg/kg), 79.9% (0.027 mg/kg) and 41.5% (0.024 mg/kg) of the TRR from the 29, 133 and 365 day plantings, respectively. The metabolite M-02 (AE C657188) was detected at 17.4% (0.031 mg/kg) and 11.8% (0.004 mg/kg) of the TRR from the 29- and 365-day plantings, respectively. It was not detected in lettuce from the 133 day planting.

Fluopicolide (AE C638206) or fluopicolide (AE C638206) plus M-02 (AE C657188) accounted for 52.3 to 79.9% of the TRR in lettuce grown as a rotational crop which increased to 55.7 to 82.5% when expressed as extractable radioactive residue.

Further metabolites of M-02 (AE C657188), M-05 (AE 1344122), M-09 (AE B102859) and M-08 (AE C653598), were also observed at low levels. Some seasonal variation in the extent of metabolism was observed. In the 133-day plot, planted in October, only fluopicolide (AE C638206) was observed in lettuce grown in soil treated with [2,6^{14}C-pyridyl]-labelled test item. The rate of formation of M-02 (AE C657188) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures. In contrast, in the 29 and 365 day plots, both planted in spring, with crops developing through the summer when the maximum formation of M-02 (AE C657188) in soil would be expected, M-02 (AE C657188) and its metabolites M-05 (AE 1344122), M-09 (AE B102859) and M-08 (AE C653598; in 365 day plot only) were also detected in lettuce. Maximum amounts observed were 0.026 mg/kg (13.0%), 0.008 mg/kg (5.3%) and 0.003 mg/kg (9.0%) for M-05 (AE 1344122), M-09 (AE B102859) and M-08 (AE C653598), respectively.

In the 29- and 365-day plots two regions of radioactivity; A and B, were observed in lettuce grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). The components in Regions A and B were concluded to correspond with multiple derivatives of fluopicolide (AE C638206) (fully characterised in wheat in which they were most abundant) which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent, and then conjugated to glucose, malonic acid, glyceric acid or amino acids. The total amount of conjugates observed in lettuce were 0.014 and 0.004 mg/kg parent equivalents (4.6% and 6.7%, respectively) for 29- and 365-day plantings treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). These were not observed in crops from the 133 day plot. This difference may be due to seasonal variation. The 29 and 365-day plots were planted in spring and the crops developed through the summer when the plants would be more metabolically active while the 133-day plots were planted in October and crops developed through the winter. The equivalent concentrations of derivatives and conjugates in the [U-^{14}C-phenyl]-labelled experiment represented such low percentages of the TRR that they were not resolved from background radioactivity.

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 87.5 to 92.3% for lettuce grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206) and 76.1 to 80.5% for lettuce grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206). In general, levels of individual components which were not identified or characterised did not exceed 10% of the TRR. In lettuce from the 29-day planting treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), an unknown component was detected at 10.5% (0.032 mg/kg parent equivalents) of the TRR. However, in this sample the total amounts of identified or characterised components expressed as a percent of the extractable radioactive residue was > 79%.

Table 6.6.1- 5 Summary of Identification and Characterisation of Residues in Lettuce following 29, 133 and 365 day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	1.013	na	100	0.115	na	100	0.619	na
Extractable Residue	98.1	0.99	na	96.5	0.11	na	97.0	0.60	na
Fluopicolide (AE C638206)	11.1	0.112	0.112	26.6	0.031	0.031	2.1	0.013	0.013
M-01 (AE C653711)	81.2	0.822	0.407	60.9	0.070	0.035	87.0	0.539	0.267
M-04 (AE C657378)	nd	nd	nd	nd	nd	nd	nd	nd	nd
M-06 (AE C643890)	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	na	nd	nd	na	nd	nd	na
Largest Single Unknown[1]	1.2	0.012	na	1.9	0.002	na	2.4	0.015	na
Total Identified and Characterised	92.3	na	na	87.5	na	na	89.1	na	na
Non-Extractable Residue	1.9	0.019	na	3.5	0.004	na	3.0	0.019	na

b) Pyridyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	0.302	na	100	0.034	na	100	0.058	na
Extractable Residue	95.2	0.29	na	96.8	0.03	na	89.6	0.05	na
Fluopicolide (AE C638206)	35.8	0.108	0.108	79.9	0.027	0.027	41.5	0.024	0.024
M-02 (AE C653188)	17.4	0.053	0.031	nd	nd	nd	11.8	0.007	0.004
M-05 (AE 1344122)	13.0	0.039	0.026	nd	nd	nd	7.8	0.005	0.003
M-08 (AE C653598)	nd	nd	nd	nd	nd	nd	9.0	0.005	0.003
M-09 (AE B102895)	5.3	0.016	0.008	nd	nd	nd	3.7	0.002	0.001
M-06 (AE C643890)	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	4.6	0.014	na	nd	nd	nd	6.7	0.004	na
Largest Single Unknown[1]	10.5	0.032	na	4.8	0.002	na	1.3	0.001	na
Total Identified and Characterised	76.1	na	na	79.9	na	na	80.5	na	na
Non-Extractable Residue	4.8	0.015	na	3.2	0.001	na	10.4	0.006	na

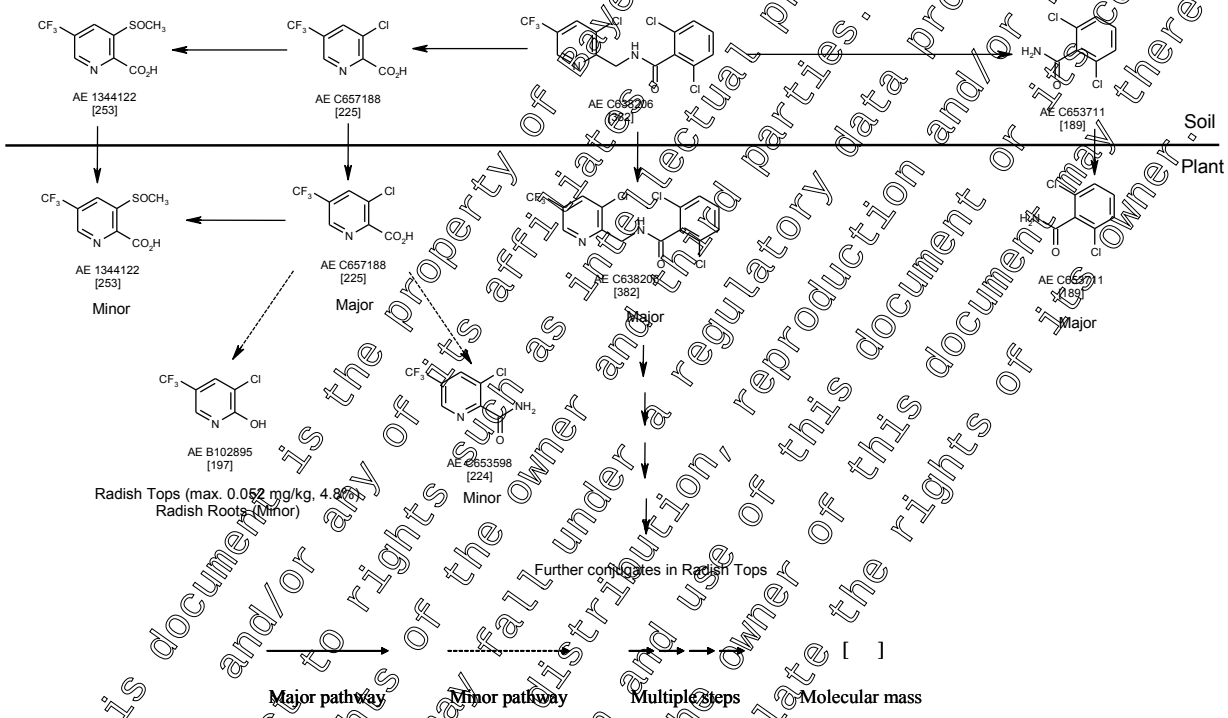
na = not applicable nd = not detected [1]Quantified in chromatograms given in report

The residues of fluopicolide (AE C638206) and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

Radish:

Radish, representative of root crops, was separated into roots and foliage at harvest. Radish roots were considered as a potential RAC for human consumption and radish tops for animal fodder. The residues of fluopicolide (AE C638206) and its metabolites detected in radishes were greatest in crops harvested after the 29-day planting and dropped significantly in those harvested after the 133- and 365-day plantings. Residue concentrations were considerably lower in radish roots (0.143 to 0.023 mg/kg parent equivalents) than in radish foliage (6.705 to 0.237 mg/kg parent equivalents). The proposed metabolic route of fluopicolide (AE C638206) in radish is given in the following figure.

Figure 6.6.1- 4 The Proposed Metabolic Pathway for AE C638206 in Radish Grown as a Confined Rotational Crop



Radish Tops:

[U-^{14}C-phenyl]-Labelled Experiment

Following application of [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) to soil, the total radioactive residues in radish tops were 6.705, 0.240 and 2.006 mg/kg parent equivalents from the 29, 133- and 365-day plantings, respectively.

Fluopicolide (AE C638206) and its metabolite M-01 (AE C653711) were identified at each harvest. Fluopicolide (AE C638206) was detected in radish tops at 24.5% (1.644 mg/kg), 15.1 % (0.036 m/kg) and 3.8 % (0.076 mg/kg) of the TRR and AE C653711 at 65.3% (2.170 mg/kg), 77.3% (0.092 mg/kg) and 87.5% (0.869 mg/kg) from the 29, 133 and 365-day plantings, respectively. Some seasonal variation in the uptake of M-01 (AE C653711) was observed. In the 133-day plot, planted with radish in October and harvested in December, the concentration of M-01 (AE C653711) observed was lower than that detected after the 365 day planting, which was planted in spring and harvested in May. The rate of formation of M-01 (AE C653711) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures.

Fluopicolide (AE C638206) and M-01 (AE C653711) accounted for 89.8 to 92.4% of the TRR in radish tops grown as a rotational crop. No other metabolites exceeded 1.7% of the TRR or 0.116 mg/kg parent equivalents.

[2,6^{14}C-pyridyl]-Labelled Experiment

Following application of [2,6^{14}C-pyridyl]-labelled AE C638206 to soil, the total radioactive residues in radish tops were 2.097, 0.237 and 0.419 mg/kg parent equivalents from the 29, 133 and 365 day plantings, respectively which is lower than the radioactive residues detected in the [U-^{14}C-phenyl]-labelled experiment.

Fluopicolide (AE C638206) was detected in radish tops at 51.1% (1.072 mg/kg), 72.2% (0.171 mg/kg) and 25.2% (0.106 mg/kg) of the TRR from the 29, 133 and 365 day plantings of soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), respectively. The concentration of parent was similar to that observed in the [U-^{14}C-phenyl]-labelled experiment in crops from the 29 and 365-day plantings but was slightly higher than those from the 133-day planting. In general, the concentrations of AE C638206 in individual RACs were comparable at each harvest in the [U-^{14}C-phenyl]-labelled and [2,6^{14}C-pyridyl]-labelled experiments. AE C657188 was detected in radish tops at 10.4% (0.128 mg/kg) and 27.1% (0.067 mg/kg) of the TRR from the 29 and 365 day plantings, respectively. It was not detected in radish tops from the 133 day planting.

fluopicolide (AE C638206) or fluopicolide (AE C638206) plus M-02 (AE C657188) accounted for 52.3 to 72.2% of the TRR in radish tops grown as a rotational crop which increased to 54.2 to 72.3% when expressed as extractable radioactive residue.

Further metabolites of M-02 (AE C657188), M-05 (AE 1344122) and M-09 (AE B102859), were also observed at low levels. Some seasonal variation in the extent of metabolism was observed. In the 133 day plot, planted in October, only AE C638206 was observed in radish tops grown in soil treated with [2,6^{14}C-pyridyl]-labelled test item. The rate of formation of M-02 (AE C657188) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures. In contrast, in the 29 and 365-day plots, both planted in spring, with crops developing through the summer when the maximum formation of AE C657188 in soil would be expected, M-02 (AE C657188) and its metabolites M-05 (AE 1344122) and M-09 (AE B102859) were also detected. The maximum concentrations observed in radish tops were 0.046 mg/kg and 0.052 mg/kg for M-05 (AE 1344122) and M-09 (AE B102859), respectively and the amounts observed in radish tops were always ≤ 6% of the TRR.

In the 29 and 365 day plots two regions of radioactivity, A and B, were observed in radish tops grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). The components in Regions A and B were concluded to correspond with multiple derivatives of fluopicolide (fully characterised in wheat in which they were most abundant) which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent, which were then conjugated to glucose, malonic acid, glyceric acid or amino acids. The total amount of conjugates observed in radish tops were 0.287 and 0.089 mg/kg parent equivalents (13.7% and 21.3%, respectively) for 29 and 365-day plantings treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). These were not observed in crops from the 133-day plot. This difference may be due to seasonal variation. The 29 and 365 Day plots were planted in spring and the crops developed through the summer when the plants would be more metabolically active while the 133-day plots were planted in October and crops developed through the winter. The equivalent concentrations of derivatives and conjugates in the [U-^{14}C-phenyl]-labelled experiment represented such low percentages of the TRR that they were not resolved from background radioactivity.

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 89.8 to 92.4% for radish tops grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 72.2 to 84.7% for those grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). In general, levels of individual components which were not identified or characterised did not exceed 10% of the TRR. In radish tops from the 29-day planting treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), an unknown component was detected at 11.3% (0.238 mg/kg parent equivalents) of the TRR. However, in this sample the total amounts of identified or characterised components expressed as a percent of the extractable radioactive residue was > 84%.

Table 6.6.1- 6 Summary of Identification and Characterisation of Residues in Radish Tops following 29, 133- and 365-day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	6.705	na	100	0.249	na	100	2.006	na
Extractable Residue	98.4	6.60	na	98.3	0.24	na	98.8	1.98	na
AE C638206	24.5	1.644	1.644	15.1	0.036	0.036	3.8	0.076	0.076
AE C653711	65.3	4.381	2.170	77.3	0.186	0.092	87.5	1.755	0.869
AE C657378	nd	nd	nd	nd	nd	nd	nd	nd	nd
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	nd	nd	nd	nd	nd	nd	nd
Largest Single Unknown[1]	1.7	0.116	na	1.7	0.004	na	1.5	0.030	na
Total Identified and Characterised	89.8	na	na	92.4	na	na	91.3	na	na
Non-Extractable Residue	0.7	0.046	na	1.7	0.004	na	1.2	0.024	na

b) Pyridyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	2.097	na	100	0.237	na	100	0.419	na
Extractable Residue	98.8	2.07	na	99.0	0.24	na	96.5	0.41	na
AE C638206	51.1	1.072	1.072	72.2	0.171	0.171	25.2	0.106	0.106
AE C657188	10.4	0.217	0.128	nd	nd	nd	27.1	0.114	0.067
AE 1344122	3.3	0.069	0.046	nd	nd	nd	5.1	0.022	0.015
AE C653598	nd	nd	nd	nd	nd	nd	nd	nd	nd
AE B102895	4.8	0.100	0.052	nd	nd	nd	6.0	0.025	0.013
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	13.7	0.287	na	nd	nd	nd	21.3	0.089	nd
Largest Single Unknown[1]	11.3	0.238	na	8.3	0.020	na	4.7	0.020	na
Total Identified and Characterised	83.3	na	na	72.2	na	na	84.7	na	na
Non-Extractable Residue	1.2	0.025	na	1.0	0.002	na	3.5	0.015	na

na = not applicable nd = not detected [1]Quantified in chromatograms given in report

The residues of fluopicolide (AE C638206) and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

Radish Roots:

[U-^{14}C-phenyl]-Labelled Experiment

Following application of [U-^{14}C-phenyl]-labelled AE C638206 to soil, the total radioactive residues in radish roots were 0.143, 0.023 and 0.036 mg/kg parent equivalents from the 29, 133 and 365-day plantings, respectively.

Fluopicolide (AE C638206) and its metabolite M-01 (AE C653711) were identified at each harvest. Fluopicolide (AE C638206) was detected in radish roots at 47.9% (0.069 mg/kg), 28.2 % (0.006 m/kg) and 24.2 % (0.009 mg/kg) of the TRR and AE C653711 at 43.2% (0.031 mg/kg), 54.9% (0.006 mg/kg) and 60.9% (0.009 mg/kg) from the 29, 133 and 365 day plantings, respectively. The concentrations of fluopicolide (AE C638206) and M-01 (AE C653711) detected in roots were considerably lower than in radish tops.

Fluopicolide (AE C638206) and M-01 (AE C653711) accounted for 83.1 to 91.1% of the TRR in radish roots grown as a rotational crop. No other metabolites exceeded 6.4% of the TRR or 0.002 mg/kg parent equivalents.

[2,6^{14}C-pyridyl]-Labelled Experiment

Following application of [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206) to soil, the total radioactive residues in radish roots were 0.116 mg/kg, 0.025 mg/kg and 0.032 mg/kg from the 29, 133 and 365-day plantings, respectively.

Fluopicolide (AE C638206) and its metabolite M-02 (AE C657188) were identified at each harvest. Fluopicolide (AE C638206) was detected in radish roots at 41.1% (0.048 mg/kg), 54.9% (0.014 m/kg) and 55.8% (0.018 mg/kg) of the TRR from the 29, 133 and-365 day plantings of soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), respectively. The concentration of parent were similar to those observed in the [U-^{14}C-phenyl]-labelled experiment. M-02 (AE C657188) was detected in radish roots at 35.5% (0.023 mg/kg), 9.6% (0.002 mg/kg) and 10.0% (0.002 mg/kg) of the TRR from the 29, 133- and 365-day plantings, respectively. The concentrations of fluopicolide (AE C638206) and M-02 (AE C657188) detected in roots were considerably lower than in radish tops.

Fluopicolide (AE C638206) and M-02 (AE C657188) accounted for 64.5 to 74.6% of the TRR in radish roots grown as a rotational crop which increased to 67.8 to 76.5% when expressed as percentage extractable radioactive residue.

Further metabolites of M-02 (AE C657188); M-05 (AE 1344122), M-08 (AE C653598) and M-09 (AE B102859), were also observed at low levels. The maximum amounts observed in radish roots were 9.6 % (0.007 mg/kg), 9.5% (0.002 mg/kg) and 19.1% (0.003 mg/kg) for M-02 (AE 1344122), M-08 (AE C653598) and M-09 (AE B102859), respectively. No conjugates were detected in radish roots. All other unidentified metabolites detected in the [2,6^{14}C-pyridyl]-labelled experiment were < 4% of the TRR and ≤ 0.005 mg/kg parent equivalents.

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 83.1 to 91.1% for radish roots grown in soil treated with [U-^{14}C-phenyl]-labelled AE C638206 and 80.6 to 86.5% for those grown in soil treated with [2,6^{14}C-pyridyl]-labelled AE C638206. Levels of individual components which were not identified or characterised did not exceed 10% of the TRR (maximum 6.4% TRR or 0.005 mg/kg parent equivalents).

Table 6.6.1- 7 Summary of Identification and Characterisation of Residues in Radish Roots following 29, 133 and 365 day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	0.143	na	100	0.023	na	100	0.036	na
Extractable Residue	97.4	0.14	na	96.8	0.02	na	96.2	0.04	na
AE C638206	47.9	0.069	0.069	28.2	0.006	0.006	24.2	0.009	0.009
AE C653711	43.2	0.062	0.031	54.9	0.013	0.006	60.9	0.022	0.011
AE C657378	nd	nd	nd	nd	nd	nd	nd	nd	nd
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	nd	nd	nd	nd	nd	nd	nd
Largest Single Unknown[1]	1.1	0.002	na	6.4	0.001	na	2.4	0.001	na
Total Identified and Characterised	91.1	na	na	83.1	na	na	85.1	na	na
Non-Extractable Residue	2.6	0.004	na	3.4	0.001	na	3.9	0.001	na

b) Pyridyl label

Plot	29 Days			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	0.116	na	100	0.025	na	100	0.032	na
Extractable Residue	97.5	0.11	na	95.1	0.02	na	95.0	0.03	na
AE C638206	41.1	0.048	0.048	54.9	0.014	0.014	55.8	0.018	0.018
AE C657188	33.5	0.039	0.025	9.6	0.002	0.002	10.0	0.003	0.002
AE 1344122	9.6	0.011	0.007	2.9	0.001	0.001	5.3	0.002	0.001
AE C653598	nd	nd	nd	nd	nd	nd	9.5	0.003	0.002
AE B102895	nd	nd	nd	19.1	0.005	0.003	nd	nd	nd
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	nd	nd	nd	nd	nd	nd	nd
Largest Single Unknown[1]	4.9	0.005	na	1.6	<0.001	na	3.5	0.001	na
Total Identified and Characterised	84.2	na	na	86.5	na	na	80.6	na	na
Non-Extractable Residue	2.5	0.003	na	4.9	0.001	na	5.0	0.002	na

na = not applicable nd = not detected [1]Quantified in chromatograms given in report

The residues of fluopicolide (AE C638206) and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

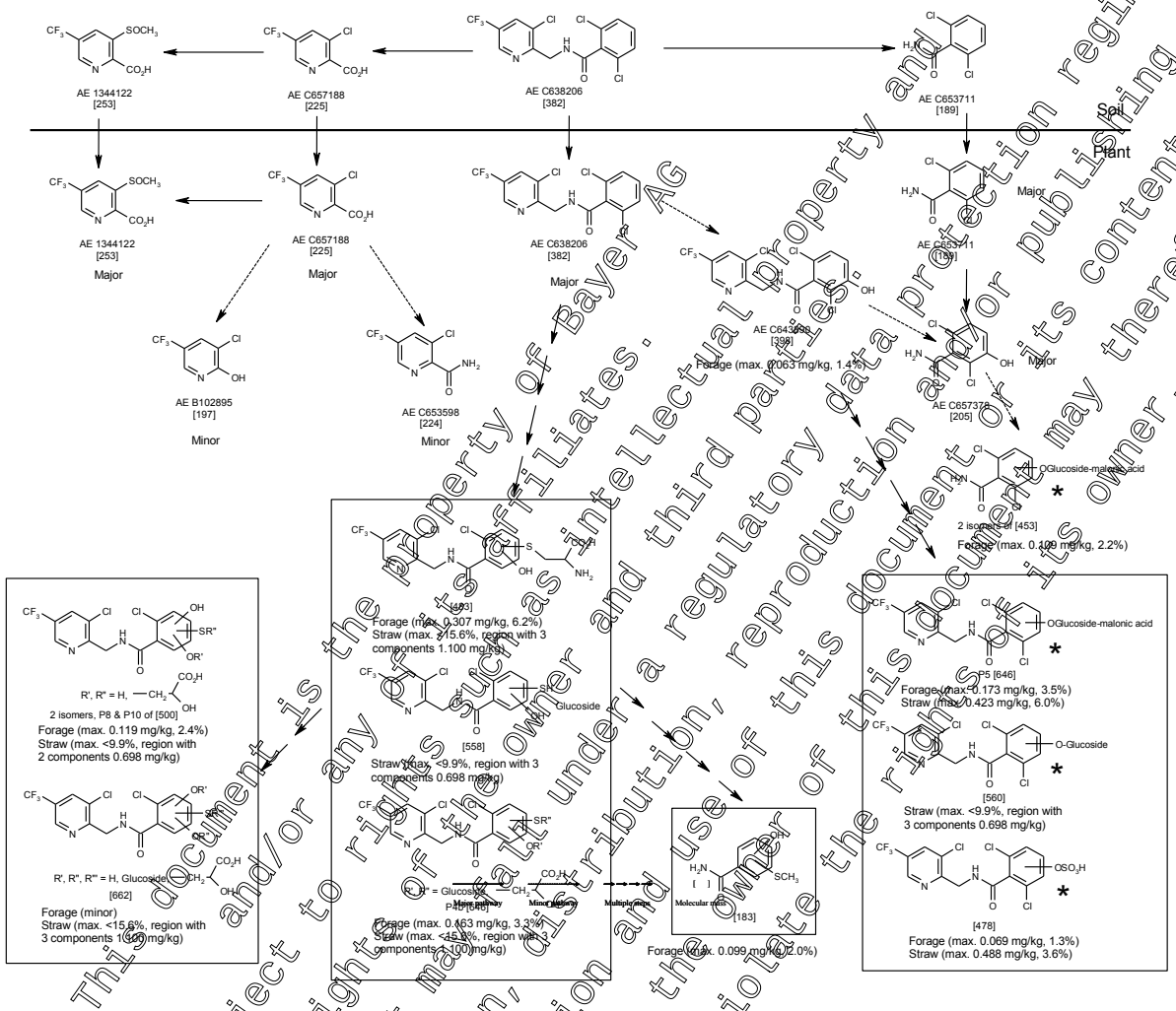
Wheat:

Wheat, representative of cereal crops, was harvested as immature and mature wheat. The immature wheat was harvested at the forage stage. Mature wheat was separated into straw (including hulls) and grain. Wheat grain was considered as a potential RAC for human consumption, while straw and forage were considered as animal fodder. The proposed metabolic route of fluopicolide (AE C638206) in wheat forage and straw is given in the following figures.

The residues of fluopicolide (AE C638206) and its metabolites detected in wheat were greatest in crops harvested after the 29-day planting and dropped significantly in those harvested after the 133- and 365-day plantings. Residue concentrations were very much lower in grain than in forage or straw. Derivatives and conjugates of fluopicolide (AE C638206) and M401 (AE C637111) were fully characterised in wheat straw and forage from the 29-day planting in which they were most abundant. These were not detected in wheat grain. Maximum amounts of individual derivatives were generally < 10% of the TRR. Only one conjugate peak was detected in excess of 10% of the TRR. P4 accounted for as much as 15.6% in the pyridyl-label straw extract. Further separation was not pursued with the straw although, in the case of forage, this peak was resolved into three components.

A total of 11 radioactive peaks were isolated from wheat straw and forage samples, listed as P1 to P11 in the analytical report of this study. The designations were assigned based on the original separation of peaks in the plant extracts. It should be noted that the designations (P-numbers) were for radioactive peaks identified as part of the crop rotational study and do not imply these are the same metabolites observed in soil and lysimeter studies with similar designations. Where a radioactive peak has been identified as a metabolite for which an authentic reference standard was available, it has been referred to by this number (AE number). Thus P2a, P2b, P2c, P4a, P4b, P4c etcetera in this summary refer to metabolites isolated from plant samples only.

Figure 6.6.1-6: The Proposed Metabolic Pathway for AE C638206 in Forage and Straw in Wheat Grown as a Confined Rotational Crop



It was not possible to define the position of substituents in the phenyl ring by mass spectroscopy. Co-chromatography with reference standards confirmed the hydroxyl groups in M-06 (AE C643890) and M-04 (AE C657378) as being in the 3 position and therefore the most probable position of the conjugates in the structures marked (*) is also in the 3 position.

Wheat Forage:

[U-^{14}C-phenyl]-Labelled Experiment

Following application of [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206)to soil, the total radioactive residues in wheat forage were 4.949, 0.225 and 0.865 mg/kg parent equivalents from the 29, 133- and 365-day plantings, respectively.

Fluopicolide (AE C638206) and its metabolites M-01 (AE C653711) and M-04 (AE C657378) were identified at each harvest. Fluopicolide (AE C638206) was detected in forage at 36.6% (1.812 mg/kg), 23.3 % (0.052 m/kg) and 4.8 % (0.042 mg/kg) of the TRR from the 29, 133 and 365 day, respectively. The metabolite M-01 (AE C653711) was detected at 6.3% (0.155 mg/kg), 5.1% (0.006 mg/kg) and 14.8% (0.063 mg/kg) of the TRR for the respective planting periods. Some seasonal variation in the uptake of M-01 (AE C653711) was observed. In the 133-day plot, planted with winter wheat in October and harvested as forage in March, the concentration of M-01 (AE C653711) observed was lower than that detected in spring wheat after the 365-day planting, planted in March and harvested in May. The rate of formation of M-01 (AE C653711) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures. M-01 (AE C653711) taken up by wheat grown as a rotational crop was further metabolised to form M-04 (AE C657378; free hydroxylated AE C653711). The same seasonal variation in the amount of M-04 (AE C657378) present was observed with the metabolite identified as 32.7% (0.870 mg/kg), 28.9% (0.035 mg/kg) and 59.3% (0.276 mg/kg) of the TRR from the 29, 133 and 365 day, respectively.

Fluopicolide (AE C638206), M-01 (AE C653711) and M-04 (AE C657378) accounted for 57.3 to 78.9% of the TRR in wheat forage grown as a rotational crop which increased to 62.1 to 85.1% when expressed as percentage of extractable radioactive residue.

All other metabolites detected in the [U-^{14}C-phenyl]-labelled experiment were < 10% of the TRR. Low amounts of the free hydroxylated parent fluopicolide (AE C638206) were observed in wheat forage from the 29-day planting (< 1.0%, <0.051 mg/kg) but was not detected at later planting periods.

Further derivatives of the phenyl ring were observed in wheat forage from the 29-day planting including glucose-malonoic acid conjugates of AE C657378. In addition to these conjugates, multiple derivatives of AE C638206 which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent, and then conjugated to glucose, malonic acid, glyceric acid or amino acids were detected in wheat forage. The total amount of conjugates observed in wheat forage grown in soil treated with [U-^{14}C-phenyl]-labelled AE C638206 were 0.970, 0.047 and 0.037 mg/kg parent equivalents (19.6%, 21.0% and 3.0%, respectively) for 29, 133 and 365 day plantings. Maximum amounts of individual derivatives were < 6.2% of the TRR.

[2,6^{14}C-pyridyl]-Labelled Experiment

Following application of [2,6^{14}C-pyridyl]-labelled AE C638206 to soil, the total radioactive residues in forage were 4.288, 0.176 and 0.243 mg/kg parent equivalents from the 29, 133 and 365 day plantings.

AE C638206 and its metabolites M-02 (AE C657188) and M-05 (AE 1344122) were identified at each harvest. Fluopicolide (AE C638206)was detected in forage at 33.7% (1.445 mg/kg), 26.2% (0.041 m/kg) and 27.8% (0.068 mg/kg) of the TRR from the 29, 133 and 365 day plantings of soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), respectively. The concentration of parent were similar to those observed in the [U-^{14}C-phenyl]-labelled experiment. The marked decline in TRR in wheat forage harvested after the 133 and 365 day plantings was in proportion to the decline observed in parent and in total pyridyl ring metabolites.

M-02 (AE C657188) was detected in forage at 43.0% (1.087 mg/kg), 5.4% (0.005 mg/kg) and 8.2% (0.012 mg/kg) of the TRR from the 29, 133- and 365-day plantings, respectively. Some seasonal variation in the uptake of M-02 (AE C657188) was observed. In the 133 day plot, planted with winter wheat in October and harvested as forage in March, the concentration of M-02 (AE C657188), and the

total concentration of pyridyl ring metabolites, observed was lower than detected in spring wheat after the 365 day planting, planted in March and harvested in May.

The rate of formation of M-02 (AE C657188) in soil from degradation of the parent would be expected to be slower in the winter due to the lower temperatures. M-05 (AE 1344122) was detected in forage at 3.8% (0.108 mg/kg), 41.0% (0.042 mg/kg) and 18.3% (0.030 mg/kg) of the TRR for the respective planting periods.

Fluopicolide (AE C638206), M-02 (AE C657188) and M-05 (AE 1344122) accounted for 54.3 to 80.5% of the TRR in wheat forage which increased to 58.0 to 82.6% when expressed as percentage of extractable radioactive residue.

Further metabolites of M-02 (AE C657188); M-08 (AE C653598) and M-09 (AE B102859), were also observed at low levels. The maximum amount of M-08 (AE C653598) observed in forage was 6.3% (0.009 mg/kg). Maximum amounts of M-09 (AE B102859) were 10.5% TRR (0.008 mg/kg) or 0.012 mg/kg (9.9% TRR). All other metabolites detected in the [2,6-^{14}C-pyridyl]-labelled experiment were < 10% of the TRR.

Low amounts of the free hydroxylated parent, M-06 (AE C643890), were observed in wheat forage from the 29 day planting but were not detected at later planting periods (1.4%, 0.003 mg/kg).

Multiple derivatives of fluopicolide (AE C638206) which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent, and then conjugated to glucose, malonic acid, glyceric acid or amino acids were detected in wheat forage. The total amount of conjugates observed in wheat forage, grown in soil treated with [2,6-^{14}C-pyridyl]-labelled fluopicolide (AE C638206), were 0.566 and 0.010 mg/kg parent equivalents (13.4% and 4.1%, respectively) for 29 and 365 day plantings. No conjugates were observed following the 133 day planting. Maximum amounts of individual derivatives were ≤ 4.3% of the TRR and are given in Table 6.6.2-13.

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 78.3 to 96.2% for wheat forage grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 74.6 to 95.3% for that grown in soil treated with [2,6-^{14}C-pyridyl]-labelled fluopicolide (AE C638206). Identified and characterised components expressed as a percentage of the extractable radioactive residue were 84.8 to 100% for wheat forage grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 79.6 to 97.7% for that grown in soil treated with [2,6-^{14}C-pyridyl]-labelled AE C638206. Levels of individual components which were not identified or characterised did not exceed 10% of the TRR (maximum 4.8% TRR and 0.073 mg/kg parent equivalents).

Table 6.6.1- 8 Summary of Identification and Characterisation of Residues in Wheat Forage following 29, 133 and 365 day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	4.949	na	100	0.225	na	100	0.865	na
Extractable Residue	95.4	4.72	na	92.3	0.21	na	92.7	0.80	na
AE C638206	36.6	1.812	1.812	23.3	0.052	0.052	4.8	0.042	0.042
AE C653711	6.3	0.312	0.155	5.1	0.011	0.006	14.8	0.128	0.063
AE C657378	32.7	1.619	0.870	28.9	0.065	0.035	59.3	0.513	0.276
AE C643890	<1.0	<0.049	<0.051	nd	nd	nd	nd	nd	nd
Total Conjugates	19.6	0.97	na	21.0	0.047	na	3.0	0.026	na
Largest Single Unknown[1]	nd	nd	nd	4.8	0.011	na	4.3	0.037	na
Total Identified and Characterised	96.2	na	na	78.3	na	na	81.9	na	na
Non-Extractable Residue	4.6	0.226	na	6.7	0.015	na	7.3[2]	0.063[2]	na

b) Pyridyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	4.288	na	100	0.156	na	100	0.243	na
Extractable Residue	97.5	4.18	na	97.2	0.15	na	93.7	0.23	na
AE C638206	33.7	1.445	1.445	26.2	0.041	0.041	27.8	0.068	0.068
AE C657188	43.0	1.844	1.087	5.4	0.008	0.005	8.2	0.020	0.012
AE 1344122	3.8	0.163	0.108	41.0	0.064	0.042	18.3	0.045	0.030
AE C653598	nd	nd	nd	nd	nd	nd	6.3	0.015	0.009
AE B102895	nd	nd	nd	10.5	0.016	0.008	9.9	0.024	0.012
AE C643890	1.4	0.060	0.063	nd	nd	nd	nd	nd	nd
Total Conjugates	13.4	0.566	na	nd	nd	nd	4.1	0.010	nd
Largest Single Unknown[1]	1.7	0.073	na	2.9	0.005	na	4.4	0.011	na
Total Identified and Characterised	95.3	na	na	83.1	na	na	74.6	na	na
Non-Extractable Residue	2.5	0.105	na	2.8	0.004	na	6.3	0.015	na

na = not applicable
nd = not detected
[1]Quantified in chromatograms given in report
[2]Non-extractable residue further extracted by acid hydrolysis

The residues of fluopicolide (AE C638206) and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

Wheat Straw:

[U-^{14}C-phenyl]-Labelled Experiment

Following application of [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206)to soil, the total radioactive residues in wheat straw were 13.560, 0.843 and 2.373 mg/kg parent equivalents in wheat straw from the 29, 133 and 365 day plantings, respectively.

Fluopicolide (AE C638206) and its metabolites M-01 (AE C653711) and M-04 (AE C657378) were identified at each harvest. Fluopicolide (AE C638206) was detected in straw at 23.1% (3.132 mg/kg), 15.5 % (0.131 m/kg) and 7.2 % (0.172 mg/kg) of the TRR from the 29, 133- and 365-day plantings, respectively.

Some seasonal variation in the uptake and metabolism of M-01 (AE C653711) was observed. The 133-day plot was planted with winter wheat in October, and the wheat developed through the winter and following summer reaching maturity after seven months in May. The total concentration of phenyl ring metabolites (that is, the sum of AE C653711 and AE C657378) observed in the 133 day plot was lower than detected in spring wheat after the 365 day planting, planted in March and harvested in June with the wheat ripening in three months through the summer. The rate of formation of M-01 (AE C653711) in soil from degradation of the parent and uptake of M-01 (AE C653711) by transpiration of the plants would be expected to be faster in summer due to the higher temperatures. M-01 (AE C653711) taken up by wheat grown as a rotational crop was further metabolised to form M-04 (AE C657378; free hydroxylated AE C653711).

M-01 (AE C653711) was detected in straw at 3.4% (0.288 mg/kg), 25.5 % (0.107 m/kg) and 5.1 % (0.060 mg/kg) and M-04 (AE C657378) at 13.6% (0.990 mg/kg), 14.6% (0.067 mg/kg) and 28.0% (0.356 mg/kg) of the TRR from the 29, 133 and 365 day plantings, respectively. The proportion of M-01 (AE C653711) metabolised to M-04 (AE C657378) was lower in the 133-day plot than the 29- and 365-day plots. The wheat planted in 29 and 365-day plot developed in two to three months through the summer when the plants would be more metabolically active.

Fluopicolide (AE C638206), M-01 (AE C653711) and M-04 (AE C657378) accounted for 40.1 to 55.6% of the TRR (56.2 to 65.7% of the extractable radioactive residue) in wheat straw. The maximum residues observed in straw were detected in wheat harvested following the 29 day planting. The radioactive residue in that crop was exhaustively identified and characterised such that > 92% of the extractable radioactive residue (ERR) in wheat straw was identified or fully characterised by LC-MS (with appropriate structures proposed). The residue in straw was composed of twelve different metabolites. All other metabolites detected in the [U-^{14}C-phenyl]-labelled experiment were < 10% of the TRR.

Multiple derivatives of Fluopicolide (AE C638206) which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent, and then conjugated to glucose, malonic acid, glyceric acid or amino acids were detected in wheat straw. The total amount of conjugates observed in straw grown in soil treated with [U-^{14}C-phenyl]-labelled AE C638206 were 3.458 mg/kg (25.5%), 0.150 mg/kg (17.9%) and 0.116 mg/kg (4.9%) for 29, 133 and 365 day plantings respectively. Maximum amounts of individual derivatives are given in Table 6.6.2-13.

[2,6^{14}C-pyridyl]-Labelled Experiment

Following application of [2,6^{14}C-pyridyl]-labelled AE C638206 to soil, the total radioactive residues in straw were 7.054, 0.348 and 1.009 mg/kg parent equivalents from the 29, 133 and 365-day plantings.

Fluopicolide (AE C638206) and its metabolites M-02 (AE C657188) and M-05 (AE 1344122) were identified at each harvest. Fluopicolide (AE C638206) was detected in straw at 34.9% (2.462 mg/kg), 25.7% (0.089 m/kg) and 27.5% (0.277 mg/kg) of the TRR from the 29, 133 and 365-day plantings of soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), respectively. The concentration of parent were similar to those observed in the [U-^{14}C-phenyl]-labelled experiment.

Some seasonal variation in the uptake of M-02 (AE C657188) and M-05 (AE 1344122) was observed. The 133 day plot was planted with winter wheat in October, and the wheat developed through the winter and following summer reaching maturity after seven months in May. The total concentration of M-02 (AE C657188) and M-05 (AE 1344122) observed in the 133 day plot was lower than detected in spring wheat after the 365 day planting, planted in March and harvested in June with the wheat ripening in three months through the summer. The rate of formation of M-02 (AE C657188) and M-05 (AE 1344122) in soil from degradation of the parent and uptake by transpiration of the plants would be expected to be faster in summer due to the higher temperatures. M-02 (AE C657188) was detected in straw at 7.0% (0.291 mg/kg), 2.1% (0.004 mg/kg) and 4.1% (0.025 mg/kg) of the TRR from the 29, 133 and 365 day plantings, respectively. The levels of M-05 (AE 1344122) detected in straw were 7.7% (0.359 mg/kg), 1.2% (0.003 mg/kg) and 14.2% (0.094 mg/kg) for the same planting periods.

Fluopicolide (AE C638206), M-02 (AE C657188) and M-05 (AE 1344122) accounted for 29.0 to 49.6% of the TRR (31.0 to 52.9% of the ERR) in wheat straw. The maximum residues observed in straw were detected in wheat harvested following the 29 day planting. The radioactive residue in that crop was exhaustively identified and characterised such that > 96% of the ERR in wheat straw was identified or fully characterised by LC-MS (with appropriate structures proposed) and was shown to be composed of nine different compounds.

Further metabolites of M-02 (AE C657188), M-08 (AE C653598) and M-09 (AE B102859), were also observed at low levels. Maximum amounts of M-08 (AE C653598) observed in straw were 9.4% (0.019 mg/kg) or 0.028 mg/kg (4.8% TRR). The maximum amount of M-09 (AE B102859) was 21.5% TRR but this was equivalent to a concentration of only 0.039 mg/kg.

Multiple derivatives of fluopicolide (AE C638206) which were associated with hydroxylated or thiolated (addition of -SH) versions of the parent and their conjugated to glucose, malonic acid, glyceric acid or amino acids were detected in wheat straw. The total amount of conjugates observed in straw, grown in soil treated with [2,6-^{14}C-pyridyl]-labelled fluopicolide (AE C638206), were 2.884 mg/kg (40.9%), 0.089 mg/kg (25.7%) and 0.195 mg/kg (19.3%) for 29, 133 and 365-day plantings, respectively. Maximum amounts of individual derivatives were generally < 10% of the TRR. Only one conjugate peak exceeded 10% in straw where P4 (see earlier comment on use of P numbers) accounted for as much as 15.6% in the pyridyl-label straw extract. Further separation was not pursued with the straw although, in the case of forage, this peak was resolved into three components.

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 45.2 to 73.3% for wheat straw grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 69.9 to 90.5% for that grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). The total amounts of identified and characterised components expressed as a percentage of the extractable radioactive residue were 69.8 to 92.0% for wheat straw grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 80.1 to 96.5% for those grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). Levels of individual components which were not identified or characterised did not exceed 5% of the TRR (maximum 4.7% TRR or 0.488 mg/kg parent equivalents).

Table 6.6.1- 9 Summary of Identification and Characterisation of Residues in Wheat Straw following 29, 133- and 365-day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	13.560	na	100	0.843	na	100	2.373	na
Extractable Residue	71.4	9.68	na	84.6	0.71	na	64.8	1.54	na
AE C638206	23.1	3.132	3.132	15.5	0.131	0.131	7.2	0.172	0.172
AE C653711	3.4	0.461	0.288	25.5	0.215	0.107	5.1	0.121	0.060
AE C657378	13.6	1.844	0.990	14.6	0.123	0.067	28.0	0.663	0.356
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	25.5	3.458	na	17.9	0.150	na	4.9	0.116	na
Largest Single Unknown[1]	3.6	0.488	na	4.7	0.040	na	3.5	0.083	na
Total Identified and Characterised	65.7	na	na	73.5	na	na	45.2	na	na
Non-Extractable Residue	28.6[2]	3.881[2]	na	15.4[2]	0.130[2]	na	35.2[2]	0.835[2]	na

b) Pyridyl label

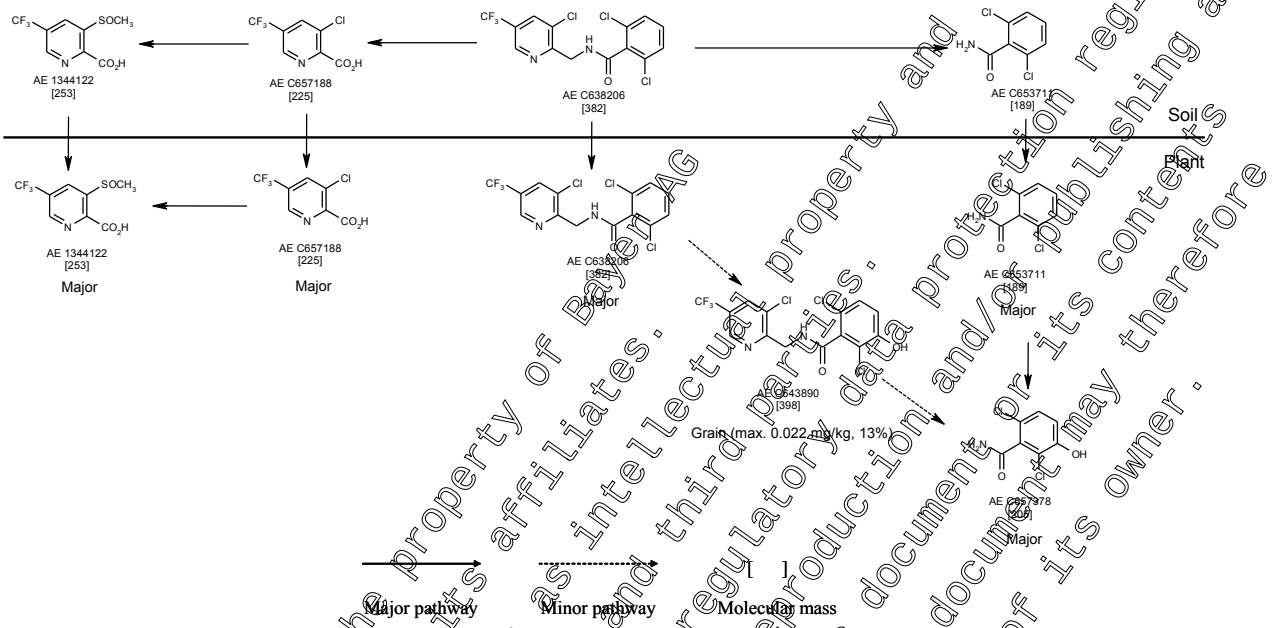
Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	7.054	na	100	0.348	na	100	1.009	na
Extractable Residue	93.8	6.62	na	93.5	0.325	na	87.3	0.88	na
AE C638206	34.9	2.462	2.462	25.7	0.089	0.089	27.5	0.277	0.277
AE C657188	7.0	0.494	0.291	2.1	0.007	0.004	4.1	0.042	0.025
AE 1344122	7.7	0.544	0.359	1.2	0.004	0.003	14.2	0.143	0.094
AE C653598	nd	nd	nd	9.4	0.033	0.019	4.8	0.048	0.028
AE B102895	nd	nd	nd	21.5	0.075	0.039	nd	nd	nd
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	40.9	2.884	na	25.7	0.089	na	19.3	0.195	na
Largest Single Unknown[1]	2.2	0.155	na	2.7	0.009	na	4.1	0.041	na
Total Identified and Characterised	90.5	na	na	85.6	na	na	69.9	na	na
Non-Extractable Residue	6.2	0.438	na	6.5	0.023	na	12.7[2]	0.128[2]	na

na = not applicable
nd = not detected
[1]Quantified in chromatograms given in report
[2]Non-extractable residue further extracted by acid and alkali hydrolysis

The residues of AE C638206 and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

Wheat Grain:

Figure 6.6.1- 5 The Proposed Metabolic Pathway for AE C638206 in Grain in Wheat Grown as a Confined Rotational Crop



[U-^{14}C-phenyl]-Labelled Experiment

Following application of [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) to soil, the total radioactive residues in wheat grain were 0.158, 0.020 and 0.054 mg/kg parent equivalents from the 29, 133 and 365-day plantings, respectively.

Fluopicolide (AE C638206) and its metabolites M-01 (AE C653711) and M-04 (AE C657378) were identified at each harvest. Fluopicolide (AE C638206) was detected in grain in very low amounts at 27.3% (0.043 mg/kg), 7.0 % (0.001 m/kg) and 7.3 % (0.004 mg/kg) of the TRR from the 29, 133- and 365-day plantings, respectively. M-01 (AE C653711) was detected in grain at 3.6% (0.003 mg/kg), 19.0 % (0.003 m/kg) and 17.9 % (0.005 mg/kg) of the TRR from the respective planting periods. M-01 (AE C653711) taken up by rotational crops was further metabolised to form M-04 (AE C657378; free hydroxylated AE C653711). M-04 (AE C657378) was detected in grain at 23.3% (0.003 mg/kg) and 17.9% (0.005 mg/kg) of the TRR from the 133 and 365-day plantings, respectively and was not detected in wheat grain from the 29 day planting.

Fluopicolide (AE C638206), M-01 (AE C653711) and M-04 (AE C657378) accounted for 30.9 to 49.7% of the TRR (38.7 to 75.6% of the extractable radioactive residue) in wheat grain. The maximum residues observed in grain were detected in wheat harvested following the 29 day planting. The residue in grain was composed of more than 10 different components. All other metabolites detected in the [U-^{14}C-phenyl]-labelled experiment were detected at <10% of the TRR and <0.01 mg/kg parent equivalents except for one polar unknown which was detected at a maximum of 13.4% (0.021 mg/kg parent equivalents).

A single finding of the free hydroxylated parent, M-06 (AE C643890), was observed in wheat grain from the 29-day planting but was not detected at later planting periods (13.1%, 0.021 mg/kg). Further derivatives or conjugates of fluopicolide (AE C638206) were not detected in wheat grain.

[2,6^{14}C-pyridyl]-Labelled Experiment

Following application of [2,6^{14}C-pyridyl]-labelled AE C638206 to soil, the total radioactive residues in grain were 2.600, 0.006 and 0.178 mg/kg parent equivalents from the 29, 133 and 365-day plantings.

Fluopicolide (AE C638206) and its metabolites M-02 (AE C657188) and M-05 (AE 1344122) were identified at each harvest. Fluopicolide (AE C638206) was detected in grain in very low amounts at 1.8% (0.046 mg/kg), 3.2% (0.003 m/kg) and 2.9% (0.005 mg/kg) of the TRR from the 29, 133 and 365 day plantings of soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206), respectively. The concentrations of parent were very similar to those observed in the [U-^{14}C-phenyl]-labelled experiment.

M-02 (AE C657188) and M-05 (AE 1344122), both pyridine carboxylic acid moieties, were, as expected from the known phloem mobility of aromatic carboxylic acids, transported to grain. M-02 (AE C657188) was detected in grain at 69.6% (1.064 mg/kg), 10.9% (0.006 mg/kg) and 14.2% (0.015 mg/kg) of the TRR from the 29, 133 and 365-day plantings, respectively. The levels of M-02 (AE 1344122) detected in grain were 13.1% (0.225 mg/kg), 66.6% (0.042 mg/kg) and 64.9% (0.077 mg/kg) for the same planting periods. These concentrations were considerably higher than the concentration of phenyl ring metabolites (AE 653711 and AE C657378) observed in grain in the [U-^{14}C-phenyl]-labelled experiment. The phenyl-ring metabolites would not be expected to be transported in the phloem system from leaves to grain as they are not carboxylic acids. M-02 (AE C657188) and M-05 (AE 1344122) are much more readily metabolised in soil than M-01 (AE C653711) and higher concentrations of the phenyl ring metabolites would be expected in rotational crops based on the different stabilities of the ring structures in soil as was found for all planting periods and plant tissues except wheat grain.

Some seasonal variation in the uptake of M-02 (AE C657188) and M-05 (AE 1344122) was observed. The 133-day plot was planted with winter wheat in October and the wheat developed through the winter and following summer reaching maturity after seven months in May. The total concentration of M-2 (AE C657188) and M-05 (AE 1344122) observed in the 133-day plot was lower than detected in spring wheat after the 365-day planting, planted in March and harvested in June with the wheat ripening in three months through the summer. The rate of formation of AE C657188 and AE 1344122 in soil from degradation of the parent and uptake by transpiration of the plants would be expected to be faster in summer due to the higher temperatures.

The proportion of M-02 (AE C657188) to M-05 (AE 1344122) was different following the 29-day planting (*ca.* 85:15 AE C657188 : AE 1344122) than observed at the 133 and 365-day plantings (*ca.* 15:85 AE C657188 : AE 1344122). M-02 (AE C657188) formed in soil was readily taken up by the growing crop. Prior to planting the soil in the 133 and 365-day plots was fallow for 133 and 272-days, respectively and during fallow periods M-02 (AE C657188) will metabolise to M-05 (AE 1344122) in soil. Once the soil was planted both were readily taken up by the growing crop.

Fluopicolide (AE C638206), M-02 (AE C657188) and M-05 (AE 1344122) accounted for 80.7 to 84.5% of the TRR (85.9 to 90.6% of the ERR) in wheat grain. All other metabolites detected in the [2,6^{14}C-pyridyl]-labelled experiment were <10% of the TRR (maximum 5.0% (0.005 mg/kg parent equivalents) or 1.9% TRR (0.048 mg/kg parent equivalents)). Further derivatives or conjugates of AE C638206 were not detected in wheat grain including the metabolites M-08 (AE C653598) and M-09 (AE B102859).

Overall:

The total amounts of identified and characterised components expressed as a percentage of the total radioactive residue were 44.0 to 49.7% for wheat grain grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 80.7 to 84.5% for that grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). The total amounts of identified and characterised components expressed as a percentage of the extractable radioactive residue were 55.1 to 75.6% for wheat grain grown in soil treated with [U-^{14}C-phenyl]-labelled fluopicolide (AE C638206) and 85.9 to 90.6% for those grown in soil treated with [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). Levels of individual components which were not identified or characterised did not exceed 10% of the TRR except for one polar unknown which was detected at a maximum of 13.4% (0.021 mg/kg parent equivalents).

Table 6.6.1- 10 Summary of Identification and Characterisation of Residues in Wheat Grain following 29, 133 and 365-day Plantings

a) Phenyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	0.158	na	100	0.020	na	100	0.054	na
Extractable Residue	79.9	0.13	na	66.3	0.01	na	65.7	0.04	na
AE C638206	27.3	0.043	0.043	7.0	0.001	0.001	7.3	0.004	0.004
AE C653711	3.6	0.006	0.003	19.0	0.003	0.003	17.9	0.010	0.005
AE C657378	nd	nd	nd	23.3	0.004	0.003	24.5	0.013	0.007
AE C643890	13.1	0.021	0.022	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	nd	nd	nd	nd	nd	nd	nd
Largest Single Unknown	13.4	0.021	na	4.5	0.001	na	3.1	0.002	na
Total Identified and Characterised	44.0	na	na	49.3	na	na	49.7	na	na
Non-Extractable Residue	13.5	0.021	na	35.8	0.007	na	34.3	0.019	na

b) Pyridyl label

Plot	29 Day			133 Day			365 Day		
	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg	%TRR	mg/kg parent equivs	mg/kg
Total Radioactive Residue (TRR)	100	2.600	na	100	0.096	na	100	0.178	na
Extractable Residue	93.3	2.43	na	94.0	0.09	na	94.2	0.17	na
AE C638206	1.8	0.046	0.046	3.2	0.003	0.003	2.9	0.005	0.005
AE C657188	69.6	1.809	1.064	10.9	0.010	0.006	14.2	0.025	0.015
AE 1344122	13.1	0.341	0.225	66.6	0.064	0.042	64.9	0.116	0.077
AE C653598	nd	nd	nd	nd	nd	nd	nd	nd	nd
AE B102895	nd	nd	nd	nd	nd	nd	nd	nd	nd
AE C643890	nd	nd	nd	nd	nd	nd	nd	nd	nd
Total Conjugates	nd	nd	nd	nd	nd	nd	nd	nd	nd
Largest Single Unknown	1.9	0.048	na	5.0	0.005	na	2.2	0.004	na
Total Identified and Characterised	84.5	na	na	80.7	na	na	82.0	na	na
Non-Extractable Residue	6.7	0.175	na	6.0	0.006	na	5.8	0.010	na

na = not applicable nd = not detected [1]Quantified in chromatograms given in report

The residues of fluopicolide (AE C638206) and its metabolites have been expressed as concentration in mg/kg parent equivalents. Metabolites have also been expressed as actual concentrations, converted from concentrations in mg/kg parent equivalents using the relevant molecular weights.

Further Conjugates:

In addition to the individual metabolites identified; nine further derivatives and conjugates of fluopicolide (AE C638206) and three of the phenyl ring were fully characterised in wheat forage and straw from the 29 day planting in which they were most abundant (see the following figure).

In 29 day forage none of the conjugates exceeded 10% of the TRR. Only one conjugate peak exceeded 10% in straw: P4 accounted for as much as 15.6% in the pyridyl labelled straw extract. Further separation was not pursued with the straw although, in the case of forage, this peak was resolved into three components.

Fluopicolide (AE C638206) initially underwent metabolism via one of two steps, either glutathionylation via elimination of one of the chloro groups in the dichlorophenyl ring or hydroxylation in position 3 of the dichlorophenyl ring to form M-06 (AE C643890). Hydroxylation will change the electophilic properties of the ring and reduce the likelihood of glutathionylation. Conjugation of the hydroxylated or thiolated (addition of -SH) versions of the parent to glucose, malonic acid, glyceric acid or amino acids was observed.

A similar hydroxylation of M-01 (AE C653711) in position 3 of the dichlorophenyl ring to form M-04 (AE C657378) was observed in wheat. Further derivatives of the phenyl ring were observed in wheat forage from the 29 day planting including 2 isomers of glucose-malonic acid conjugates of hydroxylated M-01 (AE C653711).

In wheat straw and forage from other plantings and occasionally in radish tops and lettuce, two regions of radioactivity were observed, Regions A and B. Regions A and B were resolved into several components in a 365 day wheat sample. Direct comparison to the individual components was not possible, but based on relative retention times, the components in Region A and B were concluded to correspond to conjugates in the group (P4, P5, P8, P10 and P11) characterised in 29 Day wheat. These components all displayed an intact skeleton without cleavage of the aliphatic bridge between the two rings present in the parent molecule.

As discussed before, it should be noted that the designations (P numbers) were for radioactive peaks identified as part of the crop rotational study and do not imply these are the same metabolites observed in soil and lysimeter studies with similar designations. Thus P2, P4, P5, P8, P10 etcetera in this summary refer to metabolites isolated from plant samples only.

Maximum amounts of individual derivatives are given in the following tables.

Table 6.6.1- 11 Maximum Levels of Derivatives and Conjugates Characterisation in Confined Rotational Crop Residues (following 29 day Plantings)

a) Phenyl label

Individual Conjugates		Wheat Forage		Wheat Straw	
Molecular Mass	Report Reference	%TRR	mg/kg parent equivs	%TRR	mg/kg parent equivs
Total Radioactive Residue (TRR)[1]		100	4.949	100	13.560
Total Extractable Residue		95.4	4.72	71.4	9.68
453	P2a	2.2	0.109	nd	nd
453	P2b				
183	P2c	2.0	0.099	nd	nd
Total Phenyl Ring Conjugates		4.2	0.208	nd	nd
483	P4a	6.2	0.307	8.6	1.166
646	P4b	3.3	0.163		
662	P4c	nd	nd	nd	nd
646	P5	3.5	0.173	2.6	0.352
558 and 560	P8a 2 metabolites	nd	nd	3.2	0.434
500	P8b	nd	nd	3.9	0.529
500	P10	2.4	0.119	3.6	0.488
478	P11	nd	nd	3.6	0.488
Total Intact Conjugates		15.4	0.762	25.5	3.458
Total Conjugates		19.6	0.97	25.5	3.458

b) Pyridyl label

Individual Conjugates		Wheat Forage		Wheat Straw	
Molecular Mass	Report Reference[1]	%TRR	mg/kg parent equivs	%TRR	mg/kg parent equivs
Total Radioactive Residue (TRR)		100	4.288	100	7.054
Total Extractable Residue		97.5	4.18	93.8	6.62
483	P4a	4.3	0.184	15.6	1.100
646	P4b	2.8	0.120		
662	P4c	0.8	0.034		
646	P5	2.6	0.103	6.0	0.423
558 and 560	P8a 2 metabolites	nd	nd	9.9	0.698
500	P8b				
500	P10	1.3	0.056	3.8	0.268
478	P11	1.6	0.069	5.6	0.395
Total Conjugates		13.4	0.566	40.9	2.884

na = not applicable
nd = not detected
[1] Refers to plant metabolites only

Two isomers of the hydroxylated AE C653721 conjugate (Molecular Mass 453, Report references P2a and P2b) and a hydroxylated AE C638206 conjugate (Molecular Mass 500, Report references P8b and P10) were observed.

The concentration of identified and characterised metabolites in the individual RACs for each planting period are shown in the following figues.

Figure 6.6.1- 6 Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings

a) Lettuce

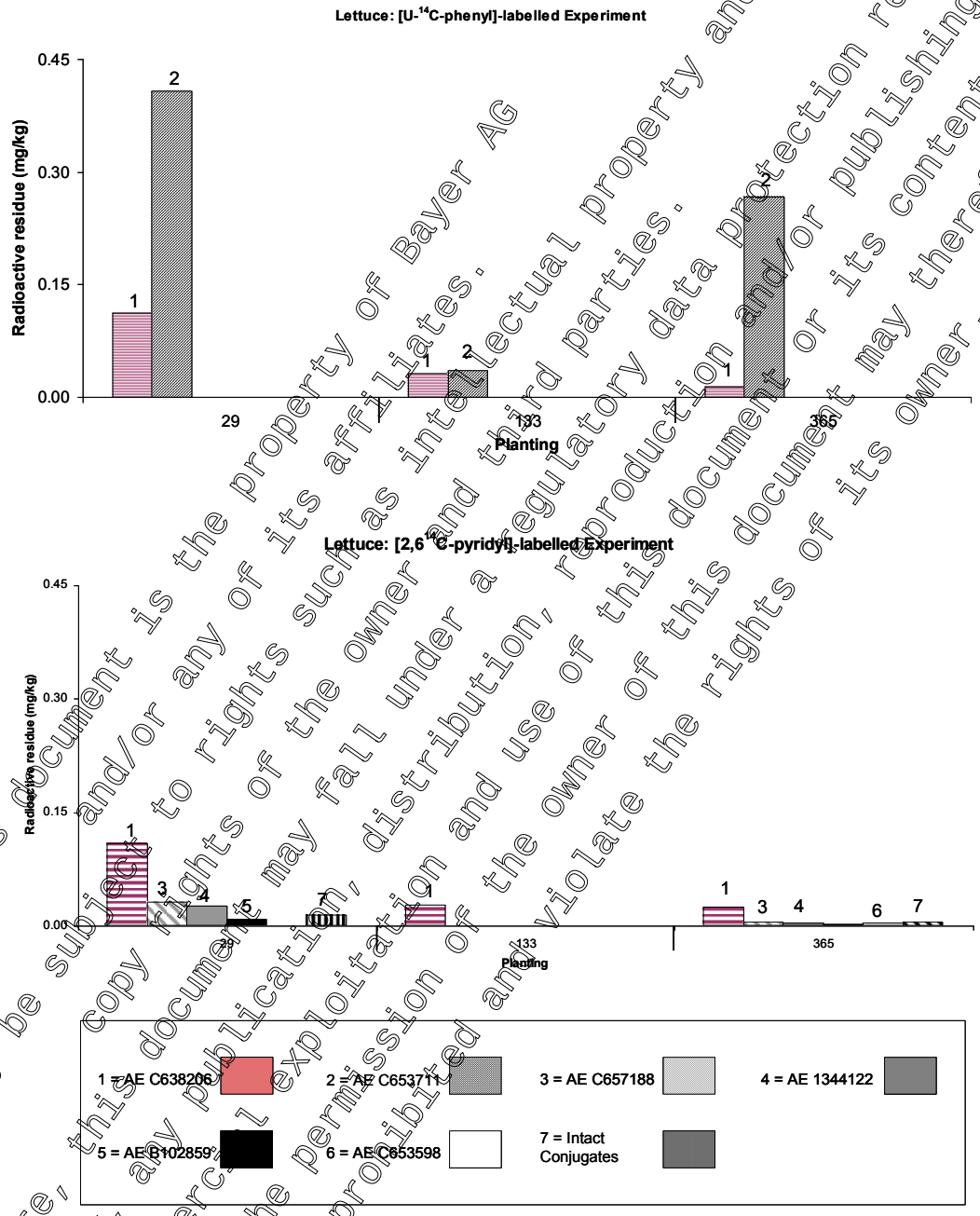


Figure 6.6.1- 7 **Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings**

b) Radish Tops

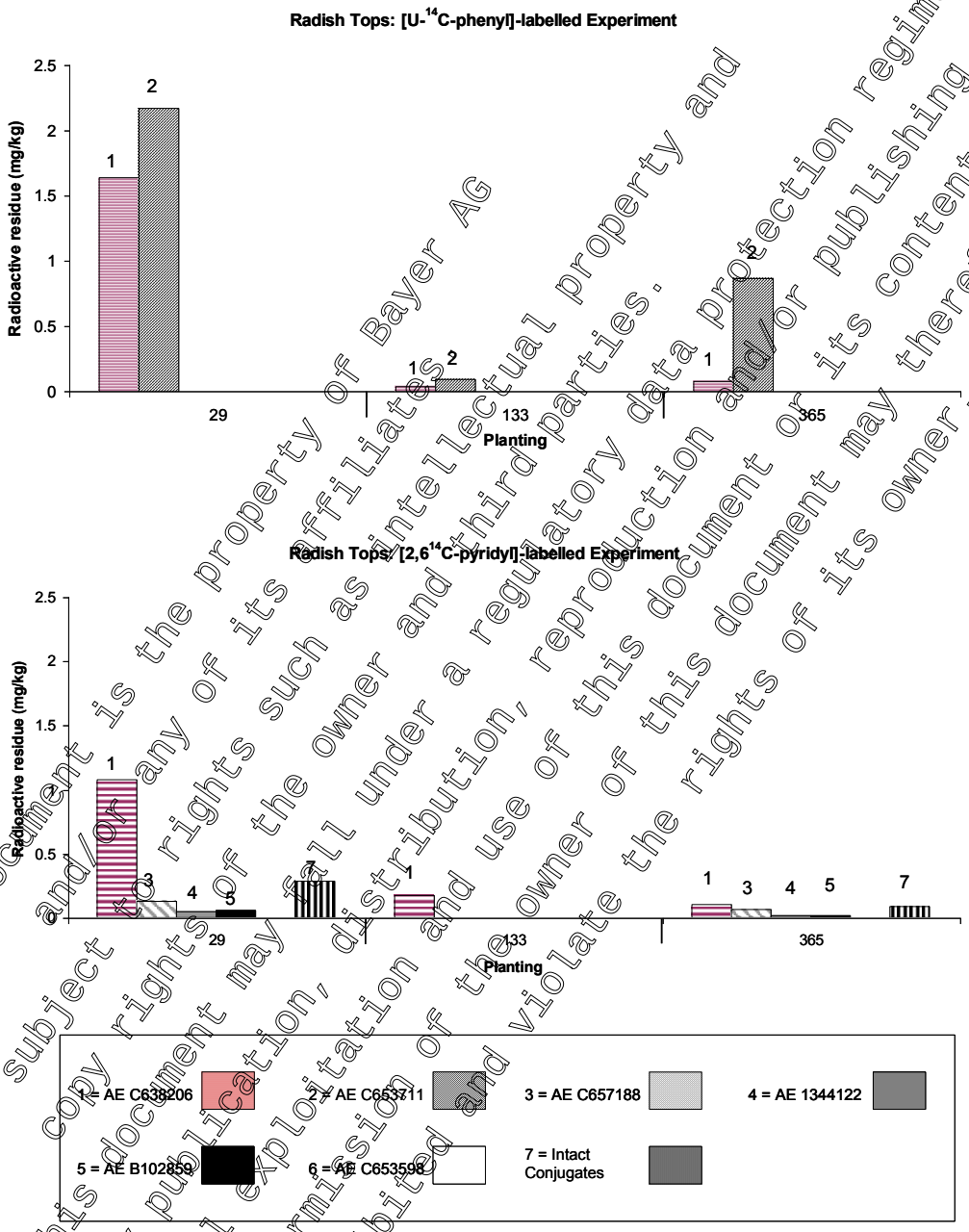


Figure 6.6.1- 8 **Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings**

c) Radish Roots

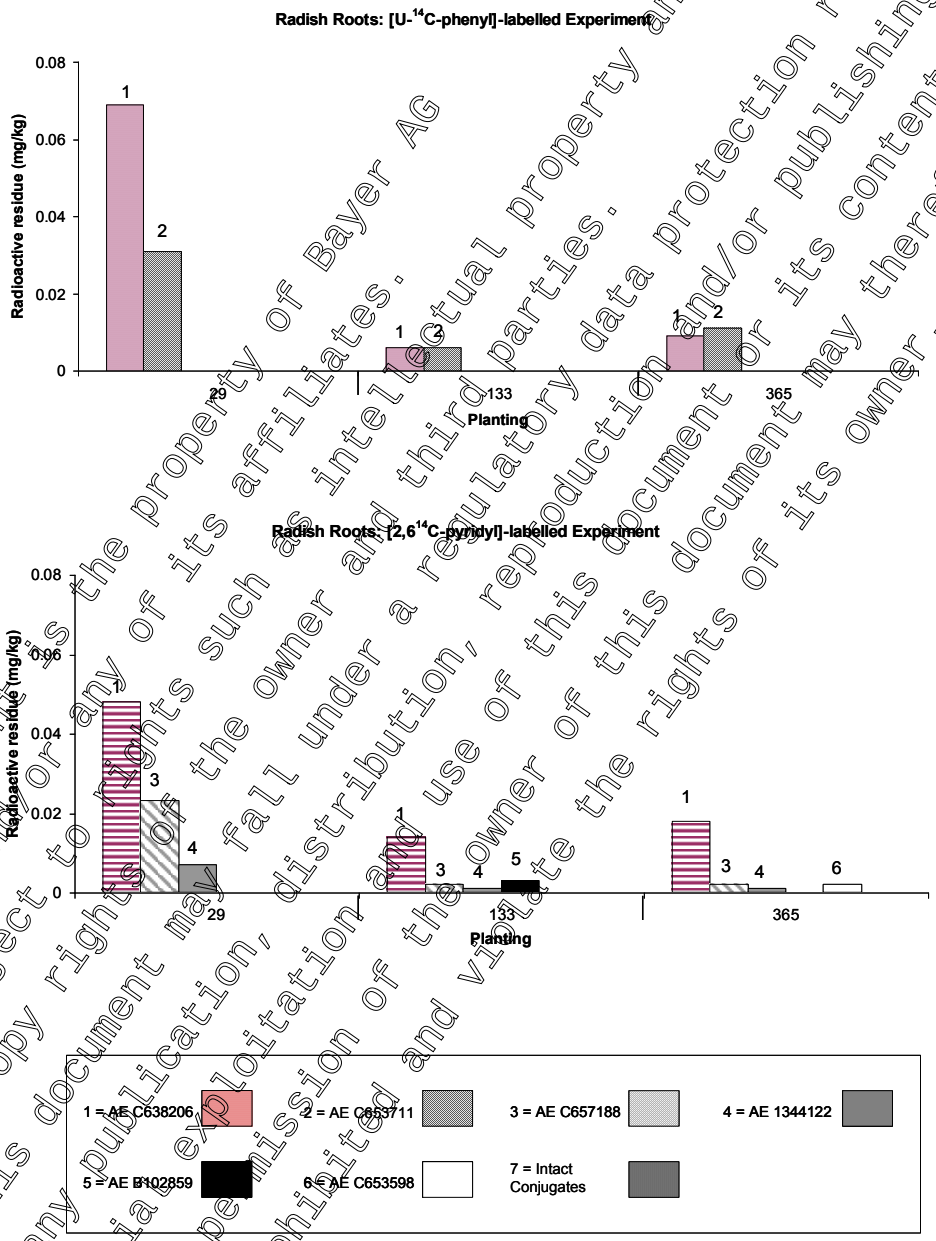


Figure 6.6.1- 9 Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings

d) Forage

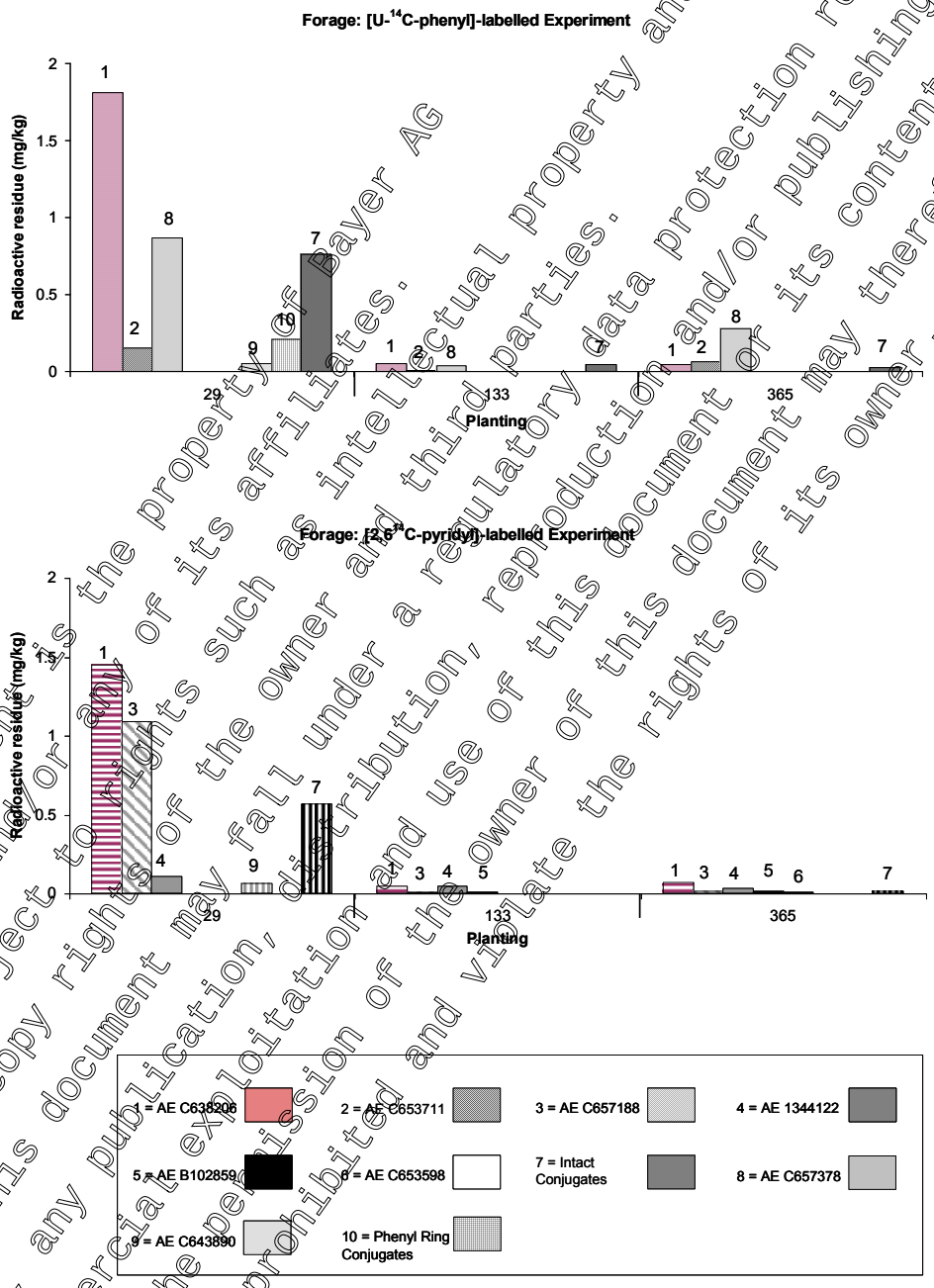


Figure 6.6.1- 10 **Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings**

e) Straw

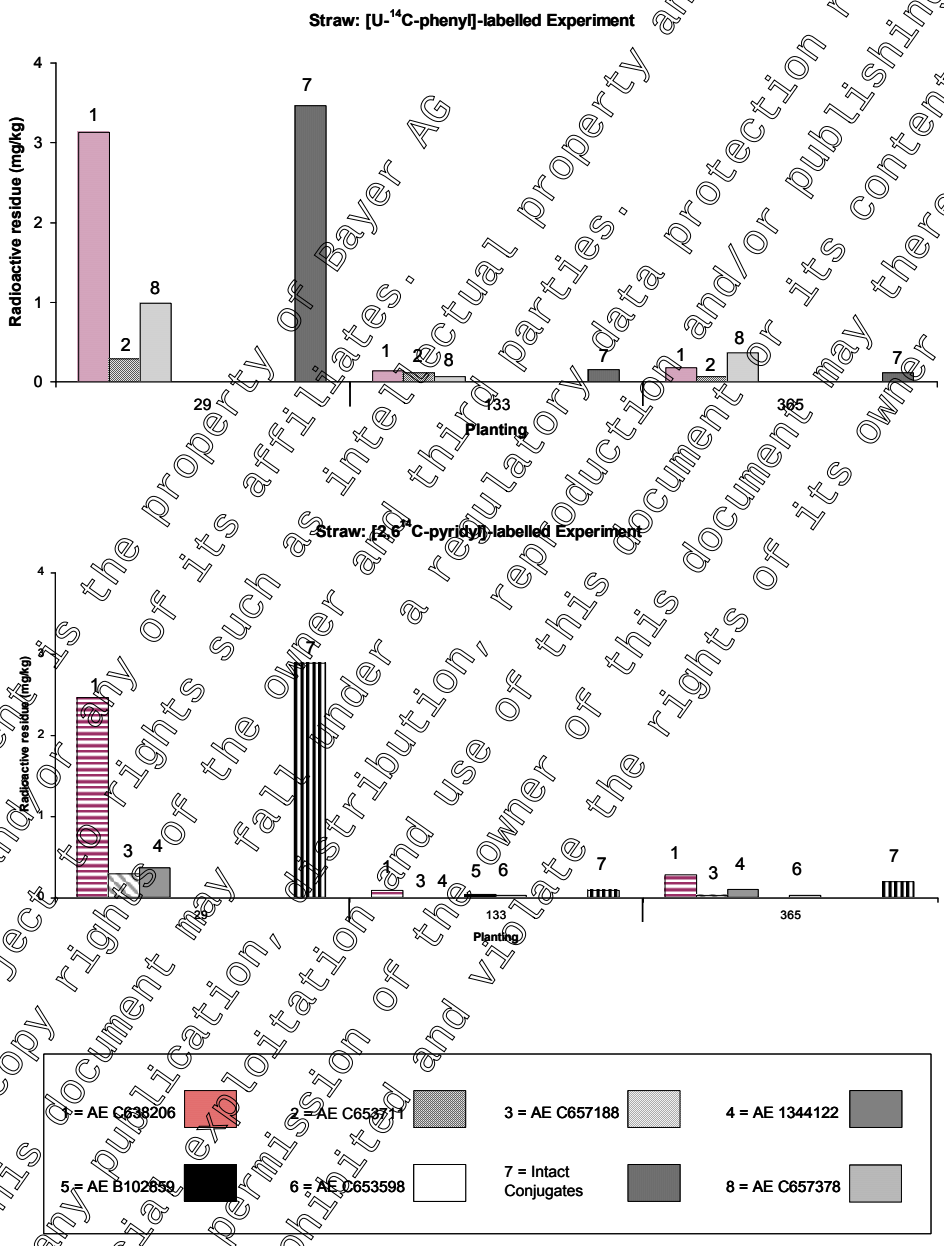
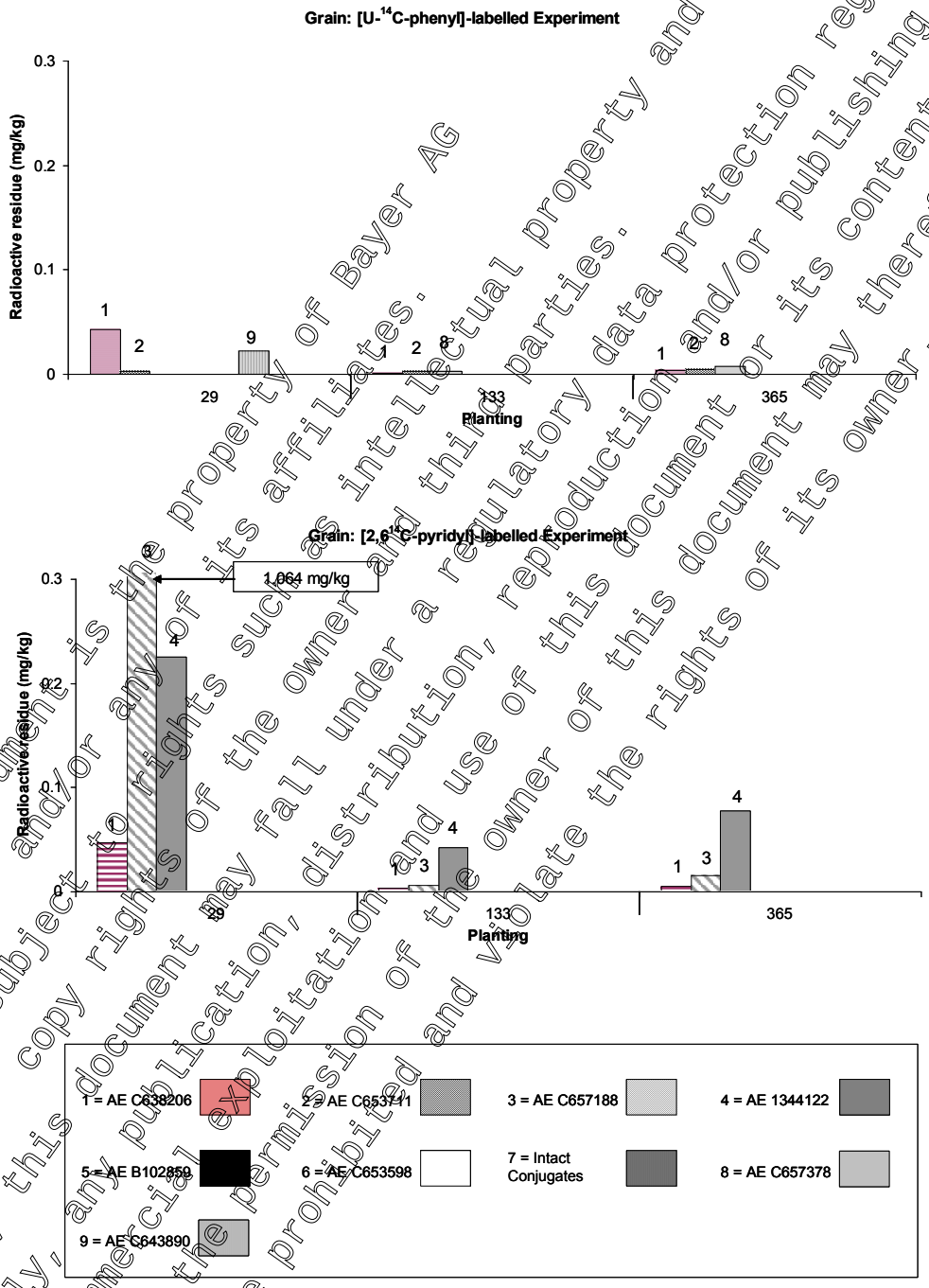


Figure 6.6.1- 11 **Summary of Identification and Characterisation of Residues in Crops following 29, 133 and 365 day Plantings**

f) Grain



Analysis of Soil from Treated Plots:

Residue values in the soil plots at harvest are outlined in the following table. The soil residue showed a general decline after treatment, although there was some variability in the results. Application of the test item was made as evenly as possible, and uniform distribution was shown by the generally consistent total crop residues when triplicate samples were harvested within a RAC with a mean relative standard deviation of 11.6%.

Fluopicolide (AE C638206) soil residues remained readily extractable over the course of the study, with only a slight increase in non-extractable residues with time. TLC analysis showed the parent compound to be the only radioactive component on Day 0. Subsequently, the major residue components in soil were the parent fluopicolide (AE C638206), M-01 (AE C653711) and M-02 (AE C657188). Similar results have been observed in laboratory soil metabolism studies.

Table 6.6.1- 12 Total radioactive residues (mg/kg AE C638206 equivalents) in soil cores (mean values)

a) Phenyl label

Soil Sampling Timepoint	29 Day		133 Day		365 Day	
	DAT	TRR (mg/kg)	DAT	TRR (mg/kg)	DAT	TRR (mg/kg)
Treatment	0	0.216	5	0.047	na	na
Planting	29	0.216	133	0.040	365	0.102
Immature Wheat[1]	68	0.051	281	0.076	410	0.047
Mature Radish	71	0.066	196	0.036	421	0.045
Mature Lettuce	83	0.056	216	0.030	421	0.045
Mature Wheat	93	0.068	335	0.103	449	nd

b) Pyridyl label

Soil Sampling Timepoint	29 Day		133 Day		365 Day	
	DAT	TRR (mg/kg)	DAT	TRR (mg/kg)	DAT	TRR (mg/kg)
Treatment	0	0.197	5	0.086	na	na
Planting	29	0.068	133	0.038	365	0.044
Immature Wheat[1]	68	0.067	281	0.028	410	0.035
Mature Radish	71	0.055	196	0.043	421	0.070
Mature Lettuce	83	0.096	216	0.046	421	0.070
Mature Wheat	93	0.061	335	0.021	449	nd

na = not applicable nd = not determined

[1]Wheat forage harvest for the 133 day planting was after lettuce and radish harvests

III. Conclusions

A confined rotational crop study was conducted with [U-^{14}C-phenyl]-labelled and [2,6^{14}C-pyridyl]-labelled fluopicolide (AE C638206). The substance was applied to soil at a rate of 400g as/ha. Following an initial 29-day fallow period, radishes, lettuces, and wheat were planted at three consecutive rotational intervals.

The total radioactivity in soil was found to decline steadily. Total radioactive residues in plant matrices declined with longer soil ageing. Mean residues in 29-day RACs ranged from 0.09 ppm (radish root) to 13.56 ppm (wheat straw), but residues declined greatly in the 133-day and 365-day ageing periods. The 133-day crop residues ranged from 0.02 ppm (radish root) to 0.84 (wheat straw). The 365-day crop residues were observed to increase slightly, ranging from 0.02 ppm (radish root) to 2.37 ppm (wheat straw). This was considered to be a result of seasonal variation. The 133-day plots were planted in October and developed through the winter when formation of soil metabolites from the degradation of parent would be slowest. In contrast, the 365-day plots were planted in March and developed through the summer when the plants would be more metabolically active.

Non-extractable residue (NER) was less than 10% or less than 0.05 mg/kg in most RACs with exception of some wheat forage and straw samples. Radioactive residues which remained non-extractable after sequential treatment with acid and base were less than 0.05 mg/kg, except in 29-day wheat straw (phenyl) where 0.310 mg/kg represented only 2.4% of the total radioactive residue.

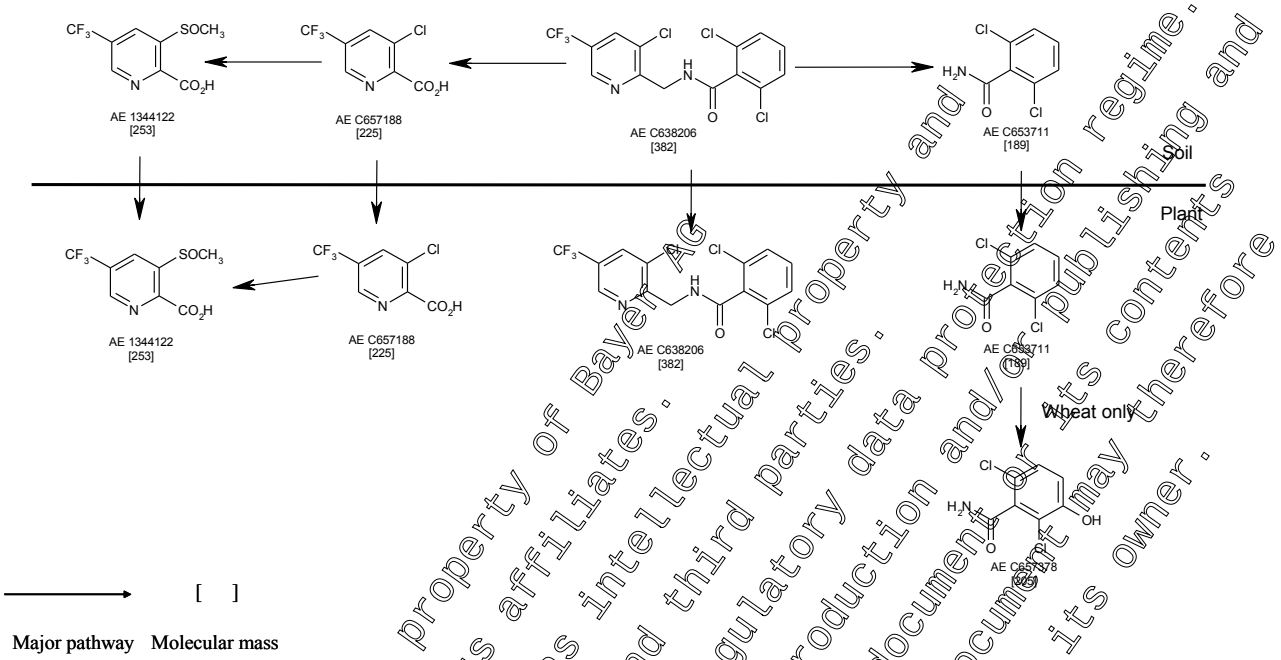
When applied to bare soil, fluopicolide (AE C638206) was readily taken up by crops in the xylem system and metabolised to numerous related components in rotational crops. Residue components identified in this study included unchanged fluopicolide (AE C638206), M-01 (AE C653711), M-04 (AE C657378), M-02 (AE C657188), M-05 (AE 1344122), M-08 (AE C653598), M-09 (AE B102859), and M-06 (AE C643890). In addition, conjugates were fully characterised utilising LC-MS. The total amounts of identified or characterised components expressed as a percent of the extractable radioactive residue was ≥ 70 % in all RACs with the exception of 29 day wheat grain (phenyl), in which the total identified was 55% of the extractable residue. In general, levels of individual components which were not identified or characterised did not exceed 10% of the TRR. In two RACs from the 29 day planting unknown individual components were detected at 11% of the TRR. However, in these samples the total amounts of identified or characterised components expressed as a percent of the extractable radioactive residue was ≥ 76%.

The principle metabolites identified in phenyl-labelled experiments were the parent fluopicolide (AE C638206), M-01 (AE C653711), and in wheat only, M-04 (AE C657378; 3-hydroxy- AE C653711). M-06 (AE C643890), which is the 3-hydroxy derivative of the parent, was detected at a quantifiable level only in 29-day wheat grain and forage (13.1%, 0.022 mg/kg and <1.0%, <0.051 mg/kg, respectively).

The principle metabolites identified in pyridyl-labelled experiments included the parent fluopicolide (AE C638206), M-02 (AE C657188), and M-05 (AE 1344122). M-08 (AE C653598), the amide congener of PCA (M-02), was detected in some 365-day RACs and in 133-day straw, but not exceeding 9.4% or 0.028 mg/kg in crops for animal fodder. It did not exceed 9.5% or 0.003 mg/kg in RACs considered as models for human consumption. M-06 (AE C643890) was detected only in 29-day wheat forage at 1.4% 0.063 mg/kg. Finally, M-09 (AE B102859) was detected at a maximum concentration of 0.052 mg/kg (4.8%) and 0.003 mg/kg (19.1%) in RACs used as models for animal fodder and human consumption respectively.

The proposed major metabolic pathway for fluopicolide (AE C6382060) in rotational crops is given in the following figure. M-04 (AE C657378) and M-05 (AE 1344122) only formed significant residues in wheat. M-04 (AE C657378) was not detected at all in other crops and M-05 (AE 1344122) was generally a minor component.

Figure 6.6.1- 12 The Major Metabolic Pathway for AE C638206 in Confined Rotational Crops



Assessment and conclusion by applicant:

Study acceptable.

Based on the findings of the confined rotational crop study, fluopicolide, M-01, M-02, M-04, M-05, M-06 and M-09 were selected as analytical targets for the open field rotational crop studies.

CA 6.6.2 Magnitude of residues in rotational crops

Risk assessment residue definition (EFSA Journal 2019;17(7):5748)

- in food of plant origin: Definition 1: Fluopicolide
  Definition 2: Metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01)
- in food of animal origin: Definition 1: Fluopicolide
  Definition 2: Metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01)

Additional analytical targets in field residues trials (see chapter 6.3):

- **Rotational crops:** M-02, M-04, M-05, M-06 and M-09

Data, on the residue of fluopicolide in rotational crops, was evaluated for the first inclusion of fluopicolide into Annex I of Council Directive 91/414/EEC (DAR, UK, 2005).

New data are available to show the residue uptake for fluopicolide residues from the soil into succeeding crops.

One study is currently available to show the residue uptake for following crops (barley, lettuce and carrots) when fluopicolide is applied at a rate of approximately 0.7 kg a.s/ha to bare soil. This study is summarised here within this section.

As this study indicates that residue uptake is likely for succeeding crops, additional studies are on-going to cover all of the 'super-groups' according to the OECD 'Draft Guidance Document on Residues in Rotational Crops' (November, 2017).

Data already evaluated during the first EU review process for inclusion on Annex I.

Data Point:	KCA 6.6.2/01
Report Author:	[redacted]
Report Year:	2003
Report Title:	Determination of the residues of AEC638206 and metabolites in potatoes and rotational crop following treatment with AE C638206 00 SC18 A1 under field conditions in southern and northern Europe 2000
Report No:	C036940
Document No:	M-221798-01-1
Guideline(s) followed in study:	BBA: Part IV, 3; EU (=EEC): 96/68/EC, Working document 7524/VI/95 rev.2, (1997; IVA: Part IA and IB
Deviations from current test guideline:	none
Previous evaluation:	yes, evaluated and accepted DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Data Point:	KCA 6.6.2/02
Report Author:	[redacted]
Report Year:	2004
Report Title:	Determination of the residues of AE C 638206 and metabolites in potatoes and rotational crop following treatment with AE C 638206 00 SC18 A1 under field conditions in southern and northern Europe 2000
Report No:	C039706
Document No:	M-227140-01-1
Guideline(s) followed in study:	EU-Ref: Council Directive 91/414/EEC of July 15,1991, Annex II, part A, point 6 and Annex III, part A, point 8 Residues in or on Treated Products, Food and Feed
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted in DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Data Point:	KCA 6.6.2/03
Report Author:	[redacted]
Report Year:	2003
Report Title:	Determination of the residues of AE C638206 and metabolites in potatoes and rotational crop following treatment with AE C638206 00 SE10 A303 under field conditions in northern Europe 2001
Report No:	C038284
Document No:	M-224665-01-1
Guideline(s) followed in study:	BBA: Part IV, 3; EU (=EEC): 96/68/EC, Working doc. 7524/VI/95 rev.2, (1997); IVA: Part IA and IB
Deviations from current test guideline:	None
Previous evaluation:	yes, evaluated and accepted in the DAR (2005)
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

The above studies were previously submitted to support the Annex I inclusion for fluopicolide and have been summarized within the DAR. These rotational crop studies determined the residues levels within succeeding crops (potatoes, wheat, faba beans and cabbage) at plant-back intervals of approximately 30, 200 and 365 days, after the treatment of potato crops which had been treated with a fluopicolide containing product.

Fluopicolide was applied to the potato crop at a maximum seasonal rate of 400 g a.s./ha (4 x 100 g a.s/ha). While this is the maximum applied rate for the representative uses, these studies do not take into consideration the plateau concentration level of fluopicolide which may potentially be within the soil; 800 g a.s./ha (based on a DT_{50} of 650 days). Consequently, a total application rate of 1200 g a.s./ha (the plateau concentration level + the maximum seasonal rate) would be a more appropriate rate to use within the rotational crop studies.

New rotational crop studies have since been completed using rate of 1200 g a.s./ha or 700 g a.s./ha (a scaling factor of 1.7 was applied to the residue results, in accordance with the proportionality principle).

These new studies are summarized within the remainder of this section. It is not considered appropriate to use the proportionality approach to scale the previously evaluated trials, due to the wide variation between the rate used in the trials (400 g a.s./ha) and the most appropriate rate (1200 g a.s./ha). Furthermore, not all the appropriate analytical targets were analysed within the field samples; M-06 and M-09 are not analysed within the studies, and M-04 and M-05 are not analysed within study [redacted] 2003; M-221798-01-1.

For these reasons, it is no longer consider appropriate to rely on the data presented within these study reports and they have been superseded with new studies which have been submitted to support the fluopicolide renewal (and summarized below). These old studies have therefore not been summarized.

New data for AIR:

Data Point:	KCA 6.6.2/04
Report Author:	[redacted]
Report Year:	2018
Report Title:	Amendment no. 1 to final report - Determination of the residues of fluopicolide in/on soil and the field rotational crops barley, carrot and lettuce after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 to bare soil in the field in Germany, the Netherlands, southern France and Italy
Report No:	16-2501
Document No:	M-623459-02-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	No
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted in lettuce, carrot and barley after application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in Germany, the Netherlands, southern France and Italy during 2016-2017. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 11.0 L/ha (equivalent to 0.688 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 20 to 30 days (1st rotation), 92 to 208 days (2nd rotation) and 287 to 380 (3rd rotation).

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 434 days prior to residue analysis.

Residues of fluopicolide, M-01, M-02 and M-09 residues were analysed using HPLC-MS/MS method 01209/M001. Method 00782/M006 (HPLC-MS/MS) was used to quantify residues of M-04, M-05 and M-06 in the samples. The limit of quantification was 0.01 mg/kg for all in the respective matrices. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ, with the exception of two instances where fluopicolide had been previously used on the plots as a maintenance product.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EV58002080
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	29-01-2019
2.	**Test Commodity**	
	Crop:	Carrot
	Variety:	Merida, Laguna, Nerac Summer, Nerja Autumn, Romance Bundle, Romance F1 Nantaise, Santorin F1, Maestro, Carvejo
	Crop part(s) or processed commodity:	Leaves (tops) and roots
	Sample size:	Not stated
3.	**Test Commodity**	
	Crop:	Lettuce
	Variety:	Aleppo, Antonet, Bente butterhead, Donela Butterhead, Kiribati F1 Oak leaf, Kyno Oak leaf, Magenta
	Crop part(s) or processed commodity:	Head leaves
	Sample size:	Not stated
4.	**Test Commodity**	
	Crop:	Barley
	Variety:	Ketos, Avalon, Naomie Winter, Irina Summer, Cassia 2 rows, Sebastian Spring Barley, Arianna, Letece
	Crop part(s) or processed commodity:	Grain, straw and green material,
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised four supervised residue trials in Germany, the Netherlands, southern France and Italy. At each trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 11.0 L/ha (equivalent to 0.688 kg/ha fluopicolide) with a water rate of 300 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ~ 8 cm.

After a period of 20-30 days after treatment (DAT), a root crop (plot 1A: carrot), a cereal crop (plot 1C: barley) were sown and lettuce (plot 1B) was planted to simulate a case of crop failure. Control plots were planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 100-140 days after treatment (DAT), barley, carrots and lettuce were planted and sown on the treated and control plots (2A, 2B and 2C). This rotational situation simulates a second use of the same plot within a single season.

At 270-365 days after treatment (DAT) barley, carrots and lettuce were planted and sown on the treated and control plots (3A, 3B and 3C). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table

Table 6.6.2- 1 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval			Remarks
		Root/tuber crop (DAT)	Leafy crop (DAT)	Cereal crop (DAT)	
16-2501-01 Germany	One application on bare soil, plant-back interval 20-30 days after treatment	1A Carrot (30)	1B Lettuce (30)	1C Barley (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 100-140 days (2A), 120-180 days (2B) and 150-210 days (2C) after treatment	2A Carrot (108)	2B Lettuce (108)	2C Barley (170)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 300-365 days (3A & 3B) and 270-330 days (3C) after treatment	3A Carrot (347)	3B Lettuce (362)	3C Barley (347*)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
16-2501-02 Netherlands	One application on bare soil, plant-back interval 20-30 days after treatment	1A Carrot (21)	1B Lettuce (21)	1C Barley (29)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 100-140 days (2A), 120-180 days (2B) and 150-210 days (2C) after treatment	2A Carrot (92)	2B Lettuce (126)	2C Barley (175)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 300-365 days (3A & 3B) and 270-	3A Carrot (377*)	3B Lettuce (380*)	3C Barley (357*)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval			Remarks
		Root/tuber crop (DAT)	Leafy crop (DAT)	Cereal crop (DAT)	
	330 days (3C) after treatment				
16-2501-03 South France	One application on bare soil, plant-back interval 20-30 days after treatment	1A Carrot (26)	1B Lettuce (26)	1C Barley (29)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 100-140 days (2A), 120-180 days (2B) and 150-210 days (2C) after treatment	2A Carrot (103)	2B Lettuce (139)	2C Barley (193)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 300-365 days (3A & 3B) and 270-330 days (3C) after treatment	3A Carrot (336)	3B Lettuce (349)	3C Barley (287)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
16-2501-04 Italy	One application on bare soil, plant-back interval 20-30 days after treatment	1A Carrot (23)	1B Lettuce (28)	1C Barley (26)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 100-140 days (2A), 120-180 days (2B) and 150-210 days (2C) after treatment	2A Carrot (111)	2B Lettuce (125)	2C Barley (208)	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops
	One application on bare soil, plant-back interval 300-365 days (3A & 3B) and 270-330 days (3C) after treatment	3A Carrot (363)	3B Lettuce (353)	3C Barley (291	1) Spray application on bare soil and incorporation 2) Planting/sowing or rotational crops

DAT = Days after treatment

* Remark: Plant-back intervals are slightly longer. The timing for replanting of rotational crops as given within OECD 504 (limited field studies) suggested 7-30 days for assessing circumstances of crop failure or closely rotated crops at 270-365 days for crops rotated the following year. Thus, the actual plant-back intervals are considered to be within an acceptable range.

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 2 Summary of the analytical methods

Method	**01209/M001**
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05 in carrot leaves, carrot roots, lettuce leaves, barley grain, barley green material and barley straw; M-06, in barley grain)
Method	**00782/M006**
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05 in carrot leaves, carrot roots, lettuce leaves, barley grain, barley green material and barley straw; M-06, in barley grain)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02 and M-09 residues was 85 and 414 days. The storage period for samples until the analysis of M-04, M-05 and M-06 residues was 94 and 434 days.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

No residues above the LOQ were found in the control samples, except for the following samples: in the control sample 16-2501-140E (barley, green material) – residues of M-01 were found (12% of the LOQ). The recoveries of this control were corrected accordingly. The individual and mean recoveries per fortification level were within the range 70-110%. The RSD values were below 20%. In trial 16-2501-03 fluopicolide was applied as a maintenance product on all plots during August 2014. This could be the reason that residues were observed above the LOQ in some control samples and resides above the LOQ in some control samples of trial 16-2501-04 are likely attributed to contamination.

Due to unusual weather effects in the field trial 16-2501-04 (Italy) the test system for barley on plots C-3C and T-3C failed, therefore the sampling of the 3rd rotation (planned plant-back intervals of 270-330 days) including all corresponding samples were cancelled.

Table 6.6.2- 3 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
16-2501-01 Germany	T-1C	27	0139E	30	218	Barley	Green material	0.060	0.013	<0.01	<0.01
	T-1C	27	0141E	75	281	Barley	Green material	0.071	0.055	<0.01	<0.01
	T-2C	170	0168E	30	361	Barley	Green material	0.032	0.02	<0.01	<0.01
	T-2C	170	0170E	75	424	Barley	Green material	0.045	0.085	<0.01	<0.01
	T-3C	347	0197E	30	408	Barley	Green material	0.037	0.019	<0.01	<0.01
	T-3C	347	0199E	75	440	Barley	Green material	0.032	0.12	<0.01	<0.01
	T-1C	27	0144E	89	304	Barley	Grain	0.033	0.014	<0.01	<0.01
	T-2C	170	0173E	89	447	Barley	Grain	0.016	0.016	<0.01	<0.01
	T-3C	347	0202E	89	472	Barley	Grain	<0.01	<0.01	<0.01	<0.01
	T-1C	27	0145E	89	304	Barley	Straw	0.11	0.046	<0.01	<0.01
	T-2C	170	0174E	89	447	Barley	Straw	0.055	0.057	<0.01	<0.01
	T-3C	347	0203E	89	472	Barley	Straw	0.041	0.014	<0.01	<0.01
	T-1A	30	0122E	47	121	Carrot	Leaf	0.062	0.059	<0.01	<0.01
	T-1A	30	0126E	49	135	Carrot	Leaf	0.057	0.039	<0.01	<0.01
	T-2A	108	0151E	47	194	Carrot	Leaf	0.036	0.2	<0.01	<0.01
	T-2A	108	0155E	49	208	Carrot	Leaf	0.022	0.11	<0.01	<0.01
	T-3A	347	0180E	47	460	Carrot	Leaf	<0.01	0.19	<0.01	<0.01
	T-3A	347	0184E	49	473	Carrot	Leaf	<0.01	0.11	<0.01	<0.01
	T-1A	30	0123E	47	121	Carrot	Root	0.065	<0.01	<0.01	<0.01
	T-1A	30	0127E	49	135	Carrot	Root	0.061	<0.01	<0.01	<0.01
	T-2A	108	0152E	47	194	Carrot	Root	0.036	0.011	<0.01	<0.01
	T-2A	108	0156E	49	208	Carrot	Root	0.032	0.011	<0.01	<0.01
	T-3A	347	0181E	47	460	Carrot	Root	0.019	0.013	<0.01	<0.01
	T-3A	347	0185E	49	473	Carrot	Root	0.014	0.014	<0.01	<0.01

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
	T-1B	30	0132E	45	65	Lettuce	Head	0.017	0.022	<0.01	<0.01
	T-1B	30	0134E	49	79	Lettuce	Head	0.021	0.019	<0.01	<0.01
	T-2B	108	0161E	46	136	Lettuce	Head	0.031	0.048	<0.01	<0.01
	T-2B	108	0163E	49	150	Lettuce	Head	0.027	0.056	<0.01	<0.01
	T-3B	362	0190E	45	402	Lettuce	Head	<0.01	0.021	<0.01	<0.01
	T-3B	362	0192E	49	416	Lettuce	Head	<0.01	0.031	<0.01	<0.01
16-2501-02 The Netherlands	T-1C	29	0139E	30	272	Barley	Green material	0.079	0.011	<0.01	<0.01
	T-1C	29	0141E	75	280	Barley	Green material	0.055	0.013	<0.01	<0.01
	T-2C	175	0168E	30	398	Barley	Green material	0.045	0.025	<0.01	<0.01
	T-2C	175	0170E	75	426	Barley	Green material	0.033	0.031	<0.01	<0.01
	T-3C	357	0197E	30	428	Barley	Green material	0.031	0.055	<0.01	<0.01
	T-3C	357	0199E	75	456	Barley	Green material	0.022	<0.01	<0.01	<0.01
	T-1C	29	0144E	89	316	Barley	Grain	0.028	<0.01	<0.01	<0.01
	T-2C	175	0173E	89	462	Barley	Grain	0.019	0.01	<0.01	<0.01
	T-3C	357	0202E	89	488	Barley	Grain	0.026	<0.01	<0.01	<0.01
	T-1C	29	0145E	89	316	Barley	Straw	0.11	0.011	<0.01	<0.01
	T-2C	175	0174E	89	462	Barley	Straw	0.086	0.025	<0.01	<0.01
	T-3C	357	0203E	89	488	Barley	Straw	0.063	<0.01	<0.01	<0.01
	T-1A	21	0122E	48	120	Carrot	Leaf	0.024	0.028	<0.01	<0.01
	T-1A	21	0126E	49	134	Carrot	Leaf	0.018	0.067	<0.01	<0.01
	T-2A	92	0151E	48	183	Carrot	Leaf	0.016	0.085	<0.01	<0.01
	T-2A	92	0155E	49	197	Carrot	Leaf	0.012	0.036	<0.01	<0.01
	T-3A	377	0180E	48	448	Carrot	Leaf	0.012	0.095	<0.01	<0.01
	T-3A	377	0184E	49	462	Carrot	Leaf	0.011	0.11	<0.01	<0.01
	T-1A	21	0123E	48	120	Carrot	Root	0.058	0.011	<0.01	<0.01

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
	T-1A	21	0127E	49	134	Carrot	Root	0.079	0.013	0.01	<0.01
	T-2A	92	0152E	48	183	Carrot	Root	0.036	0.014	<0.01	<0.01
	T-2A	92	0156E	49	197	Carrot	Root	0.02	0.011	<0.01	<0.01
	T-3A	377	0181E	48	448	Carrot	Root	0.014	0.011	<0.01	<0.01
	T-3A	377	0185E	49	462	Carrot	Root	0.01	<0.01	<0.01	<0.01
	T-1B	21	0132E	45	47	Lettuce	Head	0.034	0.027	<0.01	<0.01
	T-1B	21	0134E	49	61	Lettuce	Head	0.011	0.02	<0.01	<0.01
	T-2B	126	0161E	45	149	Lettuce	Head	0.018	0.048	<0.01	<0.01
	T-2B	126	0163E	49	163	Lettuce	Head	<0.01	0.043	<0.01	<0.01
	T-3B	380	0190E	45	411	Lettuce	Head	0.014	0.11	<0.01	<0.01
	T-3B	380	0192E	49	425	Lettuce	Head	<0.01	0.039	<0.01	<0.01
16-2501-03 France	T-1C	20	0139E	30	157	Barley	Green material	0.15	0.027	0.022	<0.01
	T-1C	20	0141E	75	220	Barley	Green material	0.13	0.057	0.032	<0.01
	T-2C	193	0168E	30	330	Barley	Green material	0.092	0.056	<0.01	<0.01
	T-2C	193	0170E	75	393	Barley	Green material	0.066	0.12	0.01	<0.01
	T-3C	287	0197E	30	376	Barley	Green material	<0.01	<0.01	<0.01	<0.01
	T-3C	287	0199E	75	440	Barley	Green material	0.093	0.17	<0.01	<0.01
	T-1C	20	0144E	89	260	Barley	Grain	0.064	<0.01	0.062	<0.01
	T-2C	193	0173E	89	433	Barley	Grain	0.038	0.013	0.012	<0.01
	T-3C	287	0202E	89	449	Barley	Grain	0.035	<0.01	0.016	<0.01
	T-1C	20	0145E	89	260	Barley	Straw	0.52	0.06	0.041	<0.01
	T-2C	193	0174E	89	433	Barley	Straw	0.14	0.038	<0.01	<0.01
	T-3C	287	0203E	89	449	Barley	Straw	0.26	0.064	0.011	<0.01
	T-1A	26	0122E	48	152	Carrot	Leaf	0.04	0.95	<0.01	<0.01
	T-1A	26	0126E	49	166	Carrot	Leaf	0.038	1.1	<0.01	<0.01

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
	T-2A	103	0151E	48	210	Carrot	Leaf	0.034	0.12	0.01	<0.01
	T-2A	103	0155E	49	225	Carrot	Leaf	0.031	0.11	<0.01	<0.01
	T-3A	336	0180E	48	453	Carrot	Leaf	0.025	0.12	<0.01	<0.01
	T-3A	336	0184E	49	467	Carrot	Leaf	0.033	0.87	<0.01	<0.01
	T-1A	26	0123E	48	152	Carrot	Root	0.077	0.013	<0.01	<0.01
	T-1A	26	0127E	49	166	Carrot	Root	0.063	0.016	<0.01	<0.01
	T-2A	103	0152E	48	210	Carrot	Root	0.036	0.036	<0.01	<0.01
	T-2A	103	0156E	49	225	Carrot	Root	0.029	0.026	<0.01	<0.01
	T-3A	336	0181E	48	453	Carrot	Root	0.031	0.021	<0.01	<0.01
	T-3A	336	0185E	49	467	Carrot	Root	0.035	0.023	<0.01	<0.01
	T-1B	26	0132E	45	56	Lettuce	Head	0.06	0.11	<0.01	<0.01
	T-1B	26	0134E	49	70	Lettuce	Head	0.033	0.089	<0.01	<0.01
	T-2B	139	0161E	47	173	Lettuce	Head	0.021	0.15	<0.01	<0.01
	T-2B	139	0163E	49	187	Lettuce	Head	<0.01	0.068	<0.01	<0.01
	T-3B	349	0190E	45	386	Lettuce	Head	0.024	0.1	<0.01	<0.01
	T-3B	349	0192E	49	400	Lettuce	Head	0.012	0.088	<0.01	<0.01
16-2501-04 Italy	T-1C	26	0139E	29	108	Barley	Green material	0.6	0.15	0.2	<0.01
	T-1C	26	0141E	75	108	Barley	Green material	0.19	0.32	0.32	<0.01
	T-2C	208	0168E	29	290	Barley	Green material	0.11	0.04	<0.01	<0.01
	T-2C	208	0170E	75	368	Barley	Green material	0.045	0.13	0.019	<0.01
	T-3C	291	0197E	29	336	Barley	Green material	0.14	0.14	0.012	<0.01
	T-1C	26	0144E	89	216	Barley	Grain	0.079	0.047	0.35	<0.01
	T-2C	208	0173E	89	398	Barley	Grain	<0.01	<0.01	<0.01	<0.01
	T-1C	26	0145E	89	216	Barley	Straw	0.88	0.6	0.61	<0.01
	T-2C	208	0174E	89	398	Barley	Straw	<0.01	<0.01	<0.01	<0.01

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
	T-1A	22	0122E	47	148	Carrot	Leaf	0.11	0.19	0.01	<0.01
	T-1A	22	0126E	49	162	Carrot	Leaf	0.1	0.35	0.016	<0.01
	T-2A	111	0151E	47	237	Carrot	Leaf	0.082	0.18	<0.01	<0.01
	T-2A	111	0155E	49	251	Carrot	Leaf	0.11	0.25	0.011	<0.01
	T-3A	336	0180E	47	459	Carrot	Leaf	0.033	0.095	<0.01	<0.01
	T-3A	336	0184E	49	473	Carrot	Leaf	0.014	0.11	<0.01	<0.01
	T-1A	22	0123E	47	148	Carrot	Root	0.047	0.018	0.01	<0.01
	T-1A	22	0127E	49	162	Carrot	Root	0.034	0.016	<0.01	<0.01
	T-2A	111	0152E	47	237	Carrot	Root	0.041	0.01	<0.01	<0.01
	T-2A	111	0156E	49	251	Carrot	Root	0.034	0.01	<0.01	<0.01
	T-3A	336	0181E	47	459	Carrot	Root	0.02	<0.01	<0.01	<0.01
	T-3A	336	0185E	49	473	Carrot	Root	0.025	<0.01	<0.01	<0.01
	T-1B	28	0132E	46	70	Lettuce	Head	0.058	0.036	<0.01	<0.01
	T-1B	28	0134E	49	84	Lettuce	Head	0.044	0.053	<0.01	<0.01
	T-2B	125	0161E	46	167	Lettuce	Head	0.04	0.025	<0.01	<0.01
	T-2B	125	0163E	49	181	Lettuce	Head	0.035	0.049	<0.01	<0.01
	T-3B	353	0190E	44	398	Lettuce	Head	0.023	0.09	<0.01	<0.01
	T-3B	353	0192E	49	412	Lettuce	Head	0.018	0.073	<0.01	<0.01

Table 6.6.2- 4 Residues in rotational crops (M-04, M-05 and M-06)

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
16-2501-01 Germany	T-1C	27	0217E	30	218	Barley	Green material	<0.01	<0.01	-
	T-1C	27	0219E	75	281	Barley	Green material	0.013	<0.01	-
	T-2C	170	0237E	30	361	Barley	Green material	<0.01	<0.01	-
	T-2C	170	0239E	75	424	Barley	Green material	0.011	<0.01	-
	T-3C	347	0257E	30	408	Barley	Green material	0.01	<0.01	-
	T-3C	347	0259E	75	440	Barley	Green material	0.01	<0.01	-
	T-1C	27	0222E	89	304	Barley	Grain	0.012	<0.01	<0.01
	T-2C	170	0242E	89	447	Barley	Grain	0.012	<0.01	<0.01
	T-3C	347	0262E	89	472	Barley	Grain	<0.01	<0.01	<0.01
	T-1C	27	0223E	89	304	Barley	Straw	0.036	<0.01	-
	T-2C	170	0243E	89	447	Barley	Straw	0.04	<0.01	-
	T-3C	347	0263E	89	472	Barley	Straw	0.039	<0.01	-
	T-1A	30	0206E	47	121	Carrot	Leaf	<0.01	0.015	-
	T-1A	30	0210E	49	135	Carrot	Leaf	<0.01	0.016	-
	T-2A	108	0226E	47	194	Carrot	Leaf	<0.01	<0.01	-
	T-2A	108	0230E	49	208	Carrot	Leaf	<0.01	<0.01	-
	T-3A	347	0246E	47	460	Carrot	Leaf	<0.01	<0.01	-
	T-3A	347	0250E	49	473	Carrot	Leaf	<0.01	<0.01	-
	T-1A	30	0207E	47	121	Carrot	Root	<0.01	<0.01	-
	T-1A	30	0211E	49	135	Carrot	Root	<0.01	<0.01	-
	T-2A	108	0227E	47	194	Carrot	Root	<0.01	<0.01	-
	T-2A	108	0231E	49	208	Carrot	Root	<0.01	<0.01	-
	T-3A	347	0247E	47	460	Carrot	Root	<0.01	<0.01	-
	T-3A	347	0251E	49	473	Carrot	Root	<0.01	<0.01	-

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
	T-1B	30	0213E	45	65	Lettuce	Head	<0.01	<0.01	-
	T-1B	30	0215E	49	79	Lettuce	Head	<0.01	<0.01	-
	T-2B	108	0233E	46	136	Lettuce	Head	<0.01	<0.01	-
	T-2B	108	0235E	49	150	Lettuce	Head	<0.01	<0.01	-
	T-3B	362	0253E	45	402	Lettuce	Head	<0.01	<0.01	-
	T-3B	362	0255E	49	416	Lettuce	Head	<0.01	<0.01	-
16-2501-02 The Netherlands	T-1C	29	0217E	30	252	Barley	Green material	<0.01	<0.01	-
	T-1C	29	0219E	75	280	Barley	Green material	<0.01	<0.01	-
	T-2C	175	0237E	30	378	Barley	Green material	<0.01	0.011	-
	T-2C	175	0239E	75	426	Barley	Green material	<0.01	0.011	-
	T-3C	357	0257E	30	428	Barley	Green material	<0.01	<0.01	-
	T-3C	357	0259E	75	456	Barley	Green material	<0.01	<0.01	-
	T-1C	29	0222E	89	316	Barley	Grain	<0.01	<0.01	<0.01
	T-2C	175	0242E	89	462	Barley	Grain	<0.01	<0.01	<0.01
	T-3C	357	0262E	89	488	Barley	Grain	<0.01	<0.01	<0.01
	T-1C	29	0223E	89	316	Barley	Straw	<0.01	<0.01	-
	T-2C	175	0243E	89	462	Barley	Straw	0.014	0.011	-
	T-3C	357	0263E	89	488	Barley	Straw	0.012	<0.01	-
	T-1A	21	0206E	48	120	Carrot	Leaf	<0.01	0.015	-
	T-1A	21	0210E	49	134	Carrot	Leaf	<0.01	0.022	-
	T-2A	92	0226E	48	183	Carrot	Leaf	<0.01	<0.01	-
	T-2A	92	0230E	49	197	Carrot	Leaf	<0.01	<0.01	-
	T-3A	377	0246E	48	448	Carrot	Leaf	<0.01	0.012	-
	T-3A	377	0250E	49	462	Carrot	Leaf	<0.01	0.015	-
	T-1A	21	0207E	48	120	Carrot	Root	<0.01	<0.01	-

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
	T-1A	21	0211E	49	134	Carrot	Root	<0.01	<0.01	-
	T-2A	92	0227E	48	183	Carrot	Root	<0.01	<0.01	-
	T-2A	92	0231E	49	197	Carrot	Root	<0.01	<0.01	-
	T-3A	377	0247E	48	448	Carrot	Root	<0.01	<0.01	-
	T-3A	377	0251E	49	462	Carrot	Root	<0.01	<0.01	-
	T-1B	21	0213E	45	47	Lettuce	Head	<0.01	<0.01	-
	T-1B	21	0215E	49	61	Lettuce	Head	<0.01	<0.01	-
	T-2B	126	0233E	45	149	Lettuce	Head	<0.01	<0.01	-
	T-2B	126	0235E	49	163	Lettuce	Head	<0.01	<0.01	-
	T-3B	380	0253E	45	441	Lettuce	Head	<0.01	<0.01	-
	T-3B	380	0255E	49	455	Lettuce	Head	<0.01	<0.01	-
16-2501-03 France	T-1C	20	0217E	30	157	Barley	Green material	<0.01	<0.01	-
	T-1C	20	0219E	75	220	Barley	Green material	<0.01	0.014	-
	T-2C	193	0237E	30	330	Barley	Green material	0.017	0.017	-
	T-2C	193	0239E	75	393	Barley	Green material	0.011	0.029	-
	T-3C	287	0257E	30	376	Barley	Green material	0.013	0.017	-
	T-3C	287	0259E	75	410	Barley	Green material	0.028	0.015	-
	T-1C	20	0222E	89	260	Barley	Grain	<0.01	<0.01	<0.01
	T-2C	193	0242E	89	433	Barley	Grain	<0.01	<0.01	<0.01
	T-3C	287	0262E	89	449	Barley	Grain	0.012	<0.01	<0.01
	T-1C	20	0223E	89	260	Barley	Straw	0.077	0.031	-
	T-2C	193	0243E	89	433	Barley	Straw	0.054	0.045	-
	T-3C	287	0263E	89	449	Barley	Straw	0.15	0.041	-
	T-1A	26	0206E	48	152	Carrot	Leaf	<0.01	0.048	-
	T-1A	26	0210E	49	166	Carrot	Leaf	<0.01	0.039	-

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
	T-2A	103	0226E	48	210	Carrot	Leaf	<0.01	0.023	-
	T-2A	103	0230E	49	225	Carrot	Leaf	<0.01	0.038	-
	T-3A	336	0246E	48	453	Carrot	Leaf	<0.01	0.02	-
	T-3A	336	0250E	49	467	Carrot	Leaf	<0.01	<0.01	-
	T-1A	26	0207E	48	152	Carrot	Root	<0.01	<0.01	-
	T-1A	26	0211E	49	166	Carrot	Root	<0.01	<0.01	-
	T-2A	103	0227E	48	210	Carrot	Root	<0.01	<0.01	-
	T-2A	103	0231E	49	225	Carrot	Root	<0.01	<0.01	-
	T-3A	336	0247E	48	453	Carrot	Root	<0.01	<0.01	-
	T-3A	336	0251E	49	467	Carrot	Root	<0.01	<0.01	-
	T-1B	26	0213E	45	70	Lettuce	Head	<0.01	<0.01	-
	T-1B	26	0215E	49	70	Lettuce	Head	<0.01	<0.01	-
	T-2B	139	0233E	47	173	Lettuce	Head	<0.01	<0.01	-
	T-2B	139	0235E	49	187	Lettuce	Head	<0.01	<0.01	-
	T-3B	349	0253E	45	386	Lettuce	Head	<0.01	<0.01	-
	T-3B	349	0255E	49	400	Lettuce	Head	<0.01	<0.01	-
16-2501-04 Italy	T-1C	26	0217E	29	108	Barley	Green material	0.016	0.046	-
	T-1C	26	0219E	75	108	Barley	Green material	0.037	0.14	-
	T-2C	208	0237E	29	290	Barley	Green material	<0.01	0.026	-
	T-2C	208	0239E	75	368	Barley	Green material	0.023	0.051	-
	T-3C	291	0257E	29	336	Barley	Green material	<0.01	0.054	-
	T-1C	26	0222E	89	216	Barley	Grain	0.024	0.026	<0.01
	T-2C	208	0242E	89	398	Barley	Grain	<0.01	<0.01	<0.01
	T-1C	26	0223E	89	216	Barley	Straw	0.17	0.62	-
	T-2C	208	0243E	89	398	Barley	Straw	<0.01	<0.01	-

Trial no. Country	Plot	PBI	Sample no.	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
	T-1A	22	0206E	47	148	Carrot	Leaf	<0.01	0.027	-
	T-1A	22	0210E	49	162	Carrot	Leaf	<0.01	0.033	-
	T-2A	111	0226E	47	237	Carrot	Leaf	<0.01	0.021	-
	T-2A	111	0230E	49	251	Carrot	Leaf	<0.01	0.023	-
	T-3A	336	0246E	47	450	Carrot	Leaf	<0.01	<0.01	-
	T-3A	336	0250E	49	473	Carrot	Leaf	<0.01	<0.01	-
	T-1A	22	0207E	47	148	Carrot	Root	<0.01	<0.01	-
	T-1A	22	0211E	49	162	Carrot	Root	<0.01	<0.01	-
	T-2A	111	0227E	47	237	Carrot	Root	<0.01	<0.01	-
	T-2A	111	0231E	49	251	Carrot	Root	<0.01	<0.01	-
	T-3A	336	0247E	47	450	Carrot	Root	<0.01	<0.01	-
	T-3A	336	0251E	49	473	Carrot	Root	<0.01	<0.01	-
	T-1B	28	0213E	46	70	Lettuce	Head	<0.01	<0.01	-
	T-1B	28	0215E	49	84	Lettuce	Head	<0.01	<0.01	-
	T-2B	125	0233E	46	167	Lettuce	Head	<0.01	<0.01	-
	T-2B	125	0235E	49	181	Lettuce	Head	<0.01	<0.01	-
	T-3B	353	0253E	44	398	Lettuce	Head	<0.01	<0.01	-
	T-3B	353	0255E	49	412	Lettuce	Head	<0.01	<0.01	-

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/05
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop barley after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 to bare soil in Germany and The Netherlands
Report No:	18-2521
Document No:	M-679637-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	No deviations from the test guideline were noted with the study report.
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on barley after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in Germany and The Netherlands during 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 351 days (ca 12 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04, M-05 and M-06). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Barley
	Variety:	Bella, Rafaela
	Crop part(s) or processed commodity:	Grain, straw and green material,
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised two supervised residue trials in Germany and The Netherlands. At each trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), barley seeds were sown on plot 1A to simulate a case of crop failure. Control plots were planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), barley seeds sown on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) barley seeds sown on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 5 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Barley plot (DAT)	
18-2521-01 Germany	One application on bare soil, plant-back interval 25-30 days after treatment	1A (26)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (159)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (320)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2521-02 Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (153)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (350)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 6 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09 barley grain, barley green material and barley straw)
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05 in barley grain, barley green material and barley straw; M-06, in barley grain)

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 7 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	93, 98, 98, 101, 103	99	3.8	0.01
	1.0	96, 96, 97, 98, 103	98	3.0	
		Overall recovery (n=10)	98	3.3	
Barley green material	0.01	85, 87, 90, 98, 100	92	7.3	0.01
	2.0	88, 93, 93, 94, 98	93	3.8	
		Overall recovery (n=10)	93	5.5	
Barley straw	0.01	78, 81, 83, 88, 90	84	5.9	0.01
	2.0	77, 81, 81, 81, 82	80	2.4	
		Overall recovery (n=10)	82	4.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 8 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	83, 88, 89, 96, 96	90	6.2	0.01
	1.0	87, 90, 91, 92, 96	91	3.6	
		Overall recovery (n=10)	91	4.8	
Barley green material	0.01	94, 96, 97, 98, 100	97	2.3	0.01
	2.0	86, 88, 90, 91, 94	90	3.4	
		Overall recovery (n=10)	93	4.9	
Barley straw	0.01	78, 84, 88, 93, 97	88	8.5	0.01
	2.0	75, 75, 78, 82, 88	80	6.9	
		Overall recovery (n=10)	84	9.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 9 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	99, 96, 91, 96, 88	94	4.7	0.01
	1.0	85, 94, 83, 88, 92	88	5.2	
		Overall recovery (n=10)	91	5.7	
Barley green material	0.01	93, 99, 92, 92, 89	93	4.0	0.01
	2.0	91, 94, 94, 85, 84	90	5.4	
		Overall recovery (n=10)	91	4.8	
Barley straw	0.01	74, 83, 83, 76, 78	79	5.2	0.01
	2.0	84, 84, 70, 74, 73	77	8.5	
		Overall recovery (n=10)	78	6.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 10 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	89, 93, 96, 102, 103	97	6.2	0.01
	1.0	101, 103, 103, 103, 105	103	1.4	
		Overall recovery (n=10)	100	5.3	
Barley green material	0.01	78, 89, 90, 94, 97	90	8.1	0.01
	2.0	97, 99, 100, 103, 105	101	3.2	
		Overall recovery (n=10)	95	8.3	
Barley straw	0.01	79, 80, 82, 83, 88	82	4.3	0.01
	2.0	80, 83, 83, 90, 91	85	5.7	
		Overall recovery (n=10)	84	5.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 11 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	91, 94, 100	95	4.8	0.01
	0.1	88, 94, 96	93	4.5	
		Overall recovery (n=6)	94	4.4	
Barley green material	0.01	85, 89, 92	89	4.0	0.01
	0.1	92, 93, 95	93	1.6	
		Overall recovery (n=6)	91	3.9	
Barley straw	0.01	91, 93, 97, 100, 102	97	4.8	0.01
	0.1	78, 81, 84, 85, 87	83	4.3	
		Overall recovery (n=10)	90	9.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 12 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	88, 92, 98	93	5.4	0.01
	0.1	88, 92, 94	91	3.3	
		Overall recovery (n=6)	92	4.1	
Barley green material	0.01	75, 82, 86	81	6.9	0.01
	0.1	85, 85, 87	86	1.3	
		Overall recovery (n=6)	83	5.3	
Barley straw	0.01	94, 94, 99, 99, 99	97	2.8	0.01
	0.1	77, 84, 85, 87, 90	84	6.1	
		Overall recovery (n=10)	91	8.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 13 Procedural recoveries for AE C643890 (M-06)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Barley grain	0.01	93, 98, 111	101	9.2	0.01
	0.1	94, 98, 108	100	7.2	
		Overall recovery (n=6)			

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05, M-06 and M-09 residues was 57 - 149 days in grain, 85 – 351 days in green material and 82 – 142 days in straw.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 14 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2521-01 Germany	T-1A	26	30	211	Barley	Green material	0.11	0.028	<0.01	<0.01
	T-1A	26	75	281	Barley	Green material	0.10	0.041	<0.01	<0.01
	T-1A	26	89	315	Barley	Grain	0.078	0.019	0.014	<0.01
	T-1A	26	89	315	Barley	Straw	0.34	0.12	0.013	<0.01
	T-2A	159	30	344	Barley	Green material	0.040	0.030	<0.01	<0.01
	T-2A	159	75	414	Barley	Green material	0.046	0.043	<0.01	<0.01
	T-2A	159	89	448	Barley	Grain	0.048	0.019	<0.01	<0.01
	T-2A	159	89	448	Barley	Straw	0.19	0.14	<0.01	<0.01
	T-3A	320	30	391	Barley	Green material	0.054	0.038	<0.01	<0.01
	T-3A	320	75	431	Barley	Green material	0.076	0.083	<0.01	<0.01
	T-3A	320	89	474	Barley	Grain	0.014	0.014	<0.01	<0.01
	T-3A	320	89	474	Barley	Straw	0.16	0.087	<0.01	<0.01
18-2521-02 The Netherlands	T-1A	27	29	103	Barley	Green material	0.017	0.017	<0.01	<0.01
	T-1A	27	75	287	Barley	Green material	0.11	0.032	<0.01	<0.01
	T-1A	27	89	314	Barley	Grain	0.11	0.040	0.013	<0.01
	T-1A	27	89	314	Barley	Straw	0.42	0.088	<0.01	<0.01
	T-2A	153	29	220	Barley	Green material	0.056	0.019	<0.01	<0.01
	T-2A	153	75	413	Barley	Green material	0.058	0.013	<0.01	<0.01
	T-2A	153	89	440	Barley	Grain	0.077	0.017	<0.01	<0.01
	T-2A	153	89	440	Barley	Straw	0.31	0.043	<0.01	<0.01
	T-3A	350	30	398	Barley	Green material	0.041	<0.01	<0.01	<0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
	T-3A	350	75	448	Barley	Green material	0.047	0.012	<0.01	<0.01
	T-3A	350	89	474	Barley	Grain	0.027	<0.01	<0.01	<0.01
	T-3A	350	89	474	Barley	Straw	0.31	0.021	<0.01	<0.01

Table 6.6.2- 15 Residues in rotational crops (M-04, M-05 and M-06)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2521-01 Germany	T-1A	26	30	211	Barley	Green material	0.012	<0.01	-
	T-1A	26	75	281	Barley	Green material	0.013	<0.01	-
	T-1A	26	89	315	Barley	Grain	0.022	<0.01	<0.01
	T-1A	26	89	315	Barley	Straw	0.11	0.026	-
	T-2A	159	30	344	Barley	Green material	0.013	<0.01	-
	T-2A	159	75	414	Barley	Green material	0.013	<0.01	-
	T-2A	159	89	448	Barley	Grain	0.020	<0.01	<0.01
	T-2A	159	89	448	Barley	Straw	0.10	0.019	-
	T-3A	320	30	391	Barley	Green material	0.013	<0.01	-
	T-3A	320	75	431	Barley	Green material	0.018	<0.01	-
	T-3A	320	89	474	Barley	Grain	0.012	<0.01	<0.01
	T-3A	320	89	474	Barley	Straw	0.058	<0.01	-

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2521-02 The Netherlands	T-1A	27	29	103	Barley	Green material	0.01	0.01	-
	T-1A	27	75	287	Barley	Green material	0.014	0.027	-
	T-1A	27	89	314	Barley	Grain	0.060	0.018	<0.01
	T-1A	27	89	314	Barley	Straw	0.055	0.055	-
	T-2A	153	29	229	Barley	Green material	<0.01	<0.01	-
	T-2A	153	75	412	Barley	Green material	<0.01	0.015	-
	T-2A	153	89	440	Barley	Grain	0.021	0.010	<0.01
	T-2A	153	89	440	Barley	Straw	0.025	0.038	-
	T-3A	350	30	398	Barley	Green material	<0.01	<0.01	-
	T-3A	350	75	448	Barley	Green material	<0.01	<0.01	-
	T-3A	350	89	474	Barley	Grain	<0.01	<0.01	<0.01
	T-3A	350	89	474	Barley	Straw	0.015	0.012	-

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/06
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop cucumber after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 on bare soil in Belgium, southern France and Spain
Report No:	18-2527
Document No:	M-679667-01-1
Guideline(s) followed in study:	Regulation (EC) No. 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies), 504. 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009), US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	No deviations from the test guideline were noted with the study report.
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on cucumber after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in Belgium, France and Spain during 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 370 days (ca. 12 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04 and M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Cucumber
	Variety:	Vert Petit De Paris, Remoir, Dasher
	Crop part(s) or processed commodity:	Fruit
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised two supervised residue trials in Germany and The Netherlands. At each trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), cucumbers were planted on plot 1A to simulate a case of crop failure. Control plots were planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), cucumbers were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) cucumbers were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table

Table 6.6.2- 16 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Cucumber plot (DAT)	
18-2527-01 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (176)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (327)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2527-02 France	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (167)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (336)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2527-03 Spain	One application on bare soil, plant-back interval 25-30 days after treatment	1A (34*)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (138)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (339)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

* Slightly outside of the planned range

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 17 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for cucumbers
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for cucumbers

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 18 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	97, 99, 102, 103	100	2.7	0.01
	0.10	89, 89, 93, 97, 104	94	6.7	
		Overall recovery (n=9)	97	5.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 19 Procedural recoveries for XE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	96, 102, 105, 107	103	4.7	0.01
	0.10	96, 96, 98, 98, 103	98	2.9	
		Overall recovery (n=9)	100	4.2	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 20 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	92, 95, 97, 98	96	2.8	0.01
	0.10	91, 93, 101, 101, 101	97	5.1	
		Overall recovery (n=9)	97	4.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 21 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	95, 97, 99, 105	99	4.4	0.01
	0.10	90, 93, 95, 100, 100	96	4.4	
		Overall recovery (n=9)	97	4.4	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 22 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	90, 92, 98, 99, 99, 104	97	5.3	0.01
	0.10	95, 101, 101, 101, 102, 104	101	3.0	
		Overall recovery (n=12)	99	4.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 23 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	73, 74, 90, 92, 95, 99	87	12.6	0.01
	0.10	73, 78, 78, 79, 81, 88	80	6.2	
		Overall recovery (n=12)	83	10.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18ºC) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05and M-09 residues was 84 – 370 days in cucumbers.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following tables.

Table 6.6.2- 24 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2527-01 Belgium	T-1A	27	73	62	Cucumber	Fruit	0.029	0.030	<0.01	<0.01
	T-1A	27	79	71	Cucumber	Fruit	0.023	0.019	<0.01	<0.01
	T-2A	176	73	218	Cucumber	Fruit	0.016	0.031	<0.01	<0.01
	T-2A	176	79	225	Cucumber	Fruit	0.011	0.024	<0.01	<0.01
	T-3A	327	73	369	Cucumber	Fruit	0.015	0.037	<0.01	<0.01
	T-3A	327	79	376	Cucumber	Fruit	<0.01	0.029	0.018	<0.01
18-2527-02 France	T-1A	27	73	68	Cucumber	Fruit	0.043	0.013	0.021	<0.01
	T-1A	27	79	73	Cucumber	Fruit	0.034	0.014	0.021	<0.01
	T-2A	167	73	210	Cucumber	Fruit	0.020	0.024	0.015	<0.01
	T-2A	167	79	217	Cucumber	Fruit	0.011	0.015	0.010	<0.01
	T-3A	336	73	379	Cucumber	Fruit	<0.01	0.031	0.010	<0.01
	T-3A	336	79	386	Cucumber	Fruit	<0.01	0.020	<0.01	<0.01
18-2527-03 Spain	T-1A	34	73	76	Cucumber	Fruit	0.039	0.019	0.027	<0.01
	T-1A	34	79	88	Cucumber	Fruit	0.029	0.014	0.017	<0.01
	T-2A	138	73	199	Cucumber	Fruit	0.040	0.017	0.013	<0.01
	T-2A	138	79	213	Cucumber	Fruit	0.028	0.015	<0.01	<0.01
	T-3A	359	73	420	Cucumber	Fruit	0.025	0.013	<0.01	<0.01
	T-3A	359	79	434	Cucumber	Fruit	0.016	0.012	<0.01	<0.01

Table 6.6.2- 25 Residues in rotational crops (M-04, M-05 and M-06)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2527-01 Belgium	T-1A	27	73	62	Cucumber	Fruit	<0.01	<0.01
	T-1A	27	79	71	Cucumber	Fruit	<0.01	<0.01
	T-2A	176	73	218	Cucumber	Fruit	<0.01	<0.01
	T-2A	176	79	225	Cucumber	Fruit	<0.01	<0.01
	T-3A	327	73	369	Cucumber	Fruit	<0.01	<0.01
	T-3A	327	79	376	Cucumber	Fruit	<0.01	<0.01
18-2527-02 France	T-1A	27	73	68	Cucumber	Fruit	<0.01	<0.01
	T-1A	27	79	73	Cucumber	Fruit	<0.01	<0.01
	T-2A	167	73	210	Cucumber	Fruit	<0.01	<0.01
	T-2A	167	79	217	Cucumber	Fruit	<0.01	<0.01
	T-3A	336	73	379	Cucumber	Fruit	<0.01	<0.01
	T-3A	336	79	386	Cucumber	Fruit	<0.01	<0.01
18-2527-03 Spain	T-1A	34	73	76	Cucumber	Fruit	<0.01	<0.01
	T-1A	34	79	85	Cucumber	Fruit	<0.01	<0.01
	T-2A	138	73	199	Cucumber	Fruit	<0.01	<0.01
	T-2A	138	79	213	Cucumber	Fruit	<0.01	<0.01
	T-3A	359	73	420	Cucumber	Fruit	<0.01	<0.01
	T-3A	359	79	434	Cucumber	Fruit	<0.01	<0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/07
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop cucumber after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 in Denmark
Report No:	18-2532
Document No:	M-679670-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies), 504. 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on cucumber after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. The trial site was established in Denmark during 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 352 days (ca 12 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04 and M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Cucumber
	Variety:	Parka
	Crop part(s) or processed commodity:	Fruit
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised one supervised residue trials site in Denmark. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), cucumbers were planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), cucumbers were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) cucumbers were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 26 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Cucumber plot (DAT)	
18-2532-01 Denmark	One application on bare soil, plant-back interval 25-30 days after treatment	1A (30)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (169)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (362)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

* Slightly outside of the planned range

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 27 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1 v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for cucumbers
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for cucumbers

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 28 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	93, 98, 98, 102, 107, 108	110	5.7	0.01
	0.10	93, 99, 105, 106, 108, 110	104	6.1	
		Overall recovery (n=12)	102	5.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 29 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	88, 93, 94, 97, 98, 99	95	4.3	0.01
	0.10	96, 104, 107, 111, 113, 115	108	6.5	
		Overall recovery (n=12)	101	8.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 30 Procedural recoveries for AE C671881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	91, 97, 98, 100, 101, 103	98	4.3	0.01
	0.10	93, 100, 101, 102, 105, 105	101	4.4	
		Overall recovery (n=12)	100	4.3	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 31 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	95, 97, 98, 99, 101, 108	100	4.6	0.01
	0.10	88, 95, 97, 97, 98, 106	97	6.0	
		Overall recovery (n=12)	98	5.3	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 32 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	88, 102, 104, 104	100	7.8	0.01
	0.10	85, 87, 87	86	1.3	
		Overall recovery (n=7)	94	9.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 33 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cucumber (fruit)	0.01	73, 101, 103, 104	95	15.6	0.01
	0.10	76, 77, 82	78	4.1	
		Overall recovery (n=7)	88	15.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05and M-09 residues was 78 – 352 days in cucumbers.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 34 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2532-01 Denmark	T-1A	30	73	63	Cucumber	Fruit	0.014	0.018	0.015	<0.01
	T-1A	30	79	83	Cucumber	Fruit	0.010	0.019	0.016	<0.01
	T-2A	169	73	202	Cucumber	Fruit	0.022	0.082	0.027	<0.01
	T-2A	169	79	209	Cucumber	Fruit	0.018	0.070	0.016	<0.01
	T-3A	362	73	395	Cucumber	Fruit	<0.01	0.035	<0.01	<0.01
	T-3A	362	79	402	Cucumber	Fruit	<0.01	0.033	<0.01	<0.01

Table 6.6.2- 35 Residues in rotational crops (M-04 and M-05)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2532-01 Denmark	T-1A	30	73	63	Cucumber	Fruit	<0.01	<0.01
	T-1A	30	79	83	Cucumber	Fruit	<0.01	<0.01
	T-2A	169	73	202	Cucumber	Fruit	<0.01	<0.01
	T-2A	169	79	209	Cucumber	Fruit	<0.01	<0.01
	T-3A	362	73	395	Cucumber	Fruit	<0.01	<0.01
	T-3A	362	79	402	Cucumber	Fruit	<0.01	<0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/08
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop strawberry after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 on bare soil in the Netherlands, Belgium and Italy
Report No:	18-2526
Document No:	M-679666-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies), 504. 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009), US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on strawberries after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in the Netherlands, Belgium and Italy 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 495 days (ca 16 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04 and M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Strawberry
	Variety:	Rumba, Elsanta, Clery, Candonga,
	Crop part(s) or processed commodity:	Fruit
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in the Netherlands, Belgium and Italy. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), strawberries were planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), strawberries were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) strawberries were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 36 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Strawberry plot (DAT)	
18-2526-01 Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (152)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (335)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2526-02 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (161)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (349)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2526-03 Italy	One application on bare soil, plant-back interval 25-30 days after treatment	1A (25)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (124)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (364)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2526-04 Italy	One application on bare soil, plant-back interval 25-30 days after treatment	1A (27)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A (159)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A (311)	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 37 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for strawberries
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for strawberries

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 38 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	93, 94, 99, 101, 104	98	4.7	0.01
	1.0	91, 92, 92, 97, 99	94	3.8	
		Overall recovery (n=10)	96	4.6	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 39 Procedural recoveries for XE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	95, 99, 100, 103, 109	101	5.2	0.01
	1.0	89, 89, 89, 91, 96	91	3.3	
		Overall recovery (n=10)	96	7.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 40 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	96, 101, 101, 102, 102	100	2.5	0.01
	1.0	89, 92, 95, 95, 96	93	3.1	
		Overall recovery (n=10)	97	4.6	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 41 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	92, 97, 101, 102, 103	99	4.6	0.01
	1.0	95, 97, 98, 101, 105	99	3.9	
		Overall recovery (n=12)	99	4.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 42 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	75, 82, 87, 90, 92	85	8.0	0.01
	0.10	86, 88, 95, 98	92	6.2	
		Overall recovery (n=9)	88	7.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 43 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Strawberry (fruit)	0.01	81, 84, 85, 85, 92	85	4.7	0.01
	0.10	79, 81, 82, 94	84	8.1	
		Overall recovery (n=9)	85	6.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18ºC) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05and M-09 residues was 48 – 495 days in strawberries.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 44 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2526-01 The Netherlands	T-1A	27	85	71	Strawberry	Fruit	0.018	0.020	< 0.01	< 0.01
	T-1A	27	87	76	Strawberry	Fruit	0.012	0.014	< 0.01	< 0.01
	T-2A	152	85	202	Strawberry	Fruit	0.017	0.025	< 0.01	< 0.01
	T-2A	152	87	208	Strawberry	Fruit	0.020	0.038	< 0.01	< 0.01
	T-3A	335	85	385	Strawberry	Fruit	0.029	0.037	< 0.01	< 0.01
	T-3A	335	87	391	Strawberry	Fruit	0.014	0.022	< 0.01	< 0.01
18-2526-02 Belgium	T-1A	27	85	79	Strawberry	Fruit	0.050	0.069	< 0.01	< 0.01
	T-1A	27	87	86	Strawberry	Fruit	0.039	0.060	< 0.01	< 0.01
	T-2A	161	85	212	Strawberry	Fruit	0.026	0.038	< 0.01	< 0.01
	T-2A	161	87	220	Strawberry	Fruit	0.028	0.044	< 0.01	< 0.01
	T-3A	349	85	400	Strawberry	Fruit	0.017	0.038	< 0.01	< 0.01
	T-3A	349	87	408	Strawberry	Fruit	0.021	0.045	< 0.01	< 0.01
18-2526-03 Italy	T-1A	25	85	68	Strawberry	Fruit	0.038	0.014	0.038	< 0.01
	T-1A	25	87	73	Strawberry	Fruit	0.037	0.015	0.042	< 0.01
	T-2A	124	85	411	Strawberry	Fruit	< 0.01	0.013	< 0.01	< 0.01
	T-2A	124	87	420	Strawberry	Fruit	< 0.01	0.011	< 0.01	< 0.01
	T-3A	364	85	420	Strawberry	Fruit	0.013	0.013	< 0.01	< 0.01
	T-3A	364	87	427	Strawberry	Fruit	0.013	0.012	< 0.01	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2526-04 Italy	T-1A	27	85	201	Strawberry	Fruit	0.037	0.018	0.023	< 0.01
	T-1A	27	87	210	Strawberry	Fruit	0.030	0.015	0.022	< 0.01
	T-2A	159	85	333	Strawberry	Fruit	0.023	0.028	0.026	< 0.01
	T-2A	159	87	342	Strawberry	Fruit	0.020	0.020	0.020	< 0.01
	T-3A	311	85	378	Strawberry	Fruit	0.021	0.023	0.01	< 0.01
	T-3A	311	87	386	Strawberry	Fruit	0.021	0.026	0.018	< 0.01

Table 6.6.2- 45 Residues in rotational crops (M-04 and M-05)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2526-01 The Netherlands	T-1A	27	85	71	Strawberry	Fruit	<0.01	<0.01
	T-1A	27	87	76	Strawberry	Fruit	<0.01	<0.01
	T-2A	152	85	202	Strawberry	Fruit	<0.01	<0.01
	T-2A	152	87	208	Strawberry	Fruit	<0.01	<0.01
	T-3A	335	85	385	Strawberry	Fruit	<0.01	<0.01
	T-3A	335	87	391	Strawberry	Fruit	<0.01	<0.01
18-2526-02 Belgium	T-1A	27	85	79	Strawberry	Fruit	<0.01	<0.01
	T-1A	27	87	86	Strawberry	Fruit	<0.01	<0.01
	T-2A	161	85	212	Strawberry	Fruit	<0.01	<0.01
	T-2A	161	87	220	Strawberry	Fruit	<0.01	<0.01
	T-3A	349	85	400	Strawberry	Fruit	<0.01	<0.01
	T-3A	349	87	408	Strawberry	Fruit	<0.01	<0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2526-03 Italy	T-1A	25	85	68	Strawberry	Fruit	<0.01	<0.01
	T-1A	25	87	73	Strawberry	Fruit	<0.01	<0.01
	T-2A	124	85	411	Strawberry	Fruit	<0.01	<0.01
	T-2A	124	87	420	Strawberry	Fruit	<0.01	<0.01
	T-3A	364	85	420	Strawberry	Fruit	<0.01	<0.01
	T-3A	364	87	427	Strawberry	Fruit	<0.01	<0.01
18-2526-04 Italy	T-1A	27	85	201	Strawberry	Fruit	<0.01	<0.01
	T-1A	27	87	210	Strawberry	Fruit	<0.01	<0.01
	T-2A	159	85	333	Strawberry	Fruit	<0.01	<0.01
	T-2A	159	87	342	Strawberry	Fruit	<0.01	<0.01
	T-3A	311	85	378	Strawberry	Fruit	<0.01	<0.01
	T-3A	311	87	386	Strawberry	Fruit	<0.01	<0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/09
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop cauliflower after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 on bare soil in the Netherlands, Belgium, Italy and Spain.
Report No:	18-2525
Document No:	M-679665-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies), 504. 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009), US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on cauliflower after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in the Netherlands, Belgium, Italy and Spain 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods.

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 461 days (ca 15 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04 and M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Cauliflower
	Variety:	Clarina, Tarifa F1, Emeraude F1, Casper RZ
	Crop part(s) or processed commodity:	Fruit
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in the Netherlands, Belgium, Italy and Spain. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), cauliflowers were planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), cauliflowers were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) cauliflowers were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 46 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Cauliflower plot (DAT)	
18-2525-01 Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 152	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 335	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2525-02 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	1A 27	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 174	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 328	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2525-03 Italy	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 139	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 320	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2525-04 Spain	One application on bare soil, plant-back interval 25-30 days after treatment	1A 28	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 153	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 362	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 47 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for cauliflower curd
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for cauliflower curd

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 48 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	89, 93, 98, 101, 111	98	8.6	0.01
	0.50	90, 92, 93, 100, 103	96	5.9	
		Overall recovery (n=10)	97	7.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 49 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	98, 99, 101, 109, 109	103	5.2	0.01
	0.50	89, 91, 91, 94, 109	95	8.6	
		Overall recovery (n=10)	99	8.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 50 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	95, 102, 104, 108, 108	103	5.2	0.01
	0.50	83, 88, 88, 91, 100	90	7.0	
		Overall recovery (n=10)	97	9.3	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 51 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	92, 96, 100, 102, 115	101	8.6	0.01
	0.50	90, 90, 96, 99, 102	95	5.6	
		Overall recovery (n=12)	98	7.6	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 52 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	92, 93, 94, 105, 105, 108, 110	101	7.6	0.01
	0.10	89, 92, 93, 94, 99, 100, 103, 105, 113	99	7.7	
		Overall recovery (n=16)	100	7.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 53 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cauliflower (curd)	0.01	87, 89, 92, 96, 96, 99, 117	97	10.3	0.01
	0.10	75, 78, 80, 82, 83, 84, 91, 92, 108	86	11.6	
		Overall recovery (n=16)	91	12.2	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05and M-09 residues was 50 – 461 days in strawberries.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 54 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2525-01 Netherlands	T-1A	26	45	97	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	26	49	111	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	152	48	242	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	152	49	256	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	335	48	425	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	335	49	439	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
18-2525-02 Belgium	T-1A	27	43	100	Cauliflower	Curd	< 0.01	< 0.01	0.031	< 0.01
	T-1A	27	49	114	Cauliflower	Curd	< 0.01	< 0.01	0.019	< 0.01
	T-2A	174	45	251	Cauliflower	Curd	< 0.01	0.016	0.021	< 0.01
	T-2A	174	49	265	Cauliflower	Curd	< 0.01	0.029	0.018	< 0.01
	T-3A	328	45	405	Cauliflower	Curd	< 0.01	0.014	0.017	< 0.01
	T-3A	328	49	419	Cauliflower	Curd	< 0.01	0.028	0.014	< 0.01
18-2525-03 Italy	T-1A	26	47	154	Cauliflower	Curd	< 0.01	< 0.01	0.025	< 0.01
	T-1A	26	49	168	Cauliflower	Curd	< 0.01	< 0.01	0.028	< 0.01
	T-2A	139	45	250	Cauliflower	Curd	< 0.01	< 0.01	0.024	< 0.01
	T-2A	139	49	264	Cauliflower	Curd	< 0.01	< 0.01	0.014	< 0.01
	T-3A	326	45	437	Cauliflower	Curd	< 0.01	< 0.01	0.013	< 0.01
	T-3A	326	49	451	Cauliflower	Curd	< 0.01	< 0.01	0.016	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2525-04 Spain	T-1A	28	45	113	Cauliflower	Curd	< 0.01	< 0.01	0.020	< 0.01
	T-1A	28	49	128	Cauliflower	Curd	< 0.010	< 0.01	0.014	< 0.01
	T-2A	153	45	238	Cauliflower	Curd	< 0.01	< 0.01	0.011	< 0.01
	T-2A	153	49	253	Cauliflower	Curd	< 0.01	< 0.01	0.010	< 0.01
	T-3A	362	45	467	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	362	49	481	Cauliflower	Curd	< 0.01	< 0.01	< 0.01	< 0.01

Table 6.6.2- 55 Residues in rotational crops (M-04 and M-05)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2525-01 Netherlands	T-1A	26	45	97	Cauliflower	Curd	<0.01	<0.01
	T-1A	26	49	111	Cauliflower	Curd	<0.01	<0.01
	T-2A	152	48	242	Cauliflower	Curd	<0.01	<0.01
	T-2A	152	49	256	Cauliflower	Curd	<0.01	<0.01
	T-3A	335	48	425	Cauliflower	Curd	<0.01	<0.01
	T-3A	335	49	439	Cauliflower	Curd	<0.01	<0.01
18-2525-02 Belgium	T-1A	27	43	100	Cauliflower	Curd	<0.01	<0.01
	T-1A	27	49	114	Cauliflower	Curd	<0.01	<0.01
	T-2A	174	45	251	Cauliflower	Curd	<0.01	<0.01
	T-2A	174	49	265	Cauliflower	Curd	<0.01	<0.01
	T-3A	328	45	405	Cauliflower	Curd	<0.01	<0.01
	T-3A	328	49	419	Cauliflower	Curd	<0.01	<0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2525-03 Italy	T-1A	26	47	154	Cauliflower	Curd	<0.01	<0.01
	T-1A	26	49	168	Cauliflower	Curd	<0.01	<0.01
	T-2A	139	45	250	Cauliflower	Curd	<0.01	<0.01
	T-2A	139	49	264	Cauliflower	Curd	<0.01	<0.01
	T-3A	326	45	437	Cauliflower	Curd	<0.01	<0.01
	T-3A	326	49	451	Cauliflower	Curd	<0.01	<0.01
18-2525-04 Spain	T-1A	28	45	113	Cauliflower	Curd	<0.01	<0.01
	T-1A	28	49	128	Cauliflower	Curd	<0.01	<0.01
	T-2A	153	45	238	Cauliflower	Curd	<0.01	<0.01
	T-2A	153	49	253	Cauliflower	Curd	<0.01	<0.01
	T-3A	362	45	467	Cauliflower	Curd	<0.01	<0.01
	T-3A	362	49	481	Cauliflower	Curd	<0.01	<0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/10
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the rotational crop maize/corn after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 on bare soil in Germany, Belgium and the Netherlands
Report No:	18-2522
Document No:	M-679662-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies), 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on maize after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in the Germany, Belgium and the Netherlands 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods.

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 569 days (ca 18 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04, M-05 and M-06). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Maize
	Variety:	ES Albatros, LG 30222, Ajaxx Duo, Avalon, Niklas, DKC 3352, LG 31205, Genialis,
	Crop part(s) or processed commodity:	Maize green material, kernel and rest of plant
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in the Netherlands, Belgium, and Germany. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), maize was planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), maize was planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) maize was planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 56 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Maize plot (DAT)	
18-2522-01 Germany	One application on bare soil, plant-back interval 25-30 days after treatment	1A 25	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 211	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 342	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2522-02 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 168	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 356	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2522-03 Germany	One application on bare soil, plant-back interval 25-30 days after treatment	1A 28	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 175	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 345	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2522-04 The Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 152	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 335	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 57 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for maize green material, kernel and rest of plant
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for maize green material, kernel and rest of plant

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 58 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	89, 91, 94, 95, 77	89	8.1	0.01
	0.50	87, 88, 89, 91, 82	87	3.8	
		Overall recovery (n=10)	88	6.1	
Maize / corn / kernel	0.01	92, 95, 97, 100, 98	96	3.2	0.01
	0.50	87, 88, 89, 90, 78	86	5.6	
		Overall recovery (n=10)	91	7.1	
Maize / corn / rest of plant	0.01	89, 91, 94, 97, 97	94	3.8	0.01
	0.50	78, 83, 87, 88, 87	85	4.9	
		Overall recovery (n=10)	89	6.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 59 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	95, 98, 98, 99, 82	94	7.5	0.01
	0.50	83, 85, 91, 93, 78	86	7.1	
		Overall recovery (n=10)	90	8.5	
Maize / corn / kernel	0.01	88, 94, 95, 97, 98	94	4.1	
	0.50	83, 90, 93, 94, 80	88	7.1	0.01
		Overall recovery (n=10)	91	6.5	
Maize / corn / rest of plant	0.01	97, 98, 101, 102, 93	98	3.6	
	0.50	84, 87, 87, 88, 79	85	4.4	0.01
		Overall recovery (n=10)	92	8.5	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 60 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	97, 98, 99, 103, 79	95	9.8	0.01
	0.50	87, 89, 89, 96, 75	87	8.7	
		Overall recovery (n=10)	91	10.0	
Maize / corn / kernel	0.01	87, 88, 88, 90, 85	88	2.1	0.01
	0.50	86, 86, 87, 89, 74	84	7.0	
		Overall recovery (n=10)	86	5.2	
Maize / corn / rest of plant	0.01	79, 83, 84, 86, 86	84	3.4	0.01
	0.50	78, 80, 82, 84, 76	80	4.0	
		Overall recovery (n=10)	82	4.2	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 61 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	84, 86, 92, 93, 91	89	4.4	0.01
	0.50	85, 89, 91, 102, 83	90	8.2	
		Overall recovery (n = 10)	90	6.3	
Maize / corn / kernel	0.01	89, 91, 91, 97, 97	93	4.0	0.01
	0.50	85, 91, 91, 94, 81	88	6.0	
		Overall recovery (n = 10)	91	5.5	
Maize / corn / rest of plant	0.01	82, 85, 88, 90, 98	89	6.8	0.01
	0.50	82, 82, 83, 87, 84	84	2.5	
		Overall recovery (n = 10)	86	5.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 62 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	76, 83, 93, 99	88	11.7	0.01
	0.10	85, 85, 86, 91, 99	89	6.7	
		Overall recovery (n = 9)	89	8.6	
Maize / corn / kernel	0.01	81, 86, 94, 95, 96	90	7.3	0.01
	0.10	86, 87, 88, 91, 92	89	2.9	
		Overall recovery (n = 10)	90	5.3	
Maize / corn / rest of plant	0.01	85, 88, 88	87	2.0	0.01
	0.10	75, 83, 85	81	6.5	
		Overall recovery (n = 6)	84	5.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 63 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	71, 86, 88, 91	84	10.6	0.01
	0.10	74, 75, 84, 84, 88	81	7.6	
		Overall recovery (n = 9)	82	8.7	
Maize / corn / kernel	0.01	76, 77, 82, 84, 84	81	4.8	0.01
	0.10	79, 80, 81, 84, 85	82	3.2	
		Overall recovery (n = 10)	82	3.9	
Maize / corn / rest of plant	0.01	84, 87, 90	87	3.4	0.01
	0.10	73, 81, 84	79	7.2	
		Overall recovery (n = 6)	83	7.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 64 Procedural recoveries for AE C643890 (M-06)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	74, 89, 97, 106	92	14.8	0.01
	0.10	85, 86, 99, 104, 108	96	10.8	
		Overall recovery (n = 9)	94	12.1	
Maize / corn / kernel	0.01	86, 94, 96, 101, 102	96	6.7	0.01
	0.10	90, 90, 95, 96, 97	94	3.6	
		Overall recovery (n = 10)	95	5.2	
Maize / corn / rest of plant	0.01	94, 96, 104	98	5.4	0.01
	0.10	81, 87, 88	85	4.4	
		Overall recovery (n = 6)	92	8.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18ºC) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05, M-06 and M-09 residues was 22 – 569 days in maize green material, kernel and rest of plant.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 65 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2522-01 Germany	T-1A	25	87	86	Maize	Green material	< 0.048	0.12	< 0.01	< 0.01
	T-1A	25	89	160	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	25	89	160	Maize	Rest of plant	0.12	0.23	0.013	< 0.01
	T-2A*	211	85	323	Maize	Green material	0.10	0.55	< 0.01	< 0.01
	T-3A*	342	85	454	Maize	Green material	0.039	0.24	< 0.01	< 0.01
18-2522-02 Belgium	T-1A	26	85	145	Maize	Green material	< 0.066	0.035	< 0.01	< 0.01
	T-1A	26	89	190	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	26	89	190	Maize	Rest of plant	0.11	0.069	< 0.01	< 0.01
	T-2A	168	85	286	Maize	Green material	0.052	0.10	< 0.01	< 0.01
	T-2A	168	89	352	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	168	89	352	Maize	Rest of plant	0.059	0.013	< 0.01	< 0.01
	T-3A	356	85	474	Maize	Green material	0.027	0.098	< 0.01	< 0.01
	T-3A	356	89	540	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	356	89	540	Maize	Rest of plant	0.038	0.021	< 0.01	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2522-03 Germany	T-1A	28	85	155	Maize	Green material	0.019	0.033	< 0.01	< 0.01
	T-1A	28	89	188	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	28	89	188	Maize	Rest of plant	0.042	0.036	< 0.01	< 0.01
	T-2A	175	85	304	Maize	Green material	0.044	0.057	< 0.01	< 0.01
	T-2A	175	89	346	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	175	89	346	Maize	Rest of plant	0.055	0.022	< 0.01	< 0.01
	T-3A	343	85	472	Maize	Green material	0.021	0.037	< 0.01	< 0.01
	T-3A	343	89	514	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	343	89	514	Maize	Rest of plant	0.041	0.018	< 0.01	< 0.01
18-2522-04 Netherlands	T-1A	26	85	135	Maize	Green material	0.011	0.013	< 0.01	< 0.01
	T-1A	26	89	137	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	26	89	137	Maize	Rest of plant	0.028	0.035	< 0.01	< 0.01
	T-2A	152	85	278	Maize	Green material	0.043	0.021	< 0.01	< 0.01
	T-2A	152	89	292	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	152	89	292	Maize	Rest of plant	0.059	0.019	< 0.01	< 0.01
	T-3A	335	85	461	Maize	Green material	0.039	0.023	< 0.01	< 0.01
	T-3A	335	89	475	Maize	Kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	335	89	475	Maize	Rest of plant	0.062	0.022	< 0.01	< 0.01

* Sampling of kernels and the rest of the maize plants was not possible since the plots were destroyed by a wild boar

Table 6.6.2- 66 Residues in rotational crops (M-04, M-05 and M-06)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2522-01 Germany	T-1A	25	87	86	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-1A	25	89	160	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-1A	25	89	160	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
	T-2A*	211	85	323	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-3A*	342	85	454	Maize	Green material	< 0.01	< 0.01	< 0.01
18-2522-02 Belgium	T-1A	26	85	145	Maize	Green material	< 0.01	0.014	< 0.01
	T-1A	26	89	190	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-1A	26	89	190	Maize	Rest of plant	< 0.01	0.012	< 0.01
	T-2A	168	85	286	Maize	Green material	< 0.01	0.011	< 0.01
	T-2A	168	89	352	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-2A	168	89	352	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
	T-3A	356	85	474	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-3A	356	89	540	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-3A	356	89	540	Maize	Rest of plant	< 0.01	< 0.01	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2522-03 Germany	T-1A	28	85	155	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-1A	28	89	188	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-1A	28	89	188	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
	T-2A	175	85	304	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-2A	175	89	346	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-2A	175	89	346	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
	T-3A	343	85	472	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-3A	343	89	514	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-3A	343	89	514	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
18-2522-04 Netherlands	T-1A	26	85	125	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-1A	26	89	137	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-1A	26	89	137	Maize	Rest of plant	< 0.01	< 0.01	< 0.01
	T-2A	152	85	278	Maize	Green material	< 0.01	< 0.01	< 0.01
	T-2A	152	89	292	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-2A	152	89	292	Maize	Rest of plant	< 0.01	0.016	< 0.01
	T-3A	335	85	461	Maize	Green material	< 0.01	0.010	< 0.01
	T-3A	335	89	475	Maize	Kernel	< 0.01	< 0.01	< 0.01
	T-3A	335	89	475	Maize	Rest of plant	< 0.01	0.012	< 0.01

* Sampling of kernels and the rest of the maize plants was not possible since the plots were destroyed by a wild boar

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/11
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop cabbage after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 on bare soil in the Netherlands, Belgium, Italy and Spain
Report No:	18-2524
Document No:	M-679664-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08; OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009); US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on cabbages after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in Italy, Spain, Belgium, and the Netherlands 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 547 days (ca 18 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04, M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Cabbage
	Variety:	Mucsuma, Colmar, Impala F1, Cambria, Green Luar-Takii
	Crop part(s) or processed commodity:	Cabbage heads
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in Italy, Spain, Belgium, and the Netherlands. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), cabbages were planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), cabbages were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) cabbages were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table.

Table 6.6.2- 67 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Cabbage plot (DAT)	
18-2524-01 Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 152	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 335	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2524-02 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	1A 27	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 170	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 351	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2524-03 Italy	One application on bare soil, plant-back interval 25-30 days after treatment	1A 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 124	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 341	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2524-04 Spain	One application on bare soil, plant-back interval 25-30 days after treatment	1A 28	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	2A 153	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	3A 362	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
DAT = Days after treatment			

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 68 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for cabbage head
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for cabbage head

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 69 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	95, 99, 101, 102, 104	100	3.4	0.01
	0.1	87, 89, 90, 91, 94	90	2.9	
		Overall recovery (n=10)	95	6.3	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 70 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	94, 95, 95, 97, 100	96	2.5	0.01
	0.1	88, 89, 92, 93, 102	93	6.0	
		Overall recovery (n=10)	95	4.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 71 Procedural recoveries for AE C657188 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	93, 98, 101, 105, 106	101	5.3	0.01
	0.1	80, 88, 88, 88, 90	87	4.5	
		Overall recovery (n=10)	94	9.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 72 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	92, 96, 98, 102, 105	99	5.2	0.01
	0.1	88, 89, 90, 90, 97	91	3.9	
		Overall recovery (n = 10)	95	6.2	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 73 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	85, 89, 89, 90, 94, 97	91	4.7	0.01
	0.1	72, 77, 79, 82, 86, 88	81	7.3	
		Overall recovery (n = 12)	86	8.4	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 74 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Cabbage (head)	0.01	77, 78, 79, 80, 80, 82	79	2.2	0.01
	0.1	72, 73, 73, 74, 74, 76	74	1.9	
		Overall recovery (n = 12)	77	4.3	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05 and M-09 residues was 28 – 547 days in cabbage heads.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 75 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2524-01 Netherlands	T-1A	26	47	123	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-1A	26	49	137	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-2A	152	48	238	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-2A	152	49	252	Cabbage	Head	<0.01	0.01	<0.01	<0.01
	T-3A	335	48	421	Cabbage	Head	<0.01	0.014	<0.01	<0.01
	T-3A	335	49	435	Cabbage	Head	<0.01	0.014	<0.01	<0.01
18-2524-02 Belgium	T-1A	27	48	124	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-1A	27	49	138	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-2A	170	48	267	Cabbage	Head	<0.01	0.015	<0.01	<0.01
	T-2A	170	49	281	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-3A	351	48	448	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-3A	351	49	462	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
18-2524-03 Italy	T-1A	26	47	87	Cabbage	Head	0.013	0.012	0.026	<0.01
	T-1A	26	49	101	Cabbage	Head	<0.01	<0.01	0.016	<0.01
	T-2A	124	47	185	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-2A	124	49	199	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-3A	341	47	417	Cabbage	Head	<0.01	0.011	<0.01	<0.01
	T-3A	341	49	430	Cabbage	Head	<0.01	0.010	<0.01	<0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2524-04 Spain	T-1A	28	44	112	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-1A	28	49	126	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-2A	153	44	237	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-2A	153	49	251	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-3A	362	47	425	Cabbage	Head	<0.01	<0.01	<0.01	<0.01
	T-3A	362	49	439	Cabbage	Head	<0.01	<0.01	<0.01	<0.01

Table 6.6.2- 76 Residues in rotational crops (M-04 and M-05)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2524-01 Netherlands	T-1A	26	47	123	Cabbage	Head	<0.01	<0.01
	T-1A	26	49	137	Cabbage	Head	<0.01	<0.01
	T-2A	152	48	238	Cabbage	Head	<0.01	<0.01
	T-2A	152	49	252	Cabbage	Head	<0.01	<0.01
	T-3A	335	48	421	Cabbage	Head	<0.01	<0.01
	T-3A	335	49	435	Cabbage	Head	<0.01	<0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2524-02 Belgium	T-1A	27	48	124	Cabbage	Head	<0.01	<0.01
	T-1A	27	49	138	Cabbage	Head	<0.01	<0.01
	T-2A	170	48	267	Cabbage	Head	<0.01	<0.01
	T-2A	170	49	281	Cabbage	Head	<0.01	<0.01
	T-3A	351	48	448	Cabbage	Head	<0.01	<0.01
	T-3A	351	49	462	Cabbage	Head	<0.01	<0.01
18-2524-03 Italy	T-1A	26	47	87	Cabbage	Head	<0.01	<0.01
	T-1A	26	49	101	Cabbage	Head	<0.01	<0.01
	T-2A	124	47	185	Cabbage	Head	<0.01	<0.01
	T-2A	124	49	199	Cabbage	Head	<0.01	<0.01
	T-3A	341	47	417	Cabbage	Head	<0.01	<0.01
	T-3A	341	49	430	Cabbage	Head	<0.01	<0.01
18-2524-04 Spain	T-1A	28	44	112	Cabbage	Head	<0.01	<0.01
	T-1A	28	49	126	Cabbage	Head	<0.01	<0.01
	T-2A	153	44	237	Cabbage	Head	<0.01	<0.01
	T-2A	153	49	251	Cabbage	Head	<0.01	<0.01
	T-3A	362	47	425	Cabbage	Head	<0.01	<0.01
	T-3A	362	49	439	Cabbage	Head	<0.01	<0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant: The study is acceptable

Data Point:	KCA 6.6.2/12
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop leek after spray application of fluopicolide & propamocarb hydrochloride SC 687.5 to bare soil in the Netherlands, Belgium, Portugal and Spain
Report No:	18-2520
Document No:	M-679661-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market OECD Guidelines for the Testing of Chemicals. Residues in Rotational Crops (Limited Field Studies). 504. 2007-01-08 OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) US EPA OCSPP Guideline No. 860.1900 Field Accumulation in Rotational Crops US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on leeks after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in the Netherlands, Belgium, Portugal and Spain 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods.

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 540 days (ca 17 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04 and M-05). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Leeks
	Variety:	Roxton, Krypton, Poulton, Lancelote, SPHEROS F1, Rijk Zwaan, Atal (Clause)
	Crop part(s) or processed commodity:	Whole plant without root
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in the Netherlands, Belgium, Portugal and Spain. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), leeks were planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), leeks were planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) leeks were planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table:

Table 6.6.2- 77 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Leeks plot (DAT)	
18-2520-01 Netherlands	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 26	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 152	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 335	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2520-02 Belgium	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 27	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 133	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 356	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2520-03 Portugal	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 28	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 172	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 354	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2520-04 Spain	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 29	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 154	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 363	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 78 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for leeks - whole plant without root
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for leeks - whole plant without root

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 79 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek whole plant without root	0.01	88; 88; 91; 92; 96	91	3.6	0.01
	0.50	87; 92; 93; 93; 97	92	3.9	
		Overall recovery (n = 10)	92	3.6	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 80 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek / whole plant without root	0.01	93; 94; 95; 97; 98	95	2.2	0.01
	0.50	84; 87; 90; 90; 92	89	3.5	
		Overall recovery (n = 10)	92	4.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 81 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek / whole plant without root	0.01	83; 86; 89; 90; 91	88	3.7	0.01
	0.50	83; 84; 84; 87; 87	85	2.2	
		Overall recovery (n = 10)	86	3.4	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 82 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek / whole plant without root	0.01	84; 90; 90; 93; 94	90	5.7	0.01
	0.50	83; 85; 87; 88; 93	87	4.3	
		Overall recovery (n = 10)	88	5.0	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 83 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek / whole plant without root	0.01	75; 80; 84; 86; 88; 89; 95; 104; 105; 106; 107; 115	93	13.4	0.01
	0.10	94; 98; 99; 99; 102; 115	101	7.2	
		Overall recovery (n = 18)	97	11.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 84 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Leek / whole plant without root	0.01	71; 72; 73; 73; 74; 74; 80; 82; 83; 93; 101; 112	82	15.9	0.01
	0.10	71; 73; 73; 74; 88; 102	80	15.4	
		Overall recovery (n = 18)	82	15.4	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05and M-09 residues was 41 – 540 days in leeks.

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table

Table 6.6.2- 85 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2520-01 Netherlands	T-1A	26	45	88	Leeks	whole plant without root	0.020	0.017	< 0.01	< 0.01
	T-1A	26	49	102	Leeks	whole plant without root	0.01	< 0.01	< 0.01	< 0.01
	T-2A	152	47	218	Leeks	whole plant without root	0.066	0.068	< 0.01	< 0.01
	T-2A	152	49	232	Leeks	whole plant without root	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	335	47	401	Leeks	whole plant without root	0.077	0.10	< 0.01	< 0.01
	T-3A	335	49	415	Leeks	whole plant without root	0.031	0.014	< 0.01	< 0.01
18-2520-02 Belgium	T-1A	27	49	169	Leeks	whole plant without root	0.038	< 0.01	< 0.01	< 0.01
	T-1A	27	49	425	Leeks	whole plant without root	0.039	< 0.01	< 0.01	< 0.01
	T-2A	133	48	245	Leeks	whole plant without root	0.037	< 0.01	< 0.01	< 0.01
	T-2A	133	49	258	Leeks	whole plant without root	0.048	< 0.01	< 0.01	< 0.01
	T-3A	356	48	468	Leeks	whole plant without root	0.028	< 0.01	< 0.01	< 0.01
	T-3A	356	49	481	Leeks	whole plant without root	0.043	< 0.01	< 0.01	< 0.01
18-2520-03 Portugal	T-1A	28	47	121	Leeks	whole plant without root	0.074	0.022	0.014	< 0.01
	T-1A	28	49	135	Leeks	whole plant without root	0.035	0.012	< 0.01	< 0.01
	T-2A	172	47	265	Leeks	whole plant without root	0.028	0.025	< 0.01	< 0.01
	T-2A	172	49	279	Leeks	whole plant without root	0.020	0.012	< 0.01	< 0.01
	T-3A	354	47	447	Leeks	whole plant without root	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	354	49	461	Leeks	whole plant without root	< 0.01	< 0.01	< 0.01	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2520-04 Spain	T-1A	29	47	107	Leeks	whole plant without root	0.11	< 0.01	0.01	< 0.01
	T-1A	29	49	121	Leeks	whole plant without root	0.076	< 0.01	< 0.01	< 0.01
	T-2A	154	45	231	Leeks	whole plant without root	0.056	0.023	< 0.01	< 0.01
	T-2A	154	49	245	Leeks	whole plant without root	0.046	0.013	< 0.01	< 0.01
	T-3A	363	45	440	Leeks	whole plant without root	0.026	0.010	< 0.01	< 0.01
	T-3A	363	49	454	Leeks	whole plant without root	0.023	< 0.01	< 0.01	< 0.01

Table 6.6.2- 86 Residues in rotational crops (M-04 and M-05)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2520-01 Netherlands	T-1A	26	45	88	Leeks	whole plant without root	< 0.01	< 0.01
	T-1A	26	49	102	Leeks	whole plant without root	< 0.01	< 0.01
	T-2A	152	47	218	Leeks	whole plant without root	0.011	< 0.01
	T-2A	152	49	232	Leeks	whole plant without root	< 0.01	< 0.01
	T-3A	335	47	401	Leeks	whole plant without root	0.023	< 0.01
	T-3A	335	49	415	Leeks	whole plant without root	0.022	< 0.01
18-2520-02 Belgium	T-1A	27	49	169	Leeks	whole plant without root	0.042	< 0.01
	T-1A	27	49	125	Leeks	whole plant without root	0.028	0.010
	T-2A	133	48	245	Leeks	whole plant without root	0.015	< 0.01
	T-2A	133	49	258	Leeks	whole plant without root	0.015	< 0.01
	T-3A	356	48	468	Leeks	whole plant without root	0.014	< 0.01
	T-3A	356	49	481	Leeks	whole plant without root	0.015	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]
18-2520-03 Portugal	T-1A	28	47	121	Leeks	whole plant without root	0.012	0.011
	T-1A	28	49	135	Leeks	whole plant without root	< 0.01	< 0.01
	T-2A	172	47	265	Leeks	whole plant without root	0.023	0.013
	T-2A	172	49	279	Leeks	whole plant without root	0.016	< 0.01
	T-3A	354	47	447	Leeks	whole plant without root	< 0.01	< 0.01
	T-3A	354	49	461	Leeks	whole plant without root	< 0.01	< 0.01
18-2520-04 Spain	T-1A	29	47	107	Leeks	whole plant without root	0.010	< 0.01
	T-1A	29	49	121	Leeks	whole plant without root	< 0.01	< 0.01
	T-2A	154	45	231	Leeks	whole plant without root	< 0.01	< 0.01
	T-2A	154	49	245	Leeks	whole plant without root	< 0.01	< 0.01
	T-3A	363	45	440	Leeks	whole plant without root	< 0.01	< 0.01
	T-3A	363	49	454	Leeks	whole plant without root	< 0.01	< 0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

Data Point:	KCA 6.6.2/13
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of the residues of fluopicolide in/on soil and the field rotational crop maize/corn after spray application of fluopicolide & propamocarb-hydrochloride SC 687.5 to bare soil in southern France, Spain, Italy and Portugal
Report No:	18-2523
Document No:	M-679663-01-1
Guideline(s) followed in study:	Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market, OECD Guidelines for the Testing of Chemicals, Residues in Rotational Crops (Limited Field Studies): 504, 2007-01-08, OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009), US EPA OCSPP Guideline No. 860.1900, Field Accumulation in Rotational Crops and US EPA OCSPP Guideline No. 860.1500 on Crop Field Trial
Deviations from current test guideline:	No deviations from the test guideline were noted with the study report.
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A rotational crop field trial was conducted on maize after the application of SC 687.5 (a suspension concentrate formulation containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride) to bare soil. Trial sites were established in the southern France, Spain, Italy and Portugal 2018-2019. One spray application of SC 687.5 was made to bare soil at a nominal application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide).

Rotational crops were planted with the following plant-back intervals (PBIs); 25 to 30 days (1st rotation), 120 to 180 days (2nd rotation) and 300 to 365 (3rd rotation). Rotational crop samples were collected at set periods

RAC samples were collected and stored frozen (<-18 °C) prior to analysis. Samples were stored for a maximum of 377 days (ca. 12 months) prior to residue analysis.

Samples were analysed for residues using the validated analytical methods 01209/M001 (for fluopicolide, M-01, M-02 and M-09) and 00782/M006 (for M-04, M-05 and M-06). The limit of quantification was 0.01 mg/kg for all analytes. Procedural recoveries of each analyte were within the acceptable range of 70-120%.

Residues in all untreated control samples and RAC rotational crop samples were ND or <LOQ.

I. MATERIALS AND METHODS

A – MATERIALS

1.	**Test Material**	Fluopicolide & Propamocarb hydrochloride SC 687.5
	Description:	Suspension concentrate
	Lot/Batch no.:	EM4L023437
	Active substance content:	Fluopicolide: 62.5 g/L (nominal) Propamocarb hydrochloride: 625 g/L (nominal)
	Expiry date:	26-03-2021
2.	**Test Commodity**	
	Crop:	Maize
	Variety:	Capuzi, DKC6728, DKC5830, Dekalb 6636, LG30600
	Crop part(s) or processed commodity:	Kernels, green material and rest of plant
	Sample size:	Not stated

B – STUDY DESIGN

1. Test Procedure

The study comprised supervised residue trials site in the southern France, Spain, Italy and Portugal. At the trial site there was one untreated plot in addition to the treated plots. The treated and untreated plots were cultivated in the same manner.

For the treated plots, one spray application of SC 687.5 was made to bare soil at an application rate of 19.2 L/ha (equivalent to 1.2 kg/ha fluopicolide) with a water rate of 200 - 400 L/ha. The application procedure was followed by incorporation of the test item into the soil via ploughing to a depth of ≤ 8 cm.

After a period of 25-30 days after treatment (DAT), maize was planted on plot 1A to simulate a case of crop failure. A control plot was planted in the same manner without the application to bare soil prior to planting/sowing.

Following a period of 120-180 days after treatment (DAT), maize was planted on the treated and control plots (2A). This rotational situation simulates a second use of the same plot within a single season.

At 300-365 days after treatment (DAT) maize was planted on the treated and control plots (3A). This rotational situation simulates a re-use of the same plot in the following season.

The study design is summarised within the following table:

Table 6.6.2- 87 Plot design and plant-back intervals

Trial No. Country	Requested plant-back interval (days) and application	Actual plant-back interval	Remarks
		Maize plot (DAT)	
18-2523-01 southern France	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 21**	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 145	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 329	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2523-02 Spain	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 22***	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 149	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 358	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2523-03 Italy	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 25	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 162	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 342	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
18-2523-04 Portugal	One application on bare soil, plant-back interval 25-30 days after treatment	**1A** 28	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 120-180 days	**2A** 172	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops
	One application on bare soil, plant-back interval 300-365 days after treatment	**3A** 354	1) Spray application on bare soil and incorporation 2) Planting/sowing of rotational crops

DAT = Days after treatment

** Due to a schedule mistake sowing was done at DAT +21 instead of DAT +25-30

*** Due to a schedule mistake sowing was done at DAT +22 instead of DAT +25-30

Samples of representative plant commodities were taken at early and full harvest maturity for each of the sub-plots and analysed for residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09.

2. Description of Analytical Procedures

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were analysed within the samples according to the following method:

Table 6.6.2- 88 Summary of the analytical methods

Method	01209/M001
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (Fluopicolide, M-01, M-02 and M-09) for maize fractions
Method	00782/M006
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (M-04 and M-05) for maize fractions

Full analytical details for these methods, and conclusions on their acceptability, are presented within document M-CA 4.

In order to check the performance of the methods, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Table 6.6.2- 89 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	93; 96; 98; 100; 108	99	5.7	0.01
	0.50	93	-	-	
	1.0	87; 90; 91; 92; 95	91	3.2	
		Overall recovery (n = 10)	95	6.0	
Maize / corn / kernel	0.01	91; 91; 94; 100; 100	95	4.8	0.01
	0.50	87; 88; 90; 90; 93; 93	90	2.8	
		Overall recovery (n = 11)	92	4.6	
Maize / corn / rest of plant	0.01	93; 94; 94; 96; 100	95	2.9	0.01
	0.50	84	-	-	
	1.0	83; 85; 86; 90; 94	88	5.0	
		Overall recovery (n = 11)	91	6.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 90 Procedural recoveries for AE C653711 (M-01)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	76; 77; 87; 89; 99	86	11.1	0.01
	0.50	96	-	-	
	1.0	83; 84; 85; 91; 92	87	4.8	
		Overall recovery (n = 11)	87	8.3	
Maize / corn / kernel	0.01	86; 94; 94; 95; 96	93	4.3	0.01
	0.50	85; 88; 90; 94; 95; 98	92	5.3	
		Overall recovery (n = 11)	92	4.7	
Maize / corn / rest of plant	0.01	92; 92; 97; 99; 102	96	4.6	0.01
	0.50	78	-	-	
	1.0	80; 82; 86; 87; 88	85	4.1	
		Overall recovery (n = 11)	89	8.7	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 91 Procedural recoveries for AE C6571881 (M-02)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	95; 97; 99; 101; 101	99	2.6	0.01
	0.50	91	-	-	
	1.0	86; 87; 88; 88; 89	88	1.3	
		Overall recovery (n = 11)	93	6.3	
Maize / corn / kernel	0.01	86; 92; 95; 96; 99	94	5.3	0.01
	0.50	82; 84; 85; 85; 89; 92	86	4.2	
		Overall recovery (n = 11)	90	6.3	
Maize / corn / rest of plant	0.01	85; 85; 90; 94; 94	90	5.0	0.01
	0.50	79	-	-	
	1.0	80; 81; 82; 85; 86	83	3.1	
		Overall recovery (n = 11)	86	6.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 92 Procedural recoveries for AE B102859 (M-09)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	87; 88; 89; 94; 106	93	8.5	0.01
	0.50	95	-	-	
	1.0	91; 92; 93; 94; 94	93	1.4	
		Overall recovery (n = 11)	93	5.5	
Maize / corn / kernel	0.01	92; 94; 94; 97; 100	95	3.3	0.01
	0.50	92; 93; 94; 94; 95; 97	94	1.8	
		Overall recovery (n = 11)	95	2.5	
Maize / corn / rest of plant	0.01	80; 81; 82; 82; 87	82	3.3	0.01
	0.50	77	-	-	
	1.0	83; 85; 87; 88; 91	87	3.5	
		Overall recovery (n = 11)	84	4.9	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 93 Procedural recoveries for AE C657378 (M-04)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	77; 80; 93	83	10.2	0.01
	0.10	83; 84; 89	85	3.8	
		Overall recovery (n = 6)	84	6.9	
Maize / corn / kernel	0.01	70; 73; 91	78	14.6	0.01
	0.10	68; 72; 90; 91; 93	83	14.3	
		Overall recovery (n = 8)	81	13.7	
Maize / corn / rest of plant	0.01	86; 92; 93	90	4.2	0.01
	0.10	89; 89; 91	90	1.3	
		Overall recovery (n = 6)	90	2.8	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 94 Procedural recoveries for AE 1344122 (M-05)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	79; 80; 92	84	8.6	0.01
	0.10	79; 83; 84	82	3.2	
		Overall recovery (n = 6)	83	6.0	
Maize / corn / kernel	0.01	77; 78; 86	80	6.1	0.01
	0.10	76; 82; 88; 88; 92	85	7.3	
		Overall recovery (n = 8)	83	7.2	
Maize / corn / rest of plant	0.01	94; 101; 102	99	4.4	0.01
	0.10	82; 82; 85	83	2.1	
		Overall recovery (n = 6)	91	10.2	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

Table 6.6.2- 95 Procedural recoveries for AE C643890 (M-06)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Maize / corn / green material	0.01	77; 81; 88	82	6.8	0.01
	0.10	86; 87; 90	88	2.4	
		Overall recovery (n = 6)	85	5.7	
Maize / corn / kernel	0.01	73; 78; 86	79	8.3	0.01
	0.10	78; 80; 87; 90; 92	85	7.2	
		Overall recovery (n = 8)	83	8.1	
Maize / corn / rest of plant	0.01	93; 102; 107	101	7.0	0.01
	0.10	88; 88; 94	90	3.8	
		Overall recovery (n = 6)	95	8.1	

RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification

3. Storage stability:

All collected samples were stored deep-frozen (< -18°C) until analysis.

The storage period for samples until the analysis of fluopicolide, M-01, M-02, M-04, M-05, M-06 and M-09 residues was 92 – 377 days in maize fractions (green material, kernels and rest of plant).

II. RESULTS AND DISCUSSION

A summary of the residue results is given in the following table.

Table 6.6.2- 96 Residues in rotational crops (fluopicolide, M-01, M-02 and M-09)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2523-01 southern France	T-1A	21	85	138	Maize	green material	0.53	0.41	0.025	< 0.01
	T-1A	21	89	180	Maize	kernel	< 0.01	0.01	< 0.01	< 0.01
	T-1A	21	89	180	Maize	rest of plant	0.39	0.22	0.039	< 0.01
	T-2A	145	85	266	Maize	green material	0.42	0.14	0.016	< 0.01
	T-2A	145	89	306	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	145	89	306	Maize	rest of plant	0.38	0.16	0.033	< 0.01
	T-3A	329	85	450	Maize	green material	0.11	0.071	< 0.01	< 0.01
	T-3A	329	89	490	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	329	89	490	Maize	rest of plant	0.075	0.074	< 0.01	< 0.01
18-2523-02 Spain	T-1A	22	85	133	Maize	green material	0.33	0.064	0.011	< 0.01
	T-1A	22	89	172	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	22	89	172	Maize	rest of plant	0.37	0.12	0.027	< 0.01
	T-2A	149	85	262	Maize	green material	0.24	0.12	< 0.01	< 0.01
	T-2A	149	89	301	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	149	89	301	Maize	rest of plant	0.42	0.25	0.023	< 0.01
	T-3A	358	85	471	Maize	green material	0.17	0.12	< 0.01	< 0.01
	T-3A	358	89	516	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	358	89	510	Maize	rest of plant	0.26	0.16	0.013	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	Fluopicolide [mg/kg]	M-01 [mg/kg]	M-02 [mg/kg]	M-09 [mg/kg]
18-2523-03 Italy	T-1A	25	85	136	Maize	green material	0.12	0.042	< 0.01	< 0.01
	T-1A	25	89	174	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-1A	25	89	174	Maize	rest of plant	0.22	0.031	0.016	< 0.01
	T-2A	162	85	306	Maize	green material	0.13	0.060	< 0.01	< 0.01
	T-2A	162	89	331	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	162	89	331	Maize	rest of plant	0.19	0.062	< 0.01	< 0.01
	T-3A	342	85	486	Maize	green material	0.060	0.040	< 0.01	< 0.01
	T-3A	342	89	511	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	342	89	511	Maize	rest of plant	0.12	0.036	< 0.01	< 0.01
18-2523-04 Portugal	T-1A	28	85	146	Maize	green material	0.31	0.072	0.018	< 0.01
	T-1A	28	89	172	Maize	kernel	< 0.01	0.017	0.019	< 0.01
	T-1A	28	89	172	Maize	rest of plant	0.77	0.32	0.031	< 0.01
	T-2A	172	85	287	Maize	green material	0.11	0.079	< 0.01	< 0.01
	T-2A	172	89	318	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-2A	172	89	318	Maize	rest of plant	0.35	0.27	0.025	< 0.01
	T-3A	354	85	469	Maize	green material	0.047	0.027	< 0.01	< 0.01
	T-3A	354	89	500	Maize	kernel	< 0.01	< 0.01	< 0.01	< 0.01
	T-3A	354	89	500	Maize	rest of plant	0.11	0.079	< 0.01	< 0.01

Table 6.6.2- 97 Residues in rotational crops (M-04, M-05 and M-06)

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2523-01 southern France	T-1A	21	85	138	Maize	green material	< 0.01	0.022	< 0.01
	T-1A	21	89	180	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-1A	21	89	180	Maize	rest of plant	0.015	0.016	< 0.01
	T-2A	145	85	266	Maize	green material	< 0.01	< 0.01	< 0.01
	T-2A	145	89	306	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-2A	145	89	306	Maize	rest of plant	< 0.01	< 0.01	0.012
	T-3A	329	85	450	Maize	green material	< 0.01	< 0.01	< 0.01
	T-3A	329	89	490	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-3A	329	89	490	Maize	rest of plant	< 0.01	< 0.01	< 0.01
18-2523-02 Spain	T-1A	22	85	133	Maize	green material	< 0.01	< 0.01	< 0.01
	T-1A	22	89	172	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-1A	22	89	172	Maize	rest of plant	< 0.01	0.014	< 0.01
	T-2A	149	85	262	Maize	green material	< 0.01	0.018	< 0.01
	T-2A	149	89	301	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-2A	149	89	301	Maize	rest of plant	0.015	0.026	< 0.01
	T-3A	358	85	471	Maize	green material	< 0.01	< 0.01	< 0.01
	T-3A	358	89	510	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-3A	358	89	510	Maize	rest of plant	0.010	0.013	< 0.01

Trial no. Country	Plot	PBI	Growth stage [BBCH]	DAT	Crop	Sample material	M-04 [mg/kg]	M-05 [mg/kg]	M-06 [mg/kg]
18-2523-03 Italy	T-1A	25	85	136	Maize	green material	< 0.01	< 0.01	< 0.01
	T-1A	25	89	174	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-1A	25	89	174	Maize	rest of plant	0.013	< 0.01	< 0.01
	T-2A	162	85	306	Maize	green material	< 0.01	< 0.01	< 0.01
	T-2A	162	89	331	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-2A	162	89	331	Maize	rest of plant	0.013	< 0.01	< 0.01
	T-3A	342	85	486	Maize	green material	< 0.01	< 0.01	< 0.01
	T-3A	342	89	511	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-3A	342	89	511	Maize	rest of plant	0.012	< 0.01	< 0.01
18-2523-04 Portugal	T-1A	28	85	146	Maize	green material	0.010	0.055	< 0.01
	T-1A	28	89	172	Maize	kernel	< 0.01	0.012	< 0.01
	T-1A	28	89	172	Maize	rest of plant	0.027	0.15	< 0.01
	T-2A	172	85	287	Maize	green material	0.014	0.064	< 0.01
	T-2A	172	89	318	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-2A	172	89	318	Maize	rest of plant	0.079	0.21	< 0.01
	T-3A	354	85	469	Maize	green material	< 0.01	0.025	< 0.01
	T-3A	354	89	500	Maize	kernel	< 0.01	< 0.01	< 0.01
	T-3A	354	89	500	Maize	rest of plant	0.019	0.043	< 0.01

III. CONCLUSIONS

Residues of fluopicolide and the metabolites M-01, M-02, M-04, M-05, M-06 and M-09 were determined using validated selective HPLC-MS/MS methods.

Assessment and conclusion by applicant:
The study is acceptable

The following studies are currently in progress and will be submitted at the indicated timepoints:

Dossier node	Draft title	Study ID	Planned submission
KCA 6.6.2	Determination of the residues of fluopicolide in/on soil and the field rotational crop pea after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 to bare soil in Belgium, Germany, France (South) and Spain	18-2530	November 2020
KCA 6.6.2	Determination of the residues of fluopicolide in/on soil and the field rotational crop barley after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 to bare soil in France (South) and Portugal	18-2531	2nd Quarter 2021
KCA 6.6.2	Determination of the residues of fluopicolide in/on soil and the field rotational crop rape after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 to bare soil in Germany, Belgium northern France and the Netherlands	18-2528 (North)	2nd Quarter 2021
KCA 6.6.2	Determination of the residues of fluopicolide in/on soil and the field rotational crop rape after spray application of Fluopicolide & Propamocarb-hydrochloride SC 687.5 to bare soil in France (South), Spain, Italy and Portugal	18-2529 (South)	2nd Quarter 2021

CA 6.7 Proposed residue definitions and maximum residue levels

CA 6.7.1 Proposed residue definitions

Fluopicolide is a first stage active substance according to Directive 91/414/EEC. It has been peer reviewed in 2005 and is included in Annex I to Directive 91/414/EEC by Commission Directive 2010/15/EU for uses as a fungicide only. The residue definitions are summarized within Table 6.7.1- 1. This is in line with the residue definition established in the Regulation (EC) No 396/2005.

Here is the extract of the document "Review of the existing maximum residue levels for fluopicolide according to Article 12 of Regulation (EC) No 396/2005" (EFSA Journal 2019;17(7):5748):

"The metabolic pathway of fluopicolide was found to be similar in the four crop groups investigated. The metabolism in rotational crops is similar to the metabolism observed in primary crops and the processing of fluopicolide is not expected to modify the nature of residues. The available studies indicate that parent compound and its metabolite 2,6-dichlorobenzamide (M-01) are the most important components of the residue. The parent compound is a relevant marker in all primary crops as well as in rotational crops and therefore the residue definition for enforcement is proposed as parent compound fluopicolide for all plant commodities. Fully validated analytical methods for enforcement of fluopicolide in the four main plant matrices are available and are fully applicable in routine according to the EURLs. The metabolite 2,6-dichlorobenzamide (M-01) is not specific to fluopicolide as it is also the main degradation product of another active substances (dichlobenil and chlorthiamide) which are not authorised in the EU. Therefore, this compound was not proposed in the residue definition for enforcement. As regards dietary risk assessment purposes, the parent fluopicolide and its metabolite 2,6-dichlorobenzamide (also referred to as BAM or M-01) are the only compounds of toxicological relevance. The other metabolites found in lower amount in primary crops and/or in rotational crops were all regarded as less toxic than the parent compound. It is noted that specific ADI and ARfD were set for 2,6-dichlorobenzamide and that fluopicolide and metabolite 2,6-dichlorobenzamide have different toxicological end points. Therefore, two separate residue definitions are set for risk assessment purpose: fluopicolide (RD-RA1) and metabolite 2,6-dichlorobenzamide (RD-RA2).The proposed residue definitions are applicable to all commodities that are under assessment in the present review."

This excerpt summarises the background to the background to the establishment of the residue definitions which were agreed and implemented at the EU level.

Further justification for the selection of the component of the respective residue definitions is outlined below.

Primary crops (risk assessment residue definition)

No changes are proposed to the current residue definitions for enforcement or risk assessment for primary crops. The primary crop metabolism for lettuce, potatoes and grapes have been previously reviewed at the EU level. The primary residues found were associated with parent fluopicolide and M-01. Minor levels of M-08 were observed, but not considered to be relevant to residue definitions. For the new oilseed rape metabolism study (seed treatment), only fluopicolide and M-01 were observed, indicating that the results by this treatment mode are comparable to those of the foliar and soil drench uses; therefore the existing residue definitions can apply to all treatment scenarios for the primary crops.

Rotational crops (risk assessment residue definition)

From the confined rotational crop study ([redacted] 2003; M-240707-03-1), metabolite M-09 was identified as an analytical target for the limited crop rotation study, due to the levels found within the tested crops. According to the toxicology studies (refer to M- CA 5.8.1), M-09 is more acutely toxic than fluopicolide (the LD_{50} for M-09 is 1030 mg/kg bw, while the corresponding value for fluopicolide is >2000 mg/kg bw). While this indicates a potential risk, the actual exposure expected from M-09 is negligible, as all of the rotational crop studies presented within section CA 6.6.2 of this document (covering matrices of barley, lettuce carrot, cabbage, maize, cucumber, strawberries and cauliflower) show that residues of M-09 do not exceed the LOQ (0.01 mg/kg in all of the tested crop fractions) for any of the tested plant-back scenarios. For this reason, metabolite M-09 is not considered to be a suitable marker for the monitoring residue definition for rotational crops, nor it is considered to be relevant for inclusion within the risk assessment residue definition for rotational crops.

Metabolites M-02, M-04, M-05 and M-06 were also identified as analytical targets based on the confined rotational crop study ([redacted] 2003; M-240707-03-1). However, it was not considered to be necessary to include these components within the residue definitions, based on the following:

M-02 The available toxicity data for M-02 demonstrated that the metabolite is not acutely toxic. In the acute oral toxicity study the LD_{50} was >2000 mg/kg bw. In a 28-day toxicity study in rats with M-02, no effects were observed up to the highest dose tested (1580 mg/kg bw). Therefore, it can be seen from the experimental data that M02 (PCA) is less toxic than M01 (BAM) both acutely, and over the short term. This is consistent with the conclusion of EFSA for the Annex 1 inclusion, M-02 is not considered to be a relevant metabolite.

M-04 The toxicity data shows that M-04 is not acutely toxic via the oral route; LD_{50} >2000 mg/kg bw/d. No effects were observed in the 28-day oral toxicity study in rats, up to and including the highest dose tested of 159.2/230.6 mg/kg bw/d in males/females. Low levels of M-04 are observed within the rotational crop studies in the tested crop fractions and at all plant-back interval. M-04 is not considered to be a relevant metabolite.

M-05 The data for M-05 was not acutely toxic in an acute oral toxicity study; LD_{50} > 2000 mg/kg bw/d. The NOAEL of 152/167 mg/kg bw/d in males/females was derived from a 28-day oral toxicity study in rats; at the LOAEL of 1495 mg/kg bw/d decreased body weight gain and kidney regeneration/degeneration were observed). Low levels of M-05 are observed within the rotational crop studies in the tested crop fractions and at all plant-back interval. M-05 is not considered to be a relevant metabolite.

M-06 No experimental toxicity data are available for M-06. However, M-06 is structurally very similar to the parent fluopicolide, being a hydroxylation product (at position 3 of the phenyl ring), which is generally considered as detoxification reaction. Therefore, M-06 is considered to be equally or less toxic compared to fluopicolide. This assumption is substantiated by the results of the QSAR analysis. Furthermore, the rotational crop studies show that there is negligible exposure potential, given that the residue of M-06 are <LOQ (<0.01 mg/kg within barley grain and maize fractions). M-06 is therefore not considered to be a relevant metabolite.

Metabolite M-08 was also identified within the confined rotational crops study, however, it was considered to be a minor metabolite and was not selected as an analytical target for the rotational crop studies.

Based on the above information, it is proposed to maintain the current residue definitions for rotational crops, which are aligned with the definitions defined for the primary crops.

Processed products (risk assessment residue definition)

The radiolabelled high temperature hydrolysis studies for fluopicolide and metabolite M-01 (refer to section CA 6.5.1), which simulate the conditions associated with baking, brewing and boiling, showed that both components remained sufficiently stable following the processing procedures, with negligible degradation noted. Based on this information, it is considered appropriate to maintain the current residue definitions for processed commodities, which are aligned with the definitions defined for the primary crops.

Livestock products (risk assessment residue definition)

The livestock metabolism studies for Metabolite M-01 (BAM) have yet to be finalised. Once these studies are complete, full consideration of the residue definition will be made in an update to this section.

Consideration of all the above, leads to the following proposed residue definitions for fluopicolide:

Table 6.7.1- 1 Residue definitions for fluopicolide

Category	Residues definition
Enforcement (post-registration) residue definition for primary crops:	Fluopicolide
Enforcement (post-registration) residue definition for products of livestock origin:	Fluopicolide
Data generation (pre-registration) residue definition for primary crops:	1. Fluopicolide 2. Metabolite M-01 (BAM)
Data generation (pre-registration) residue definition for products of livestock origin:	1. Fluopicolide 2. Metabolite M-01 (BAM)
Data generation (pre-registration) residue definition for processed plant commodities:	1. Fluopicolide 2. Metabolite M-01 (BAM)
Data generation (pre-registration) residue definition for succeeding crops:	1. Fluopicolide 2. Metabolite M-01 (BAM)

CA 6.7.2 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed

The EU MRLs for fluopicolide were published in the Annex II and Annex III Part B of the Regulation (EC) No. 396/2005 via the Regulation (EC) No. 839/2008. The currently enforced EU MRLs for fluopicolide are defined within Regulation (EU) 2018/832. The current EU MRLs are based on the residue definition of the parent compound only (fluopicolide).

The proposed MRLs are included within Table 6.7.2- 1. The proposed changes are based on the following criteria:

- The MRL derived from the residue trials data for primary crops (refer to section CA 6.3) supports a higher MRL.
- The data generated on the surrogate rotation crops support a higher MRL (assuming that the crop is commonly rotated).

Proposals to maintain the existing EU MRLs have been made for specific commodities (Table 6.7.2- 1) according to the following criteria:

- There is no use intended for the commodity and the commodity is not rotated (permanent or semi-permanent crop).
- The existing MRL is higher than (or equal to) the MRL supported by the primary crop data or rotational crop data (whichever is highest).

Table 6.7.2- 1: Current EU MRLs and proposed MRLs for fluopicolide

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0100000	FRUITS, FRESH or FROZEN; TREE NUTS			
0110000	Citrus fruits	0.01*	0.01*	No use intended for the commodity
0110010	Grapefruits	0.01*	0.01*	No use intended for the commodity
0110020	Oranges	0.01*	0.01*	No use intended for the commodity
0110030	Lemons	0.01*	0.01*	No use intended for the commodity
0110040	Limes	0.01*	0.01*	No use intended for the commodity
0110050	Mandarins	0.01*	0.01*	No use intended for the commodity
0110990	Others	0.01*	0.01*	No use intended for the commodity
0120000	Tree nuts	0.01*	0.01*	No use intended for the commodity
0120010	Almonds	0.01*	0.01*	No use intended for the commodity
0120020	Brazil nuts	0.01*	0.01*	No use intended for the commodity
0120030	Cashew nuts	0.01*	0.01*	No use intended for the commodity
0120040	Chestnuts	0.01*	0.01*	No use intended for the commodity
0120050	Coconuts	0.01*	0.01*	No use intended for the commodity
0120060	Hazelnuts/cobnuts	0.01*	0.01*	No use intended for the commodity
0120070	Macadamias	0.01*	0.01*	No use intended for the commodity
0120080	Pecans	0.01*	0.01*	No use intended for the commodity
0120090	Pine nut kernels	0.01*	0.01*	No use intended for the commodity
0120100	Pistachios	0.01*	0.01*	No use intended for the commodity
0120110	Walnuts	0.01*	0.01*	No use intended for the commodity
0120990	Others	0.01*	0.01*	No use intended for the commodity
0130000	Pome fruits	0.01*	0.01*	No use intended for the commodity
0130010	Apples	0.01*	0.01*	No use intended for the commodity
0130020	Pears	0.01*	0.01*	No use intended for the commodity
0130030	Quinces	0.01*	0.01*	No use intended for the commodity
0130040	Medlars	0.01*	0.01*	No use intended for the commodity
0130050	Loquats/Japanese medlars	0.01*	0.01*	No use intended for the commodity
0130990	Others	0.01*	0.01*	No use intended for the commodity

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0140000	Stone fruits	0.01*	0.01*	No use intended for the commodity
0140010	Apricots	0.01*	0.01*	No use intended for the commodity
0140020	Cherries (sweet)	0.01*	0.01*	No use intended for the commodity
0140030	Peaches	0.01*	0.01*	No use intended for the commodity
0140040	Plums	0.01*	0.01*	No use intended for the commodity
0140990	Others	0.01*	0.01*	No use intended for the commodity
0150000	Berries and small fruits			
0151000	Grapes	2	2	No change required based on the data available in this dossier
0151010	Table grapes	2	2	No change required based on the data available in this dossier
0151020	Wine grapes	2	2	No change required based on the data available in this dossier
0152000	Strawberries	0.01*	0.1	Based on Rotational crop study results
0153000	Cane fruits			
0153010	Blackberries	3	3	No change required based on the data available in this dossier
0153020	Dewberries	0.01*	0.01*	No use intended for the commodity
0153030	Raspberries (red and yellow)	0.01*	0.01*	No use intended for the commodity
0153990	Others	0.01*	0.01*	No use intended for the commodity
0154000	other small fruits and berries	0.01*	0.01*	No use intended for the commodity
0154010	Blueberries	0.01*	0.01*	No use intended for the commodity
0154020	Cranberries	0.01*	0.01*	No use intended for the commodity
0154030	Currants (black, red and white)	0.01*	0.01*	No use intended for the commodity
0154040	Gooseberries (green, red and yellow)	0.01*	0.01*	No use intended for the commodity
0154050	Rose hips	0.01*	0.01*	No use intended for the commodity
0154060	Mulberries (black and white)	0.01*	0.01*	No use intended for the commodity
0154070	Azaroles/Mediterranean medlars	0.01*	0.01*	No use intended for the commodity
0154080	Elderberries	0.01*	0.01*	No use intended for the commodity
0154990	Others	0.01*	0.01*	No use intended for the commodity

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0160000	Miscellaneous fruits with…	0.01*	0.01*	No use intended for the commodity
0161000	edible peel	0.01*	0.01*	No use intended for the commodity
0161010	Dates	0.01*	0.01*	No use intended for the commodity
0161020	Figs	0.01*	0.01*	No use intended for the commodity
0161030	Table olives	0.01*	0.01*	No use intended for the commodity
0161040	Kumquats	0.01*	0.01*	No use intended for the commodity
0161050	Carambolas	0.01*	0.01*	No use intended for the commodity
0161060	Kaki/Japanese persimmons	0.01*	0.01*	No use intended for the commodity
0161070	Jambuls/jambolans	0.01*	0.01*	No use intended for the commodity
0161990	Others	0.01*	0.01*	No use intended for the commodity
0162000	inedible peel, small	0.01*	0.01*	No use intended for the commodity
0162010	Kiwi fruits (green, red, yellow)	0.01*	0.01*	No use intended for the commodity
0162020	Litchis/lychees	0.01*	0.01*	No use intended for the commodity
0162030	Passionfruits/maracujas	0.01*	0.01*	No use intended for the commodity
0162040	Prickly pears/cactus fruits	0.01*	0.01*	No use intended for the commodity
0162050	Star apples/cainitos	0.01*	0.01*	No use intended for the commodity
0162060	American persimmons/Virginia kaki	0.01*	0.01*	No use intended for the commodity
0162990	Others	0.01*	0.01*	No use intended for the commodity
0163000	inedible peel, large	0.01*	0.01*	No use intended for the commodity
0163010	Avocados	0.01*	0.01*	No use intended for the commodity
0163020	Bananas	0.01*	0.01*	No use intended for the commodity
0163030	Mangoes	0.01*	0.01*	No use intended for the commodity
0163040	Papayas	0.01*	0.01*	No use intended for the commodity
0163050	Granate apples/pomegranates	0.01*	0.01*	No use intended for the commodity
0163060	Cherimoyas	0.01*	0.01*	No use intended for the commodity
0163070	Guavas	0.01*	0.01*	No use intended for the commodity
0163080	Pineapples	0.01*	0.01*	No use intended for the commodity
0163090	Breadfruits	0.01*	0.01*	No use intended for the commodity
0163100	Durians	0.01*	0.01*	No use intended for the commodity
0163110	Soursops/guanabanas	0.01*	0.01*	No use intended for the commodity
0163990	Others	0.01*	0.01*	No use intended for the commodity

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0200000	VEGETABLES, FRESH or FROZEN			
0210000	Root and tuber vegetables			
0211000	potatoes	0.03	0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0212000	tropical root and tuber vegetables	0.01	0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0212010	Cassava roots/manioc	0.01	0.3	
0212020	Sweet potatoes	0.01	0.3	
0212030	Yams	0.01	0.3	
0212040	Arrowroots	0.01	0.3	
0212990	Others	0.01	0.3	
0213000	other root and tuber vegetables except sugar beets	0.15	0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0213010	Beetroots	0.15	0.3	
0213020	Carrots	0.15	0.3	
0213030	Celeriacs/turnip rooted celeries	0.15	0.3	
0213040	Horseradishes	0.15	0.3	
0213050	Jerusalem artichokes	0.15	0.3	
0213060	Parsnips	0.15	0.3	
0213070	Parsley roots/Hamburg roots parsley	0.15	0.3	
0213080	Radishes	0.15	0.3	
0213090	Salsifies	0.15	0.3	
0213100	Swedes/rutabagas	0.15	0.3	
0213110	Turnips	0.15	0.3	
0213990	Others	0.15	0.3	

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0220000	Bulb vegetables			
0220010	Garlic	0.3	0.3	No change necessary.
0220020	Onions	1	1	No change necessary.
0220030	Shallots	0.3	0.3	No change necessary.
0220040	Spring onions/green onions and Welsh onions	10	10	No change necessary.
0220990	Others	0.01*	0.3	Based on extrapolation from the rotational crop data for leeks. Refer to section M-CA 6.6.2 for further details.
0230000	Fruiting vegetables			
0231000	Solanaceae and Malvaceae	1	1	No change necessary.
0231010	Tomatoes	1	1	No change necessary.
0231020	Sweet peppers/bell peppers	1	1	No change necessary.
0231030	Aubergines/eggplants	1	1	No change necessary.
0231040	Okra/lady's fingers	1	1	No change necessary.
0231990	Others	1	1	No change necessary.
0232000	cucurbits with edible peel	0.5	0.5	No change necessary.
0232010	Cucumbers	0.5	0.5	No change necessary.
0232020	Gherkins	0.5	0.5	No change necessary.
0232030	Courgettes	0.5	0.5	No change necessary.
0232990	Others	0.5	0.5	No change necessary.
0233000	cucurbits with inedible peel	0.5	0.5	No change necessary.
0233010	Melons	0.5	0.5	No change necessary.
0233020	Pumpkins	0.5	0.5	No change necessary.
0233030	Watermelons	0.5	0.5	No change necessary.
0233990	Others	0.5	0.5	No change necessary.
0234000	sweet corn	0.01*	0.1	Based on extrapolation from the rotational crop data for strawberries. Refer to section M-CA 6.6.2 for further details.
0239000	other fruiting vegetables	0.01*	0.1	Based on extrapolation from the rotational crop data for strawberries. Refer to section M-CA 6.6.2 for further details.

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0240000	Brassica vegetables (excluding brassica roots and brassica baby leaf crops)			
0241000	flowering brassica	2	2	No change necessary.
0241010	Broccoli	2	2	No change necessary.
0241020	Cauliflowers	2	2	No change necessary.
0241990	Others	2	2	No change necessary.
0242000	head brassica			
0242010	Brussels sprouts	0.2	0.2	No change necessary.
0242020	Head cabbages	0.2	0.2	No change necessary.
0242990	Others	0.01*	0.03	Based on extrapolation from the rotational crop data for cabbage. Refer to section M-CA 6.6.2 for further details
0243000	leafy brassica			
0243010	Chinese cabbages/pe-tsai	2	2	No change necessary.
0243020	Kales	2	2	No change necessary.
0243990	Others	0.1	0.1	No change necessary.
0244000	kohlrabies	0.03	0.03	No change necessary.
0250000	Leaf vegetables, herbs and edible flowers			
0251000	lettuces and salad plants			
0251010	Lamb's lettuces/corn salads	9	9	No change necessary.
0251020	Lettuces	9	9	No change necessary.
0251030	Escaroles/broad-leaved endives	1.5	1.5	No change necessary.
0251040	Cresses and other sprouts and shoots	9	9	No change necessary.
0251050	Land cresses	9	9	No change necessary.
0251060	Roman rocket/rucola	9	9	No change necessary.
0251070	Red mustards	9	9	No change necessary.
0251080	Baby leaf crops (including brassica species)	9	9	No change necessary.
0251990	Others	9	9	No change necessary.

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0252000	spinaches and similar leaves			
0252010	Spinaches	6	6	No change necessary.
0252020	Purslanes	6	6	No change necessary.
0252030	Chards/beet leaves	6	6	No change necessary.
0252990	Others	6	6	No change necessary.
0253000	grape leaves and similar species	0.01*	0.01*	No change necessary.
0254000	watercresses	0.01*	0.01*	No change necessary.
0255000	witloofs/Belgian endives	0.01*	0.3	Based on extrapolation from the rotational crop data for carrots (or lettuce). Refer to section M-CA 6.6.2 for further details.
0256000	herbs and edible flowers	9	9	No change necessary.
0256010	Chervil	9	9	No change necessary.
0256020	Chives	9	9	No change necessary.
0256030	Celery leaves	9	9	No change necessary.
0256040	Parsley	9	9	No change necessary.
0256050	Sage	9	9	No change necessary.
0256060	Rosemary	9	9	No change necessary.
0256070	Thyme	9	9	No change necessary.
0256080	Basil and edible flowers	9	9	No change necessary.
0256090	Laurel/bay leaves	9	9	No change necessary.
0256100	Tarragon	9	9	No change necessary.
0256990	Others	9	9	No change necessary.
0260000	Legume vegetables	0.01*	0.01*	No change necessary.
0260010	Beans (with pods)	0.01*	0.01*	No change necessary.
0260020	Beans (without pods)	0.01*	0.01*	No change necessary.
0260030	Peas (with pods)	0.01*	0.01*	No change necessary.
0260040	Peas (without pods)	0.01*	0.01*	No change necessary.
0260050	Lentils	0.01*	0.01*	No change necessary.
0260990	Others	0.01*	0.01*	No change necessary.

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0270000	Stem vegetables			
0270010	Asparagus	0.01*	0.3	Based on extrapolation from the rotational crop data for leeks. Refer to section M-CA 6.6.2 for further details.
0270020	Cardoons	0.01*	0.3	
0270030	Celeries	0.01*	0.3	
0270040	Florence fennels	0.01*	0.3	
0270050	Globe artichokes	0.01*	0.3	
0270060	Leeks	1.5	1.5	No change necessary
0270070	Rhubarbs	0.01*	0.3	Based on extrapolation from the rotational crop data for leeks. Refer to section M-CA 6.6.2 for further details
0270080	Bamboo shoots	0.01*	0.3	
0270090	Palm hearts	0.01*	0.3	
0270990	Others	0.01*	0.3	
0280000	Fungi, mosses and lichens	0.01*	0.01*	No use intended for the commodity
0280010	Cultivated fungi	0.01*	0.01*	No use intended for the commodity
0280020	Wild fungi	0.01*	0.01*	No use intended for the commodity
0280990	Mosses and lichens	0.01*	0.01*	No use intended for the commodity
0290000	Algae and prokaryotes organisms	0.01*	0.01*	No use intended for the commodity
0300000	PULSES	0.01*	0.02	Based on extrapolation from the rotational crop data for pulses. Refer to section M-CA 6.6.2 for further details.
0300010	Beans	0.01*	0.02	
0300020	Lentils	0.01*	0.02	
0300030	Peas	0.01*	0.02	
0300040	Lupins/lupini beans	0.01*	0.02	
0300990	Others	0.01*	0.02	
0400000	OILSEEDS AND OIL FRUITS	0.01*	0.15	Based on extrapolation from the rotational crop data for oilseeds. Refer to section M-CA 6.6.2 for further details.
0401000	Oilseeds	0.01*	0.15	
0401010	Linseeds	0.01*	0.15	
0401020	Peanuts/groundnuts	0.01*	0.15	
0401030	Poppy seeds	0.01*	0.15	
0401040	Sesame seeds	0.01*	0.15	
0401050	Sunflower seeds	0.01*	0.15	
0401060	Rapeseeds/canola seeds	0.01*	0.15	
0401070	Soyabeans	0.01*	0.15	
0401080	Mustard seeds	0.01*	0.15	
0401090	Cotton seeds	0.01*	0.15	

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0401100	Pumpkin seeds	0.01*	0.15	
0401110	Safflower seeds	0.01*	0.15	
0401120	Borage seeds	0.01*	0.15	
0401130	Gold of pleasure seeds	0.01*	0.15	
0401140	Hemp seeds	0.01*	0.15	
0401150	Castor beans	0.01*	0.15	
0401990	Others	0.01*	0.15	
0402000	Oil fruits	0.01*	0.15	
0402010	Olives for oil production	0.01*	0.15	
0402020	Oil palms kernels	0.01*	0.15	
0402030	Oil palms fruits	0.01*	0.15	
0402040	Kapok	0.01*	0.15	
0402990	Others	0.01*	0.15	
0500000	CEREALS	0.01*		
0500010	Barley	0.01*	0.3	
0500020	Buckwheat and other pseudocereals	0.01*	0.3	Based on extrapolation from the rotational crop data for barley. Refer to section M-CA 6.6.2 for further details
0500030	Maize/corn	0.01*	0.01	No change necessary, no residue observed in the rotational crop.
0500040	Common millet/proso millet	0.01*	0.3	Based on extrapolation from the rotational crop data for barley. Refer to section M-CA 6.6.2 for further details
0500050	Oat	0.01*	0.3	
0500060	Rice	0.01*	0.3	
0500070	Rye	0.01*	0.3	
0500080	Sorghum	0.01*	0.3	
0500090	Wheat	0.01*	0.3	
0500990	Others	0.01*	0.3	
0600000	TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS			
0610000	Teas	0.02*	0.02*	No use intended for the commodity
0620000	Coffee beans	0.02*	0.02*	No use intended for the commodity

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0630000	Herbal infusions from			
0631000	flowers	0.02*	0.3	Based on extrapolation from the rotational crop data for lettuce. Refer to section M-CA 6.6.2 for further details.
0631010	Chamomile	0.02*	0.3	
0631020	Hibiscus/roselle	0.02*	0.3	
0631030	Rose	0.02*	0.3	
0631040	Jasmine	0.02*	0.3	
0631050	Lime/linden	0.02*	0.3	
0631990	Others	0.02*	0.3	
0632000	leaves and herbs	0.02*	0.3	
0632010	Strawberry	0.02*	0.3	
0632020	Rooibos	0.02*	0.3	
0632030	Mate/maté	0.02*	0.3	
0632990	Others	0.02*	0.3	
0633000	roots			
0633010	Valerian	7	7	No change necessary
0633020	Ginseng	0.02*	0.3 / 7	To be set at least to 0.3 mg/kg. Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details. However, in the draft regulation to be voted in June SCOPAFF a value of 7 is proposed for the group.
0633990	Others	0.02*	0.3 / 7	
0639000	any other parts of the plant	0.02*	0.3	Based on extrapolation from the rotational crop data for carrots and lettuce. Refer to section M-CA 6.6.2 for further details.
0640000	Cocoa beans	0.02*	0.02*	No use intended for the commodity
0650000	Carobs/Saint John's breads	0.02*	0.02*	No use intended for the commodity
0700000	HOPS	0.7	0.7	No use intended for the commodity
0800000	SPICES		0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0810000	Seed spices	0.02*	0.3	Based on extrapolation from the rotational crop data for lettuce. Refer to section M-CA 6.6.2 for further details.
0810010	Anise/aniseed	0.02*	0.3	
0810020	Black caraway/black cumin	0.02*	0.3	
0810030	Celery	0.02*	0.3	
0810040	Coriander	0.02*	0.3	
0810050	Cumin	0.02*	0.3	

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0810060	Dill	0.02*	0.3	
0810070	Fennel	0.02*	0.3	
0810080	Fenugreek	0.02*	0.3	
0810090	Nutmeg	0.02*	0.3	
0810990	Others	0.02*	0.3	
0820000	Fruit spices	0.02*	0.02*	No use intended for the commodity
0820010	Allspice/pimento	0.02*	0.02*	No use intended for the commodity
0820020	Sichuan pepper	0.02*	0.02*	No use intended for the commodity
0820030	Caraway	0.02*	0.02*	No use intended for the commodity
0820040	Cardamom	0.02*	0.02*	No use intended for the commodity
0820050	Juniper berry	0.02*	0.02*	No use intended for the commodity
0820060	Peppercorn (black, green and white)	0.02*	0.02*	No use intended for the commodity
0820070	Vanilla	0.02*	0.02*	No use intended for the commodity
0820080	Tamarind	0.02*	0.02*	No use intended for the commodity
0820990	Others	0.02*	0.02*	No use intended for the commodity
0830000	Bark spices	0.02*	0.02*	No use intended for the commodity
0830010	Cinnamon	0.02*	0.02*	No use intended for the commodity
0830990	Others	0.02*	0.02*	No use intended for the commodity
0840000	Root and rhizome spices	0.02*	0.3	Based on extrapolation from the rotational crop data for carrot. Refer to section M-CA 6.6.2 for further details
0840010	Liquorice	0.02*	0.3	
0840020	Ginger	0.02*	0.3	
0840030	Turmeric/curcuma	0.02*	0.3	
0840040	Horseradish	-	0.3	
0840990	Others	0.02*	0.3	
0850000	Bud spices	0.02*	0.3	
0850010	Cloves	0.02*	0.3	
0850020	Capers	0.02*	0.3	
0850990	Others	0.02*	0.3	
0860000	Flower pistil spices	0.02*	0.3	Based on extrapolation from the rotational crop data for lettuce. Refer to section M-CA 6.6.2 for further details.
0860010	Saffron	0.02*	0.3	
0860990	Others	0.02*	0.3	
0870000	Aril spices	0.02*	0.3	
0870010	Mace	0.02*	0.3	
0870990	Others	0.02*	0.3	

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
0900000	SUGAR PLANTS			
0900010	Sugar beet roots	0.15	0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0900020	Sugar canes	0.01*	0.3	Based on extrapolation from the rotational crop data for leeks. Refer to section M-CA 6.6.2 for further details.
0900030	Chicory roots	0.01*	0.3	Based on extrapolation from the rotational crop data for carrots. Refer to section M-CA 6.6.2 for further details.
0900990	Others	0.01*	0.3	
1000000	PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS			
1010000	Commodities from	0.01*	0.01*	**
1011000	swine	0.01*	0.01*	**
1011010	Muscle	0.01*	0.01*	**
1011020	Fat	0.01*	0.01*	**
1011030	Liver	0.01*	0.01*	**
1011040	Kidney	0.01*	0.01*	**
1011050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1011990	Others	0.01*	0.01*	**
1012000	bovine	0.01*	0.01*	**
1012010	Muscle	0.01*	0.01*	**
1012020	Fat	0.01*	0.01*	**
1012030	Liver	0.01*	0.01*	**
1012040	Kidney	0.01*	0.01*	**
1012050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1012990	Others	0.01*	0.01*	**
1013000	sheep	0.01*	0.01*	**
1013010	Muscle	0.01*	0.01*	**
1013020	Fat	0.01*	0.01*	**
1013030	Liver	0.01*	0.01*	**
1013040	Kidney	0.01*	0.01*	**
1013050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1013990	Others	0.01*	0.01*	**

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
1014000	goat	0.01*	0.01*	**
1014010	Muscle	0.01*	0.01*	**
1014020	Fat	0.01*	0.01*	**
1014030	Liver	0.01*	0.01*	**
1014040	Kidney	0.01*	0.01*	**
1014050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1014990	Others	0.01*	0.01*	**
1015000	equine	0.01*	0.01*	**
1015010	Muscle	0.01*	0.01*	**
1015020	Fat	0.01*	0.01*	**
1015030	Liver	0.01*	0.01*	**
1015040	Kidney	0.01*	0.01*	**
1015050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1015990	Others	0.01*	0.01*	**
1016000	poultry	0.01*	0.01*	**
1016010	Muscle	0.01*	0.01*	**
1016020	Fat	0.01*	0.01*	**
1016030	Liver	0.01*	0.01*	**
1016040	Kidney	0.01*	0.01*	**
1016050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1016990	Others	0.01*	0.01*	**
1017000	other farmed terrestrial animals	0.01*	0.01*	**
1017010	Muscle	0.01*	0.01*	**
1017020	Fat	0.01*	0.01*	**
1017030	Liver	0.01*	0.01*	**
1017040	Kidney	0.01*	0.01*	**
1017050	Edible offals (other than liver and kidney)	0.01*	0.01*	**
1017990	Others	0.01*	0.01*	**

Code	Commodity	Current MRLs (mg/kg)	Proposed MRLs (mg/kg)	Justification for proposed MRLs
1020000	Milk	0.02	0.02	**
1020010	Cattle	0.02	0.02	**
1020020	Sheep	0.02	0.02	**
1020030	Goat	0.02	0.02	**
1020040	Horse	0.02	0.02	**
1020990	Others	0.02	0.02	**
1030000	Birds eggs	0.01*	0.01*	**
1030010	Chicken	0.01*	0.01*	**
1030020	Duck	0.01*	0.01*	**
1030030	Geese	0.01*	0.01*	**
1030040	Quail	0.01*	0.01*	**
1030990	Others	0.01*	0.01*	**
1040000	Honey and other apiculture products	0.05*	0.05*	No change necessary – current MRL supported by data from the honey residue study. Refer to section CA 6.10.1 for further details.
1050000	Amphibians and Reptiles	0.01*	0.01*	
1060000	Terrestrial invertebrate animals	0.01*	0.01*	**
1070000	Wild terrestrial vertebrate animals	0.01*	0.01*	**

** Livestock feeding studies are currently on-going – updates to the proposed MRLs for livestock commodities will be made once the data from these studies is available.

The EU MRLs listed within the 'Current MRLs' column are aligned with those set within Commission Regulation (EU) No. 2018/832, these MRLs were enforced at the time this document was prepared. The Article 12 MRL review report for fluopicolide (EFSA Journal 2019;17(7):5748) was published during July 2019, and recommends new MRLs for a number of commodities – where necessary, these changes are also noted in the table.

CA 6.7.3 Proposed maximum residue levels (MRLs) and justification of the acceptability of the levels proposed for imported products (import tolerance)

MRLs based on imported products into the EU (import tolerances) are not proposed within this dossier, as the setting of import tolerances has not been requested by the applicant (previously, or as part of this renewal dossier).

CA 6.8 Proposed safety intervals

Pre-harvest interval (in days) for each relevant crop

Pre-harvest intervals for each crop were determined based on good agricultural practices (GAPs) recommended for biological control of pests on the proposed label, and have been used in the field residue trials supporting MRLs on crop commodities. A list of proposed PHIs for the crops in this submission is presented in Table 6.8-1 (these PHIs are established based on the representative renewal GAPs included within Document D1).

Table 6.8-1 Summary of pre-harvest intervals (PHIs)

Representative crop	Pre-harvest interval – PHI (days)
Potato	7
Lettuce	7
Cucumber	1
Oilseed rape	Not applicable for commodities which have been seed treated

Re-entry period (in days) for livestock, to areas to be grazed

Of the representative crops included within this submission, none of the commodities are typically grazed (*in situ*) by livestock animals.

Re-entry period (in hours or days) for man to crops, buildings or spaces treated

Under the practical conditions of use, there is no reason for workers to enter the crop shortly after treatment. The general approach of avoiding re-entry until the spray solution has dried is recommended, for the representative SC formulation. No restriction is required for the representative FS seed treatment product, due to the nature of the application mode.

Withholding period (in days) for animal feedingstuffs

For potatoes, a specific withholding period is not required for livestock – only the PHI of 7 days should be observed. As fluopicolide is applied to oilseed rape as a seed treatment, a withholding period is not necessary as the raw agricultural commodity is not consumed by livestock. For other livestock feed items (including potatoes), the dietary burden takes into account the residues incurred according to GAP and therefore no additional withholding periods are required.

Waiting period (in days) between last application and sowing or planting the crops to be protected

Not applicable. Fluopicolide is applied as a post-emergence treatment for the potatoes, cucumbers and lettuce uses. Not applicable for the seed-treated oilseed rape use, due to the nature of this application mode.

Waiting period (in days) between application and handling treated product

The general approach of avoiding handling until the spray solution has dried is recommended.

Waiting period (in days) between last application and sowing or planting succeeding crops

No specific plant-back restriction is required following the proposed uses of fluopicolide, based on the data contained within section 6.6.2. The consumer risk assessment takes into account the most critical residue levels incurred within succeeding crops and therefore no additional withholding periods are required.

CA 6.9 Estimation of the potential and actual exposure through diet and other sources

The ADI and ARfD for fluopicolide and M-01 are summarised in the table below - these toxicological endpoints are used in the dietary exposure calculations:

Dietary reference values for fluopicolide and M-01 using in the PRIMo model input

End Point	Value	Study	Safety factor	Comments
Fluopicolide				
Acceptable Daily Intake (ADI)	0.08 mg/kg bw/day	78-week dietary study in mice, supported by the 2-year dietary study in rats	100	EFSA Scientific Report (2009) 299
Acute Reference Dose (ARfD)	Not required – refer to document N1, section 6.3			
Metabolite M-01				
Acceptable Daily Intake (ADI)	0.05 mg/kg bw/day	Long term (two-year) rat and dog studies	100	EFSA Scientific Report (2009) 299
Acute Reference Dose (ARfD)	0.3 mg/kg bw	Developmental toxicity study in rabbits	100	EFSA Scientific Report (2009) 299

TMDI calculation

The TMDI was estimated using the EFSA PRIMo 3.1. The calculation of the TMDI was performed assuming that all food crops contained residues at the proposed MRLs (the values specified in Table 6.7.2- 1) for fluopicolide.

MRLs are not set for M-01, as it is not considered to be a suitable marker compound (as it is a common metabolite of other active substances used as plant protection products). As such, a TMDI calculation for M-01 has not been undertaken.

The summary output of the calculations for fluopicolide are presented in Appendix 3.

PRIMo version 3.1

The TMDI calculations for fluopicolide indicated no exceedances of any of the ADI for any of the consumer diets included within PRIMo version 3.1.

The highest calculated TMDI is for NL toddler with an estimated TMDI of 26% of ADI. The highest contributor to NL toddler diet is spinach with 5% of ADI. All other diets were <26%, indicating no chronic risk to consumers, using the proposed MRLs as worst-case values in the calculation

The results of the PRIMo calculations indicate that there is no unacceptable chronic risk to human health from the consumption of commodities treated with fluopicolide according to the representative intended uses/GAPs.

NEDI calculation

For fluopicolide, the diet with the highest intake was NL Toddler, with an intake of 6% of the ADI. The highest contributor to the NL toddler diet was milk (1% of the ADI).

For M-01, the diet with the highest intake was NL Toddler, with an intake of 5% of the ADI. The highest contributor to the NL toddler diet was milk (2% of the ADI).

The results indicate that there is no unacceptable chronic risk to human health from the consumption of commodities treated with fluopicolide according to the representative intended uses/GAPs.

NESTI calculation / Acute dietary exposure

For fluopicolide, an ARfD is not required, so an acute consumer risk assessment is not needed.

For M-01, the commodity with the highest %ARfD is melons (4% of the ARfD) for children, and Escaroles (2% of the ARfD) for adults. All other commodities have a %ARfD less than these values for the respective child / adult consumer groups.

The results indicate that there is no unacceptable acute risk to human health from the consumption of commodities treated with fluopicolide according to the representative intended uses/GAPs.

Drinking water assessment

Drinking water assessments were required for M-01, M-05 and M-10, as the as the calculated / observed maximum annual leachate concentrations exceeded 0.75 µg/L. Based on the levels of the metabolites expected within drinking water, none of the calculated consumer intakes exceeded the respective ADIs established for these metabolites.

Table 6.9- 01 Consumer intakes of M-01, M-05 and M-10, via drinking water

Consumer group	Drinking water intakes expressed as % of the respective ADIs		
	M-01 (ADI = 0.05 mg/kg bw/day)	**M-05** (ADI = 0.076 mg/kg bw/day)	**M-10** (ADI = 1.7 mg/kg bw/day)
Adult (body weight = 70 kg, assumed to drink 2 L of water per day)	0.399%	0.034%	0.003%
Adult (body weight = 60 kg, assumed to drink 2 L of water per day)	0.465%	0.040%	0.003%
Child (body weight = 12 kg, assumed to drink 1 L of water per day)	1.163%	0.099%	0.009%
Child (body weight = 10 kg, assumed to drink 1 L of water per day)	1.396%	0.119%	0.010%
Infant (body weight = 5 kg, assumed to drink 0.75 L of water per day)	2.094%	0.178%	0.015%

The intakes were far below 100% of the ADIs, which showed a significant margin of safety and demonstrates that there is no significant risk for consumers. The results of these calculations are presented within Document N5.

Stereogenic metabolites

It is noted that metabolite M-05 possesses a stereogenic sulfur atom (within the sulfoxide moiety), consequently this metabolite can potentially exist in two isomeric forms. An assessment of the impact of the stereogenic nature of this metabolite was therefore considered with respect to consumer safety. A consumer risk assessment took into consideration potential M-05 intakes via food and drinking water, which showed that there was a wide margin of safety (the combined exposures were far less than 100% of the ADI for M-05). A summary of this assessment is contained within Document N4 and full details of the assessment for M-05 are contained within a supplementary document ([redacted] 2020; M-687285-02-1).

Data Point:	KCA 6.9/01
Report Author:	[redacted]
Report Year:	2020
Report Title:	Fluopicolide - Statement on potential for formation of stereogenic elements: M-05 (AE 1344122)
Report No:	VC/19/038A
Document No:	M-687285-02-1
Guideline(s) followed in study:	None
Deviations from current test guideline:	Not applicable
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	not applicable
Acceptability/Reliability:	Yes

Summary

The fungicide fluopicolide does not contain any stereogenic centres. The sulfonylation of M-02 (AE C657188, PCA) within soil and plants, results in the formation of M-05 (AE 1344122) which possesses a chiral center at the sulfur atom of the sulfoxide moiety, which could exist as a pair of enantiomers.

The metabolite M-05 is found within succeeding crops at very low levels at each of the three representative plant back intervals (refer to section CA 6.6.2). Residues within the tested crops were generally <0.01 mg/kg, with the exception of barley grains, corn kernels, pea pods, dry peas, and leeks, where positive residues of M-05 were observed (though the highest residue levels did not exceed 0.04 mg/kg for M-05 within these commodities). Nonetheless, the observation of positive residues necessitated a consumer dietary intake calculation to be conducted for M-05.

Dietary intake calculations for consumers using the EFSA PRIMo version 3.1 calculator (with a derived ADI value of 0.076 mg/kg bw/day for M-05) show that the potential intake by consumers is low (<3% of the ADI) and there are no expected chronic or acute effects expected for consumers as a result of exposure to M-05 at these low levels. Intakes of M-05 associated with the consumption of drinking water are also very low (<1% of the ADI), and do not reveal a potential risk to consumers when compared with the ADI. As the combined drinking water and dietary intakes expected for consumers is far below 100%, it is considered that there is a wide safety margin for consumers.

Given these results, the presence of two stereogenic forms of M-05 is not expected to impact the risk assessment for fluopicolide. Further details are contained within the supplementary document.

Assessment and conclusion by applicant:

The reasoned case is considered to be acceptable.

CA 6.10 Other studies

CA 6.10.1 Effect on the residue level in pollen and bee products

A new study ([redacted] 2020; M-681610-01-1) has been generated to address the data requirement to consider residues within honey (for the purposes of MRL setting), as outlined within the current EU guidance: SANTE/11956/2016 rev. 9. A summary of this study is included later within this section.

In the study, *phacelia tanacetifolia* plants were treated at an exaggerated rate (4 x 100 g a.s. /ha) compared to the critical GAP rates which are intended for the uses on the representative crops sought for the fluopicolide renewal (total max. 400 g FLC / ha (per crop), refer to document IO1 of this dossier), yet the levels of fluopicolide and M-01 are very low (<0.05 mg/kg for fluopicolide and <0.01 mg/kg). Following the decision logic located in Appendix J of SANTE/11956/2016 rev. 9, an MRL of 0.02 mg/kg for fluopicolide in honey can be calculated using the OECD MRL calculator (it should however be noted that there is a high level of uncertainty in the calculated MRL due to the small size of the dataset and the censoring of the three values which were <LOQ). For M-01, no further consideration is deemed necessary, as the residue levels for this metabolite in the produced honey for all four trials were <LOQ (<0.01 mg/kg).

Fluopicolide is only registered for use within the EU as a plant protection product. The compound does not have a role in veterinary medicines and is not present within any registered biocidal products, and consequently no specific MRLs are set for fluopicolide within these respective regulatory frameworks. The EU MRL for fluopicolide within honey should therefore be based solely on the available data for fluopicolide applied as a plant protection product.

On this basis of the available information, it is not considered to be necessary to amend the currently established EU MRL for fluopicolide in honey from the default value of 0.05 mg/kg.

Data Point:	KCA 6.10.1/01
Report Author:	[redacted]
Report Year:	2020
Report Title:	Determination of residues of BCS-CS55621 (FXN) and fluopicolide (FLC) in honey after four applications of FXN + FLC SC 230 in Phacelia tanacetifolia at 4 sites in Northern and Southern Europe in 2019
Report No:	S19-01063
Document No:	M-681610-01-1
Guideline(s) followed in study:	OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published in September 2009) EC (2018) Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey (SANTE/11956/2016 rev. 9) Commission Regulation (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009 (Oct. 2009)
Deviations from current test guideline:	None
Previous evaluation:	No, not previously submitted
GLP/Officially recognised testing facilities:	Yes, conducted under GLP/Officially recognised testing facilities
Acceptability/Reliability:	Yes

Executive Summary

A total of four residue semi-field trials were conducted in northern Europe (Germany) and southern Europe (Spain) on *phacelia tanacetifolia*, during 2019. Four applications of 'FXN + FLC SC 230' (a product containing 200 g/L of fluopicolide) were made at a target rate of 0.10 kg a.s. / ha.

For each site, two tunnels were established containing flowering *phacelia tanacetifolia*: one tunnel acted as a control (untreated) and in the second tunnel, the *phacelia tanacetifolia* were treated with 'FXN + FLC SC 230'. The beehives were introduced to the tunnels and the honeybees were allowed to forage the nectar from the *phacelia tanacetifolia* plants and produce mature honey.

Residue levels (fluopicolide, M-01) within the mature honey were quantified using analytical method 01592. The results show that the residue levels in honey were low. The highest fluopicolide residue in honey was 0.014 mg/kg (residues were not found above 0.01 mg/kg in the other three trials). For M-01, no residues above the LOQ (0.01 mg/kg) were found in honey obtained from any of the four treatment plots.

Residue data for fluoxapiprolin and its metabolites were also reported, but these results have not been included within this study summary, as they are not relevant to the EU renewal of fluopicolide.

I. MATERIALS AND METHODS

A. MATERIALS

1.	**Test Item:**	FXN + FLC SC 230 (nominal 200 g/L of fluopicolide)
	Batch no.:	2019-000969
	Active Ingredient / Purity:	202.9 g/L fluopicolide (analysed content)
	Storage:	Ambient (5 °C – 30 °C), dry and in the dark
	Expiry date:	April 2021
2.	**Test commodity:**	*Phacelia tanacetifolia*, honey produced from the nectar foraged from the treated plants
	Crop part:	Plant material was not analysed
	Product:	Honey (fresh and dried)

B. STUDY DESIGN AND METHODS

Field phase:

Four semi-field residue trials were conducted on *phacelia tanacetifolia* in the Northern European (Germany) and the Southern European (Spain) residue trials zones during 2019. Four applications of FLC + FXN SC 230 (containing 200 g /L fluopicolide) were made to the trials sites at rates of 0.1 kg a.s. / ha.

On each trial site, tunnels confining the honeybees (*Apis mellifera* L.) were established on the control and the treated plots. To conform to the data requirements outlined within SANTE/11956/2016 rev. 9, the following parameters were implemented into the trial design:

Table 6.10.1- 1 Plot details for the semi-field trials

	Trial No.			
	S19-01063-01	**S19-01063-02**	**S19-01063-03**	**S19-01063-04**
Distance between trial sites	>10 km	>10 km	>10 km	>10 km
Plot / tunnel size (width x length)	5 m x 40 m	5 m x 40 m	5 m x 40 m	5 m x 40 m
Closest distance between control and treated plots	>10 m	>10 m	>10 m	>10 m
Minimum distance to the edge of the field	>3 m	>3 m	>3 m	>3 m
Minimum Buffer zone to next use of competing chemistry	>10 m	>10 m	>10 m	>10 m
Treated area	~185 m^2	~185 m^2	~200 m^2	~200 m^2
Plants per hectare	15 kg/ha	15 kg/ha	10 kg/ha	10 kg/ha

One beehive was set-up per tunnel for the control and treated plots. Colony assessments were performed before the before the hives were set-up in the tunnels and after the sampling of the honey.

Honey was collected from initially empty combs which were introduced in the hive shortly before the 3rd application. Mature honey was collected once the lowering of the *phacelia* had ended or if the water content was <20% or after comb closure (whichever occurred first).

A summary of the application details is presented in the following table:

Table 6.10.1- 2 Application details

Applied product	Number of applications	Applied rate	Application interval	Growth stage at last treatment	DALA
FXN + FLC SC 230 *	4	0.10 kg a.s. / ha	Approx. 7 days	BBCH 65-67	8 / 9 days (German trials) 1 / 2 days (Spanish trials)

* Product contains fluopicolide (200 g/L)
DALA = Days after last application

The trials were conducted in the following locations:

Table 6.10.1- 3 Trial details and regions

Trial No.	Country	Location	Crop / variety
S19-01063-01	Germany	75177, Pforzheim, Baden-Württemberg	*Phacelia tanacetifolia* / Balo
S19-01063-02	Germany	76297, Stutensee, Baden-Württemberg	*Phacelia tanacetifolia* / Balo
S19-01063-03	Spain	02690, Alpera / Albacete	*Phacelia tanacetifolia* / Stala
S19-01063-03	Spain	46620, Ayora, Comunidad	*Phacelia tanacetifolia* / Stala

The product was applied onto the *phacelia tanacetifolia* using spray applicators.

Analytical method

Residues of fluopicolide and the metabolite M-01 were analysed within the samples according to the following method:

Table 6.10.1- 4 Summary of the analytical method

Method	01592
Extraction	Diluted with acetone/water (1/1, v/v)
Detection	HPLC-MS/MS
LOQ	0.01 mg/kg (for fluopicolide, M-01, in honey)

Full details and acceptable validation data to support this method are presented within document M-CA 4, which comply with the EU regulatory requirements outlined within SANCO/3029/99 rev 4.

In order to check the performance of the method, recovery determinations were included in each set of analysis. Control samples from the study were fortified and used as the recovery samples. All the recovery determinations were performed in parallel to the analyses of control and treated samples from the study.

Recoveries were not corrected for apparent residues in the control samples used for these recoveries.

Table 6.10.1- 5 Procedural recoveries for Fluopicolide

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Honey	0.01	111, 111, 109	110	1.0	0.01
	0.10	99, 101, 93	98	4.3	
		Overall recovery (n=6)	**104**	**7.2**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with fluopicolide, determined as fluopicolide and calculated as fluopicolide

Table 6.10.1- 6 Procedural recoveries for M-01 (AE C653711)

Sample matrix	Fortification level (mg/kg)	Recovery values (%)	Mean recovery value (%)	RSD (%)	LOQ (mg/kg)
Honey	0.01	107, 107, 104	106	1.6	0.01
	0.10	98, 97, 90	95	4.6	
		Overall recovery (n=6)	**101**	**6.7**	

RSD = Relative standard deviation, LOQ = Practical limit of quantification
Fortified with AE C653711, determined as AE C653711 and calculated as AE C653711

Storage stability:

The storage period of deep-frozen samples (at -18°C or below) for fluopicolide and the metabolite M-01 ranged between 52 and 93 days.

Acceptable storage stability data are available (presented within this document under point CA 6.1) which demonstrate the stability of fluopicolide and M-01 when stored in high water matrices (at -18°C or below) for up to 180 days. These available data are sufficient to support the storage period between sampling and extraction.

The storage stability study for honey also included an assessment of the stability of these compounds in the extracts over an 8-day period. The stability of fluopicolide and M-01 was acceptably demonstrated for this period, which covers the time between the extraction and the analysis in the analytical phase of this honey residue study.

II. RESULTS AND DISCUSSION

The residues field trials results provided within the study report are summarised within the following table.

While the applied test formulation also contained fluoxapiprolin, only residues values for fluopicolide and M-01 have been presented, as these are the only components which are relevant to the fluopicolide renewal.

Residues ≥0.01 mg/kg (LOQ) were not observed in the samples obtained from the control plots. Residues were found to be low in all of the samples obtained from the treated plots – in all but one case, residues were <0.01 mg/kg for fluopicolide and M-01. The highest residues observed was 0.014 mg/kg (for fluopicolide in the second trial conducted within Spain).

Table 6.10.1- 7 Residues of fluopicolide and M-01 in honey produced from the nectar of treated *phacelia tanacetifolia* plants

Trial No. Country	Growth stage at sampling*	DALT	Honey: fresh or dried	Residues (mg/kg)		Sugar content of honey (%)
				Fluopicolide	M-01	
S19-01063-01 Germany	68	9	Fresh	<0.01	<0.01	77.0
	68	9	Dried**	<0.01	<0.01	80.3
S19-01063-02 Germany	69	8	Fresh	<0.01	<0.01	80.0
S19-01063-03 Spain	65	1	Fresh	<0.01	<0.01	81.1
S19-01063-03 Spain	66	2	Fresh	0.014	<0.01	80.8

DALT = Days after last treatment
* Growth stage of phacelia at sampling
** Drying period = 3 days

III. CONCLUSION

Four independent residue trials have been conducted in Northern Europe (Germany) and Southern Europe (Spain), under semi-field conditions. For each site, two tunnels were established containing flowering *phacelia tanacetifolia*: one tunnel acted as a control (untreated) and in the second tunnel, the phacelia *tanacetifolia* were treated at a rate of 4 x 100 g a.s. / ha. The beehives were introduced to the tunnels and the honeybees were allowed to forage the nectar from the *phacelia tanacetifolia* plants and produce honey. Mature honey was sampled from the combs and residue levels were quantified using HPLC-MS/MS. The results of the trials are as follows:

Northern European trials	Southern European trials
Fluopicolide: 2 x <0.01 mg/kg	Fluopicolide: <0.01 and 0.014 mg/kg
Metabolite M-01: 2 x <0.01 mg/kg	Metabolite M-01: 2 x <0.01 mg/kg

No residues were detected above the LOQ for the honey produced from the control plots.

The trials were designed to conform to the requirements outlined within SANTE/11956/2016 rev. 9 (for the field phase) and with SANCO/3029/99 revision 4 (for the analytical phase).

Assessment and conclusion by applicant:

Residues of fluopicolide did not exceed 0.014 mg/kg within honey produced from the nectar of *phacelia tanacetifolia,* which had been treated with a fluopicolide containing product. Levels of BAM (M-01) were <0.01 mg/kg in all analysed honey samples.

APPENDIX 1 - Livestock dietary burden calculations

Farmed fish

The intakes for fish were calculated using the Fraunhofer Institute Dietary Burden Calculator 2.0.3. The input values are based on those used for other conventionally farmed livestock (refer to section CA 6.4). The input values for fluopicolide and M-01 are tabulated within Table 1A- 1 and Table 1A- 2 (respectively). The raw output from the calculations follows the input tables for each substance, representative fish species.

Table 1A- 1 Input values for commodities which form part of the fish diet, which contain residues of fluopicolide

Category	Crop	Commodity	Residue input value	Residue value (mg/kg)
By-Products	Brewer's grain	dried	STMR-P	0.93
By-Products	Canola meal	Solvent extracted	STMR-P	0.03
By-Products	Coconut/Copra	meal decorticated	STMR-P	0
By-Products	Corn	feed meal	STMR-P	0.01
By-Products	Corn	bran	STMR-P	0.01
By-Products	Corn	gluten feed	STMR-P	0.01
By-Products	Corn	gluten meal	STMR-P	0.01
By-Products	Corn	starch	STMR-P	0.01
By-Products	Corn	Distiller's dried grains with solubles	STMR-P	0.01
By-Products	Corn	Condensed distillers solubles	STMR-P	0.01
By-Products	Cottonseed	meal decorticated	STMR-P	0.03
By-Products	Linseed	meal, solv. extr.	STMR-P	0.03
By-Products	Lupin seed white	meal (treated)	STMR-P	0.03
By-Products	Mustard	Meal, solv. extr.	STMR-P	0.03
By-Products	Palm	kernel meal	STMR-P	0
By-Products	Peanut/ meal	meal decorticated	STMR-P	0
By-Products	Potato	protein	STMR-P	0.11
By-Products	Rice	polishings	STMR-P	0
By-Products	Rice	hulls	STMR-P	0
By-Products	Sesame seed	meal	STMR-P	0.03
By-Products	Safflower	Meal decorticated	STMR-P	0.03
By-Products	Soybean	Meal decorticated	STMR-P	0.03
By-Products	Sunflower	meal decorticated, solv. extr.	STMR-P	0.03
By-Products	Wheat	bran	STMR-P	0.93
By-Products	Wheat	flour	STMR-P	0.93
By-Products	Wheat	germ	STMR-P	0.93
By-Products	Wheat	middlings	STMR-P	0.93
By-Products	Wheat	gluten meal	STMR-P	0.93
Cereal Grains/ Crop Seeds	Cow pea	seed	STMR-P	0.01
Cereal Grains/ Crop Seeds	Faba bean	seed	STMR-P	0.01
Cereal Grains/ Crop Seeds	Lupin (white)	seed	STMR-P	0.01
Cereal Grains/ Crop Seeds	Pea	seed	STMR-P	0.01
Cereal Grains/ Crop Seeds	Lupin	seed, head processed	STMR-P	0.01
Cereal Grains/ Crop Seeds	Rice	Broken grains	STMR-P	0
Cereal Grains/ Crop Seeds	Wheat	Grain (extruded)	STMR-P	0.93
Fat	Vegetable oil	oil	STMR-P	0.03

Table 1A- 2 Input values for commodities which form part of the fish diet, which contain residues of M-01

Category	Crop	Commodity	Residue input value	Residue value (mg/kg)
By-Products	Brewer's grain	dried	STMR-P	0.02
By-Products	Canola meal	Solvent extracted	STMR-P	0.06
By-Products	Coconut/Copra	meal decorticated	STMR-P	
By-Products	Corn	feed meal	STMR-P	0.01
By-Products	Corn	bran	STMR-P	0.01
By-Products	Corn	gluten feed	STMR-P	0.01
By-Products	Corn	gluten meal	STMR-P	0.01
By-Products	Corn	starch	STMR-P	0.01
By-Products	Corn	Distiller's dried grains with solubles	STMR-P	0.01
By-Products	Corn	Condensed distillers solubles	STMR-P	0.01
By-Products	Cottonseed	meal decorticated	STMR-P	0.09
By-Products	Linseed	meal, solv. extr.	STMR-P	0.09
By-Products	Lupin seed white	meal (roated)	STMR-P	0.01
By-Products	Mustard	Meal, solv. extr.	STMR-P	0.09
By-Products	Palm	kernel meal	STMR-P	0
By-Products	Peanut meal	meal decorticated	STMR-P	0
By-Products	Potato	protein	STMR-P	0.02
By-Products	Rice	polishing	STMR-P	0
By-Products	Rice	hulls	STMR-P	0
By-Products	Sesame seed	meal	STMR-P	0
By-Products	Safflower	Meal decorticated	STMR-P	0.09
By-Products	Soybean	Meal decorticated	STMR-P	0.09
By-Products	Sunflower	meal decorticated, solv. extr.	STMR-P	0.09
By-Products	Wheat	bran	STMR-P	0.02
By-Products	Wheat	flour	STMR-P	0.02
By-Products	Wheat	germ	STMR-P	0.02
By-Products	Wheat	middlings	STMR-P	0.02
By-Products	Wheat	gluten meal	STMR-P	0.02
Cereal Grains/ Crop Seeds	Cow pea	seed	STMR	0.01
Cereal Grains/ Crop Seeds	Faba bean	seed	STMR	0.01
Cereal Grains/ Crop Seeds	Lupin (white)	seed	STMR	0.01
Cereal Grains/ Crop Seeds	Pea	seed	STMR	0.01
Cereal Grains/ Crop Seeds	Lupin	seed, head processed	STMR	0.01
Cereal Grains/ Crop Seeds	Rice	Broken grains	STMR	0
Cereal Grains/ Crop Seeds	Wheat	Grain (extruded)	STMR	0.02
Fat	Vegetable oil	oil	STMR-P	0.09

Fluopicolide – 0.726 mg/kg common carp

Dietary Burden Calculation concerning New Substance

DietaryBurdenCalculator 2.0.3

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

INPUT
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Target content for Common carp:

Crude fat	10.00%
Crude protein	35.00%

Maximum principal content of components in the diet:

Brewer's grain (dried)	15.00%
Canola meal (Solvent extracted)	10.00%
Corn (feed meal)	35.00%
Corn (bran)	20.00%
Corn (gluten feed)	20.00%
Corn (gluten meal)	20.00%
Corn (starch)	35.00%
Corn (Distiller's dried grains with solubles)	35.00%
Corn (Condensed distillers solubles)	10.00%
Cottonseed (meal decorticated)	15.00%
Linseed (meal, solv. extr.)	7.00%
Lupin seed white (meal (treated))	15.00%
Mustard (Meal, solv. extr.)	10.00%
Potato (protein)	3.00%
Sesame seed (meal)	20.00%
Safflower (Meal decorticated)	7.00%
Soybean (Meal decorticated)	30.00%
Sunflower (meal decorticated, solv. extr.)	20.00%
Wheat (bran)	5.00%
Wheat (flour)	15.00%
Wheat (germ)	5.00%
Wheat (middlings)	20.00%
Wheat (gluten meal)	5.00%
Cow pea (seed)	15.00%
Faba bean (seed)	15.00%
Lupin (white) (seed)	15.00%
Pea (seed)	15.00%
Lupin (seed, head processed)	9.00%
Wheat (Grain (extruded))	15.00%
Vegetable oil (oil)	10.00%
Fish meal(PC)	100.00%
Starch(CC)	100.00%
Oil(F)	100.00%

Percent dry matter of components:

Brewer's grain (dried)	92.0%
Canola meal (Solvent extracted)	91.0%
Corn (feed meal)	87.8%
Corn (bran)	87.5%
Corn (gluten feed)	90.1%
Corn (gluten meal)	91.3%
Corn (starch)	90.2%
Corn (Distiller's dried grains with solubles)	90.8%
Corn (Condensed distillers solubles)	90.6%
Cottonseed (meal decorticated)	90.8%
Linseed (meal, solv. extr.)	90.0%
Lupin seed white (meal (treated))	89.5%
Mustard (Meal, solv. extr.)	89.9%
Potato (protein)	89.4%
Sesame seed (meal)	92.4%
Safflower (Meal decorticated)	91.0%
Soybean (Meal decorticated)	89.5%
Sunflower (meal decorticated, solv. extr.)	92.6%
Wheat (bran)	88.7%
Wheat (flour)	88.0%
Wheat (germ)	88.7%
Wheat (middlings)	89.4%
Wheat (gluten meal)	91.4%
Cow pea (seed)	88.0%
Faba bean (seed)	88.0%
Lupin (white) (seed)	88.0%
Pea (seed)	90.0%
Lupin (seed, head processed)	88.0%
Wheat (Grain (extruded))	87.7%
Vegetable oil (oil)	-

New Substance residues in the components:

Brewer's grain (dried) (STMR-P)	0.930 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.030 mg/kg
Corn (feed meal) (STMR-P)	0.010 mg/kg
Corn (bran) (STMR-P)	0.010 mg/kg
Corn (gluten feed) (STMR-P)	0.010 mg/kg
Corn (gluten meal) (STMR-P)	0.010 mg/kg
Corn (starch) (STMR-P)	0.010 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.010 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.010 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.030 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.030 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.030 mg/kg

Mustard (Meal, solv. extr.) (STMR-P)	0.030 mg/kg
Potato (protein) (STMR-P)	0.110 mg/kg
Sesame seed (meal) (STMR-P)	0.030 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.030 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.030 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.030 mg/kg
Wheat (bran) (STMR-P)	0.930 mg/kg
Wheat (flour) (STMR-P)	0.930 mg/kg
Wheat (germ) (STMR-P)	0.930 mg/kg
Wheat (middlings) (STMR-P)	0.930 mg/kg
Wheat (gluten meal) (STMR-P)	0.930 mg/kg
Cow pea (seed) (STMR-P)	0.010 mg/kg
Faba bean (seed) (STMR-P)	0.010 mg/kg
Lupin (white) (seed) (STMR-P)	0.010 mg/kg
Pea (seed) (STMR-P)	0.010 mg/kg
Lupin (seed, head processed) (STMR-P)	0.010 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.930 mg/kg
Vegetable oil (oil) (STMR-P)	0.030 mg/kg

New Substance residues in the components (dry matter):

Brewer's grain (dried) (STMR-P)	1.011 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.033 mg/kg
Corn (feed meal) (STMR-P)	0.011 mg/kg
Corn (bran) (STMR-P)	0.011 mg/kg
Corn (gluten feed) (STMR-P)	0.011 mg/kg
Corn (gluten meal) (STMR-P)	0.011 mg/kg
Corn (starch) (STMR-P)	0.011 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.011 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.011 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.033 mg/kg

Linseed (meal, solv. extr.) (STMR-P)	0.033 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.034 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.033 mg/kg
Potato (protein) (STMR-P)	0.123 mg/kg
Sesame seed (meal) (STMR-P)	0.032 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.033 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.034 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.032 mg/kg
Wheat (bran) (STMR-P)	1.048 mg/kg
Wheat (flour) (STMR-P)	1.057 mg/kg
Wheat (germ) (STMR-P)	1.048 mg/kg
Wheat (middlings) (STMR-P)	1.040 mg/kg
Wheat (gluten meal) (STMR-P)	1.018 mg/kg
Cow pea (seed) (STMR-P)	0.011 mg/kg
Faba bean (seed) (STMR-P)	0.011 mg/kg
Lupin (white) (seed) (STMR-P)	0.011 mg/kg
Pea (seed) (STMR-P)	0.011 mg/kg
Lupin (seed, head processed) (STMR-P)	0.011 mg/kg
Wheat (grain (extruded)) (STMR-P)	1.060 mg/kg
Vegetable oil (oil) (STMR-P)	0.030 mg/kg

RESULTS
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Maximum dietary burden based on New Substance is 0.726 mg/kg (dry matter).

The respective composition of the feed is:

Brewer's grain (dried)	15.00%
Canola meal (Solvent extracted)	0.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	0.00%
Linseed (meal, solv. extr.)	0.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	0.00%
Potato (protein)	3.00%
Sesame seed (meal)	0.00%
Safflower (Meal decorticated)	0.00%
Soybean (Meal decorticated)	0.00%
Sunflower (meal decorticated, solv. extr.)	0.00%
Wheat (bran)	5.00%
Wheat (flour)	15.00%
Wheat (germ)	5.00%
Wheat (middlings)	20.00%
Wheat (gluten meal)	5.00%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	4.42%
Vegetable oil (oil)	5.81%
Fish meal(PC)	21.77%
Starch(CC)	0.00%
Oil(F)	0.00%

The dietary load of New Substance caused by the individual components is:

Brewer's grain (dried)	20.88%
Canola meal (Solvent extracted)	0.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	0.00%
Linseed (meal, solv. extr.)	0.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	0.00%
Potato (protein)	0.51%
Sesame seed (meal)	0.00%
Safflower (Meal decorticated)	0.00%
Soybean (Meal decorticated)	0.00%

Sunflower (meal decorticated, solv. extr.)	0.00%
Wheat (bran)	7.22%
Wheat (flour)	21.83%
Wheat (germ)	7.22%
Wheat (middlings)	28.65%
Wheat (gluten meal)	7.01%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	6.45%
Vegetable oil (oil)	0.24%
Fish meal(PC)	0.00%
Starch(CC)	0.00%

Oil(F) 0.00%

Fluopicolide – 0.483 mg/kg rainbow trout

Dietary Burden Calculation concerning New Substance

DietaryBurdenCalculator 2.0.3

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

INPUT

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Target content for Rainbow trout:

Crude fat	15.00%
Crude protein	42.00%

Maximum principal content of components in the diet:

Brewer's grain (dried)	10.00%
Canola meal (Solvent extracted)	8.00%
Corn (feed meal)	20.00%
Corn (bran)	5.00%
Corn (gluten feed)	10.00%
Corn (gluten meal)	15.00%
Corn (starch)	15.00%
Corn (Distiller's dried grains with solubles)	10.00%
Corn (Condensed distillers solubles)	3.00%
Cottonseed (meal decorticated)	5.00%
Linseed (meal, solv. extr.)	5.00%
Lupin seed white (meal (treated))	9.00%
Mustard (Meal, solv. extr.)	5.00%
Potato (protein)	2.00%
Sesame seed (meal)	10.00%
Safflower (Meal decorticated)	5.00%
Soybean (Meal decorticated)	15.00%
Sunflower (meal decorticated, solv. extr.)	10.00%
Wheat (bran)	2.00%
Wheat (flour)	10.00%

Wheat (germ)	2.00%
Wheat (middlings)	10.00%
Wheat (gluten meal)	2.00%
Cow pea (seed)	15.00%
Faba bean (seed)	15.00%
Lupin (white) (seed)	15.00%
Pea (seed)	15.00%
Lupin (seed, head processed)	3.00%
Wheat (Grain (extruded))	10.00%
Vegetable oil (oil)	15.00%
Fish meal(PC)	100.00%
Starch(CC)	100.00%
Oil(F)	100.00%

Percent dry matter of components:

Brewer's grain (dried)	92.0%
Canola meal (Solvent extracted)	91.0%
Corn (feed meal)	87.8%
Corn (bran)	87.5%
Corn (gluten feed)	90.1%
Corn (gluten meal)	91.3%
Corn (starch)	90.2%
Corn (Distiller's dried grains with solubles)	90.8%
Corn (Condensed distillers solubles)	90.6%
Cottonseed (meal decorticated)	90.8%
Linseed (meal, solv. extr.)	90.0%
Lupin seed white (meal (treated))	89.5%
Mustard (Meal, solv. extr.)	89.9%
Potato (protein)	89.4%
Sesame seed (meal)	92.4%
Safflower (Meal decorticated)	91.0%
Soybean (Meal decorticated)	89.5%
Sunflower (meal decorticated, solv. extr.)	92.6%
Wheat (bran)	88.7%
Wheat (flour)	88.0%
Wheat (germ)	88.7%
Wheat (middlings)	89.4%
Wheat (gluten meal)	91.4%
Cow pea (seed)	88.0%
Faba bean (seed)	88.0%
Lupin (white) (seed)	88.0%
Pea (seed)	90.0%
Lupin (seed, head processed)	88.0%
Wheat (Grain (extruded))	87.7%
Vegetable oil (oil)	-

New Substance residues in the components:

Brewer's grain (dried) (STMR-P)	0.930 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.030 mg/kg
Corn (feed meal) (STMR-P)	0.010 mg/kg
Corn (bran) (STMR-P)	0.010 mg/kg
Corn (gluten feed) (STMR-P)	0.010 mg/kg

Corn (gluten meal) (STMR-P)	0.010 mg/kg
Corn (starch) (STMR-P)	0.010 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.010 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.010 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.030 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.030 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.030 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.030 mg/kg
Potato (protein) (STMR-P)	0.110 mg/kg
Sesame seed (meal) (STMR-P)	0.030 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.030 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.030 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.030 mg/kg
Wheat (bran) (STMR-P)	0.930 mg/kg
Wheat (flour) (STMR-P)	0.930 mg/kg
Wheat (germ) (STMR-P)	0.930 mg/kg
Wheat (middlings) (STMR-P)	0.930 mg/kg
Wheat (gluten meal) (STMR-P)	0.930 mg/kg
Cow pea (seed) (STMR-P)	0.010 mg/kg
Faba bean (seed) (STMR-P)	0.010 mg/kg
Lupin (white) (seed) (STMR-P)	0.010 mg/kg
Pea (seed) (STMR-P)	0.010 mg/kg
Lupin (seed, head processed) (STMR-P)	0.010 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.930 mg/kg
Vegetable oil (oil) (STMR-P)	0.030 mg/kg

New Substance residues in the components (dry matter):

Brewer's grain (dried) (STMR-P)	1.011 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.033 mg/kg
Corn (feed meal) (STMR-P)	0.011 mg/kg

Corn (bran) (STMR-P)	0.011 mg/kg
Corn (gluten feed) (STMR-P)	0.011 mg/kg
Corn (gluten meal) (STMR-P)	0.011 mg/kg
Corn (starch) (STMR-P)	0.011 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.011 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.011 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.033 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.033 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.034 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.033 mg/kg
Potato (protein) (STMR-P)	0.123 mg/kg
Sesame seed (meal) (STMR-P)	0.032 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.033 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.034 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.032 mg/kg
Wheat (bran) (STMR-P)	1.048 mg/kg
Wheat (flour) (STMR-P)	1.057 mg/kg
Wheat (germ) (STMR-P)	1.048 mg/kg
Wheat (middlings) (STMR-P)	1.040 mg/kg
Wheat (gluten meal) (STMR-P)	1.018 mg/kg
Cow pea (seed) (STMR-P)	0.011 mg/kg
Faba bean (seed) (STMR-P)	0.011 mg/kg
Lupin (white) (seed) (STMR-P)	0.011 mg/kg
Pea (seed) (STMR-P)	0.011 mg/kg
Lupin (seed, head processed) (STMR-P)	0.011 mg/kg
Wheat (Grain (extruded)) (STMR-P)	1.060 mg/kg
Vegetable oil (oil) (STMR-P)	0.030 mg/kg

RESULTS
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Maximum dietary burden based on New Substance is 0.483 mg/kg (dry matter).

The respective composition of the feed is:

Brewer's grain (dried)	10.00%
Canola meal (Solvent extracted)	0.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	0.00%
Linseed (meal, solv. extr.)	0.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	0.00%
Potato (protein)	2.00%
Sesame seed (meal)	0.00%
Safflower (Meal decorticated)	0.00%
Soybean (Meal decorticated)	0.00%
Sunflower (meal decorticated, solv. extr.)	0.00%
Wheat (bran)	2.00%
Wheat (flour)	10.00%
Wheat (germ)	2.00%
Wheat (middlings)	10.00%
Wheat (gluten meal)	2.00%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	9.77%
Vegetable oil (oil)	11.09%
Fish meal(PC)	41.13%
Starch(CC)	0.00%
Oil(F)	0.00%

The dietary load of New Substance caused by the individual components is:

Brewer's grain (dried)	20.95%
Canola meal (Solvent extracted)	0.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	0.00%
Linseed (meal, solv. extr.)	0.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	0.00%
Potato (protein)	0.51%
Sesame seed (meal)	0.00%
Safflower (Meal decorticated)	0.00%
Soybean (Meal decorticated)	0.00%

Sunflower (meal decorticated, solv. extr.)	0.00%
Wheat (bran)	4.35%
Wheat (flour)	21.90%
Wheat (germ)	4.35%
Wheat (middlings)	21.56%
Wheat (gluten meal)	4.22%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	21.48%
Vegetable oil (oil)	0.69%
Fish meal(PC)	0.00%
Starch(CC)	0.00%
Oil(F)	0.00%

M-01 – common carp 0.089 mg/kg

Dietary Burden Calculation concerning New Substance

DietaryBurdenCalculator 2.0.3

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

INPUT

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Target content for Common carp:

Crude fat	10.00%
Crude protein	35.00%

Maximum principal content of components in the diet:

Brewer's grain (dried)	15.00%
Canola meal (Solvent extracted)	10.00%
Corn (feed meal)	35.00%
Corn (bran)	20.00%
Corn (gluten feed)	20.00%
Corn (gluten meal)	20.00%
Corn (starch)	35.00%
Corn (Distiller's dried grains with solubles)	35.00%
Corn (Condensed distillers solubles)	10.00%
Cottonseed (meal decorticated)	15.00%
Linseed (meal, solv. extr.)	7.00%
Lupin seed white (meal (treated))	15.00%
Mustard (Meal, solv. extr.)	10.00%
Potato (protein)	3.00%
Safflower (Meal decorticated)	7.00%
Soybean (Meal decorticated)	30.00%
Sunflower (meal decorticated, solv. extr.)	20.00%
Wheat (bran)	5.00%
Wheat (flour)	15.00%
Wheat (germ)	5.00%
Wheat (middlings)	20.00%

Wheat (gluten meal)	5.00%
Cow pea (seed)	15.00%
Faba bean (seed)	15.00%
Lupin (white) (seed)	15.00%
Pea (seed)	15.00%
Lupin (seed, head processed)	9.00%
Wheat (Grain (extruded))	15.00%
Vegetable oil (oil)	10.00%
Fish meal(PC)	100.00%
Starch(CC)	100.00%
Oil(F)	100.00%

Percent dry matter of components:

Brewer's grain (dried)	92.0%
Canola meal (Solvent extracted)	91.0%
Corn (feed meal)	87.8%
Corn (bran)	87.5%
Corn (gluten feed)	90.1%
Corn (gluten meal)	91.3%
Corn (starch)	90.2%
Corn (Distiller's dried grains with solubles)	90.8%
Corn (Condensed distillers solubles)	90.6%
Cottonseed (meal decorticated)	90.8%
Linseed (meal, solv. extr.)	90.0%
Lupin seed white (meal (treated))	89.5%
Mustard (Meal, solv. extr.)	89.9%
Potato (protein)	89.4%
Safflower (Meal decorticated)	91.0%
Soybean (Meal decorticated)	89.5%
Sunflower (meal decorticated, solv. extr.)	92.6%
Wheat (bran)	88.7%
Wheat (flour)	88.0%
Wheat (germ)	88.7%
Wheat (middlings)	89.4%
Wheat (gluten meal)	91.4%
Cow pea (seed)	88.0%
Faba bean (seed)	88.0%
Lupin (white) (seed)	88.0%
Pea (seed)	90.0%
Lupin (seed, head processed)	88.0%
Wheat (Grain (extruded))	87.7%
Vegetable oil (oil)	-

New Substance residues in the components:

Brewer's grain (dried) (STMR-P)	0.020 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.090 mg/kg
Corn (feed meal) (STMR-P)	0.010 mg/kg
Corn (bran) (STMR-P)	0.010 mg/kg
Corn (gluten feed) (STMR-P)	0.010 mg/kg
Corn (gluten meal) (STMR-P)	0.010 mg/kg
Corn (starch) (STMR-P)	0.010 mg/kg

Corn (Distiller's dried grains with solubles) (STMR-P)	0.010 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.010 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.090 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.090 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.010 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.090 mg/kg
Potato (protein) (STMR-P)	0.020 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.090 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.090 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.090 mg/kg
Wheat (bran) (STMR-P)	0.020 mg/kg
Wheat (flour) (STMR-P)	0.020 mg/kg
Wheat (germ) (STMR-P)	0.020 mg/kg
Wheat (middlings) (STMR-P)	0.020 mg/kg
Wheat (gluten meal) (STMR-P)	0.020 mg/kg
Cow pea (seed) (STMR-P)	0.010 mg/kg
Faba bean (seed) (STMR-P)	0.010 mg/kg
Lupin (white) (seed) (STMR-P)	0.010 mg/kg
Pea (seed) (STMR-P)	0.010 mg/kg
Lupin (seed, head processed) (STMR-P)	0.010 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.020 mg/kg
Vegetable oil (oil) (STMR-P)	0.090 mg/kg

New Substance residues in the components (dry matter):

Brewer's grain (dried) (STMR-P)	0.022 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.099 mg/kg
Corn (feed meal) (STMR-P)	0.011 mg/kg
Corn (bran) (STMR-P)	0.011 mg/kg
Corn (gluten feed) (STMR-P)	0.011 mg/kg
Corn (gluten meal) (STMR-P)	0.011 mg/kg

Corn (starch) (STMR-P)	0.011 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.011 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.011 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.099 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.100 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.011 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.100 mg/kg
Potato (protein) (STMR-P)	0.022 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.099 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.101 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.097 mg/kg
Wheat (bran) (STMR-P)	0.023 mg/kg
Wheat (flour) (STMR-P)	0.023 mg/kg
Wheat (germ) (STMR-P)	0.023 mg/kg
Wheat (middlings) (STMR-P)	0.022 mg/kg
Wheat (gluten meal) (STMR-P)	0.022 mg/kg
Cow pea (seed) (STMR-P)	0.011 mg/kg
Faba bean (seed) (STMR-P)	0.011 mg/kg
Lupin (white) (seed) (STMR-P)	0.011 mg/kg
Pea (seed) (STMR-P)	0.011 mg/kg
Lupin (seed, head processed) (STMR-P)	0.011 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.023 mg/kg
Vegetable oil (oil) (STMR-P)	0.090 mg/kg

RESULTS
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Maximum dietary burden based on New Substance is 0.089 mg/kg (dry matter).

The respective composition of the feed is:

Brewer's grain (dried)	0.00%
Canola meal (Solvent extracted)	10.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	10.82%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	15.00%
Linseed (meal, solv. extr.)	7.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	10.00%
Potato (protein)	0.00%
Safflower (Meal decorticated)	7.00%
Soybean (Meal decorticated)	13.13%
Sunflower (meal decorticated, solv. extr.)	20.00%
Wheat (bran)	0.00%
Wheat (flour)	0.00%
Wheat (germ)	0.00%
Wheat (middlings)	0.00%
Wheat (gluten meal)	0.00%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain extruded)	0.00%
Vegetable oil (oil)	8.05%
Fish meal(PC)	0.00%
Starch(CC)	0.00%
Oil(F)	0.00%

The dietary load of New Substance caused by the individual components is:

Brewer's grain (dried)	0.00%
Canola meal (Solvent extracted)	11.14%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	0.00%
Corn (starch)	1.35%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	16.75%
Linseed (meal, solv. extr.)	7.89%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	11.28%
Potato (protein)	0.00%
Safflower (Meal decorticated)	7.80%
Soybean (Meal decorticated)	13.74%
Sunflower (meal decorticated, solv. extr.)	21.90%
Wheat (bran)	0.00%

Wheat (flour)	0.00%
Wheat (germ)	0.00%
Wheat (middlings)	0.00%
Wheat (gluten meal)	0.00%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	0.00%
Vegetable oil (oil)	8.16%
Fish meal(PC)	0.00%
Starch(CC)	0.00%
Oil(F)	0.00%

M-01 rainbow trout – 0.068 mg/kg

Dietary Burden Calculation concerning New Substance

DietaryBurdenCalculator 2.0.3

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

INPUT

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Target content for Rainbow trout:

Crude fat	15.00%
Crude protein	42.00%

Maximum principal content of components in the diet:

Brewer's grain (dried)	10.00%
Canola meal (Solvent extracted)	8.00%
Corn (feed meal)	20.00%
Corn (bran)	5.00%
Corn (gluten feed)	10.00%
Corn (gluten meal)	15.00%
Corn (starch)	15.00%
Corn (Distiller's dried grains with solubles)	10.00%
Corn (Condensed distillers solubles)	3.00%
Cottonseed (meal decorticated)	5.00%
Linseed (meal, solv. extr.)	5.00%
Lupin seed white (meal (treated))	9.00%
Mustard (Meal, solv. extr.)	5.00%
Potato (protein)	2.00%
Safflower (Meal decorticated)	5.00%
Soybean (Meal decorticated)	15.00%
Sunflower (meal decorticated, solv. extr.)	10.00%
Wheat (bran)	2.00%
Wheat (flour)	10.00%
Wheat (germ)	2.00%
Wheat (middlings)	10.00%
Wheat (gluten meal)	2.00%
Cow pea (seed)	15.00%

Faba bean (seed)	15.00%
Lupin (white) (seed)	15.00%
Pea (seed)	15.00%
Lupin (seed, head processed)	3.00%
Wheat (Grain (extruded))	10.00%
Vegetable oil (oil)	15.00%
Fish meal(PC)	100.00%
Starch(CC)	100.00%
Oil(F)	100.00%

Percent dry matter of components:

Brewer's grain (dried)	92.0%
Canola meal (Solvent extracted)	91.0%
Corn (feed meal)	87.8%
Corn (bran)	87.5%
Corn (gluten feed)	90.1%
Corn (gluten meal)	91.3%
Corn (starch)	90.2%
Corn (Distiller's dried grains with solubles)	90.8%
Corn (Condensed distillers solubles)	90.6%
Cottonseed (meal decorticated)	90.8%
Linseed (meal, solv. extr.)	90.0%
Lupin seed white (meal (treated))	89.5%
Mustard (Meal, solv. extr.)	89.9%
Potato (protein)	89.4%
Safflower (Meal decorticated)	91.0%
Soybean (Meal decorticated)	89.5%
Sunflower (meal decorticated, soly. extr.)	92.6%
Wheat (bran)	88.7%
Wheat (flour)	88.0%
Wheat (germ)	88.7%
Wheat (middlings)	89.4%
Wheat (gluten meal)	91.4%
Cow pea (seed)	88.0%
Faba bean (seed)	88.0%
Lupin (white) (seed)	88.0%
Pea (seed)	90.0%
Lupin (seed, head processed)	88.0%
Wheat (Grain (extruded))	87.7%
Vegetable oil (oil)	-

New Substance residues in the components:

Brewer's grain (dried) (STMR-P)	0.020 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.090 mg/kg
Corn (feed meal) (STMR-P)	0.010 mg/kg
Corn (bran) (STMR-P)	0.010 mg/kg
Corn (gluten feed) (STMR-P)	0.010 mg/kg
Corn (gluten meal) (STMR-P)	0.010 mg/kg
Corn (starch) (STMR-P)	0.010 mg/kg
Corn (Distiller's dried grains with solubles) (STMR-P)	0.010 mg/kg

Corn (Condensed distillers solubles) (STMR-P)	0.010 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.090 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.090 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.010 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.090 mg/kg
Potato (protein) (STMR-P)	0.020 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.090 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.090 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.090 mg/kg
Wheat (bran) (STMR-P)	0.020 mg/kg
Wheat (flour) (STMR-P)	0.020 mg/kg
Wheat (germ) (STMR-P)	0.020 mg/kg
Wheat (middlings) (STMR-P)	0.020 mg/kg
Wheat (gluten meal) (STMR-P)	0.020 mg/kg
Cow pea (seed) (STMR-P)	0.010 mg/kg
Faba bean (seed) (STMR-P)	0.010 mg/kg
Lupin (white) (seed) (STMR-P)	0.010 mg/kg
Pea (seed) (STMR-P)	0.010 mg/kg
Lupin (seed, head processed) (STMR-P)	0.010 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.020 mg/kg
Vegetable oil (oil) (STMR-P)	0.090 mg/kg

New Substance residues in the components (dry matter):

Brewer's grain (dried) (STMR-P)	0.022 mg/kg
Canola meal (Solvent extracted) (STMR-P)	0.099 mg/kg
Corn (feed meal) (STMR-P)	0.011 mg/kg
Corn (bran) (STMR-P)	0.011 mg/kg
Corn (gluten feed) (STMR-P)	0.011 mg/kg
Corn (gluten meal) (STMR-P)	0.011 mg/kg
Corn (starch) (STMR-P)	0.011 mg/kg

Corn (Distiller's dried grains with solubles) (STMR-P)	0.011 mg/kg
Corn (Condensed distillers solubles) (STMR-P)	0.011 mg/kg
Cottonseed (meal decorticated) (STMR-P)	0.099 mg/kg
Linseed (meal, solv. extr.) (STMR-P)	0.100 mg/kg
Lupin seed white (meal (treated)) (STMR-P)	0.011 mg/kg
Mustard (Meal, solv. extr.) (STMR-P)	0.100 mg/kg
Potato (protein) (STMR-P)	0.022 mg/kg
Safflower (Meal decorticated) (STMR-P)	0.099 mg/kg
Soybean (Meal decorticated) (STMR-P)	0.101 mg/kg
Sunflower (meal decorticated, solv. extr.) (STMR-P)	0.097 mg/kg
Wheat (bran) (STMR-P)	0.023 mg/kg
Wheat (flour) (STMR-P)	0.023 mg/kg
Wheat (germ) (STMR-P)	0.023 mg/kg
Wheat (middlings) (STMR-P)	0.022 mg/kg
Wheat (gluten meal) (STMR-P)	0.022 mg/kg
Cow pea (seed) (STMR-P)	0.011 mg/kg
Faba bean (seed) (STMR-P)	0.011 mg/kg
Lupin (white) (seed) (STMR-P)	0.011 mg/kg
Pea (seed) (STMR-P)	0.011 mg/kg
Lupin (seed, head processed) (STMR-P)	0.011 mg/kg
Wheat (Grain (extruded)) (STMR-P)	0.023 mg/kg
Vegetable oil (oil) (STMR-P)	0.090 mg/kg

RESULTS
=======

Maximum dietary burden based on New Substance is 0.068 mg/kg (dry matter).

The respective composition of the feed is:

Brewer's grain (dried)	8.82%
Canola meal (Solvent extracted)	8.00%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	15.00%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	5.00%
Linseed (meal, solv. extr.)	5.00%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	5.00%
Potato (protein)	2.00%
Safflower (Meal decorticated)	5.00%
Soybean (Meal decorticated)	15.00%
Sunflower (meal decorticated, solv. extr.)	10.00%
Wheat (bran)	0.00%
Wheat (flour)	0.00%
Wheat (germ)	2.00%
Wheat (middlings)	0.00%
Wheat (gluten meal)	2.00%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain extruded)	0.00%
Vegetable oil (oil)	12.14%
Fish meal(PC)	5.04%
Starch(CC)	0.00%
Oil(F)	0.00%

The dietary load of New Substance caused by the individual components is:

Brewer's grain (dried)	2.80%
Canola meal (Solvent extracted)	11.56%
Corn (feed meal)	0.00%
Corn (bran)	0.00%
Corn (gluten feed)	0.00%
Corn (gluten meal)	2.40%
Corn (starch)	0.00%
Corn (Distiller's dried grains with solubles)	0.00%
Corn (Condensed distillers solubles)	0.00%
Cottonseed (meal decorticated)	7.24%
Linseed (meal, solv. extr.)	7.31%
Lupin seed white (meal (treated))	0.00%
Mustard (Meal, solv. extr.)	7.31%
Potato (protein)	0.65%
Safflower (Meal decorticated)	7.22%
Soybean (Meal decorticated)	22.04%
Sunflower (meal decorticated, solv. extr.)	14.20%
Wheat (bran)	0.00%

Wheat (flour)	0.00%
Wheat (germ)	0.66%
Wheat (middlings)	0.00%
Wheat (gluten meal)	0.64%
Cow pea (seed)	0.00%
Faba bean (seed)	0.00%
Lupin (white) (seed)	0.00%
Pea (seed)	0.00%
Lupin (seed, head processed)	0.00%
Wheat (Grain (extruded))	0.00%
Vegetable oil (oil)	15.97%
Fish meal(PC)	0.00%
Starch(CC)	0.00%
Oil(F)	0.00%

APPENDIX 2 - TIER 2 summaries of residue trials

Reference	**CA 6.3.2/01 - [redacted], 2003 (M-232144-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (North), Germany and the United Kingdom	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	Propamocarb hydrochloride (625 g/L) and fluopicolide (62.5 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	AE B066752 04 SC61 A102	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
										FLC	M-01	M-02		
	(a)	(b)					(c)		(a)				(d)	(e)
Report No 02R286 Trial No 02R286-1 Germany (04808 Falkenhain)	Potato / Princess	1. 18.4.2002 2. 22.06.2002 to 02.07.2002 3. 05.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	300 300 300 300	0.033 0.033 0.033 0.033	08.07.2002 (7 days) 15.07.2002 (7 days) 22.07.2002 (7 days) 29.07.2002	69 85 89 91	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 02R286 Trial No 02R286-2 United Kingdom (CB7 4UP Cambridgeshire)	Potato / Maris Piper	1. 26.4.2002 2. 25.06.2002 to 25.07.2002 3. 22.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	320 320 320 320	0.031 0.031 0.031 0.031	25.07.2002 (7 days) 01.08.2002 (7 days) 08.08.2002 (7 days) 15.08.2002	46 47 47 48	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R286 Trial No 02R286-3 France, North (80700 Cremery)	Potato / Bintje	1. 24.4.2002 2. 14.07.2002 to 30.07.2002 3. 18.09.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	21.08.2002 (8 days) 29.08.2002 (7 days) 05.09.2002 (6 days) 11.09.2002	91 93 95 97	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R286 Trial No 02R286-4 France, North (02400 Lucy le Bocage)	Potato / Bintje	1. 15.4.2002 2. 15.06.2002 to 15.07.2002 3. 31.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	08.08.2002 (6 days) 14.08.2002 (6 days) 20.08.2002 (6 days) 26.08.2002	47 48 48 48	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/02-[redacted], 2003 (M-232146-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South), Italy and Spain	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	Propamocarb hydrochloride (625 g/L) and fluopicolide (62.5 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	AE B066752 04 SC61 A102	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)		(a)	FLC	M-01	M-02	(d)	(e)
Report No 02R287 Trial No 02R287-1 France, South (69380 Chazay)	Potato / Bintje	1. 16.4.2002 2. 05.06.2002 to 15.06.2002 3. 24.07.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	26.06.2002 (7 days) 03.07.2002 (7 days) 10.07.2002 (7 days) 17.07.2002	85 89 91 91	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R287 Trial No 02R287-2 France, South (47400 Gontaud-de-Nogaret)	Potato / Charlotte	1. 10.03.2002 2. 01.06.2002 to 18.06.2002 3. 09.07.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	11.06.2002 (7 days) 18.06.2002 (7 days) 25.06.2002 (7 days) 02.07.2002	73 81 91 95	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 02R287 Trial No 02R287-3 Italy (70056 Molfetta)	Potato / Spunta Olandese	1. 08.02.2002 2. 20.05.2002 to 30.05.2002 3. 13.06.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	500 500 500 500	0.020 0.020 0.020 0.020	16.05.2002 (7 days) 23.05.2002 (7 days) 30.05.2002 (7 days) 06.06.2002	35 39 91 93	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R287 Trial No 02R287-4 Spain (41310 Brenes)	Potato / Spunta	1. 16.01.2002 2. N/A 3. 20.05.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	300 300 300 300	0.033 0.033 0.033 0.033	22.04.2002 (7 days) 29.04.2002 (7 days) 06.05.2002 (7 days) 13.05.2002	44 45 47 47	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 0.02	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/03-[redacted], 2003 (M-214893-02-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (North), Germany and United Kingdom	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (95 g/L)	Other active ingredients in the formulation:	-
Formulation type (e.g. WG):	SE		
Commercial product name:	AE C638206 00 SE10 A303	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL (c)	Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 01R282 Trial No 01R282-1 Germany (04808 Falkenhain)	Potato / Secura	1. 01/05/2001 2. 20/06/2001 to 30/06/2001 3. 13/08/2001	Spray, flat-fan	0.125 0.125 0.125	300 300 300	0.042 0.042 0.042	23/07/2001 (7 days) 30/07/2001 (7 days) 06/08/2001	48 48 49	Tubers Tubers Tubers Tubers Tubers	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 01R282 Trial No 01R282-2 United Kingdom (NR147DU Suffolk)	Potato / Premier	1. 05/04/2001 2. 25/06/2001 to 30/07/2001 3. 24/07/2001	Spray, flat-fan	0.125 0.125 0.125	250 250 250	0.050 0.050 0.050	03/07/2001 (6 days) 09/07/2001 (8 days) 17/07/2001	63 69 47(1)	Tubers Tubers Tubers Tubers Tubers	0.01 0.01 <0.01 0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 01R282 Trial No 01R282-3 United Kingdom (CB7 4UP Cambridgeshire)	Potato / Maris Piper	1. 01/05/2001 2. 08/07/2001 to 05/08/2001 3. 24/08/2001	Spray, flat-fan	0.125 0.125 0.125	302 302 302	0.041 0.041 0.041	03/08/2001 (7 days) 10/08/2001 (7 days) 17/08/2001	44 47 47	Tubers Tubers Tubers Tubers Tubers Tubers	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 01R282 Trial No 01R282-4 France - North (51 520 La Veuve)	Potato / Monalisa	1. 12/05/2001 2. 06/07/2001 to 26/08/2001 3. 18/09/2001	Spray, flat-fan	0.125 0.125 0.125	250 250 250	0.050 0.050 0.050	29/08/2001 (4 days) 03/09/2001 (8 days) 11/09/2001	72 71 75	Tubers Tubers Tubers Tubers Tubers Tubers	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 01R282 Trial No 01R282-5 France - North (62 123 Series Au Bois)	Potato / Desiree	1. 15/05/2001 2. 10/07/2001 to 25/07/2001 3. 17/09/2001	Spray, flat-fan	0.125 0.125 0.125	250 250 250	0.050 0.050 0.050	27/08/2001 (7 days) 03/09/2001 (7 days) 10/09/2001	72 72 72	Tubers Tubers Tubers Tubers Tubers Tubers	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/04 - [redacted] 2003 (M-214897-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South), Italy and Spain	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (95 g/L)	Other active ingredients in the formulation:	-
Formulation type (e.g. WG):	SE		
Commercial product name:	AE C638206 00 SE10 A303	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 01R283 Trial No 01R283-1 France, South (33190 Fontet)	Potato / Concurent	1. 16.04.2001 2. 08.06.2001 to 25.06.2001 3. 02.07.2001	Spray, flat-fan	0.125	250	0.050	11.06.2001 (7 days)	59	Tuber Tuber	0.013 <0.01	<0.01 <0.01	<0.01 <0.01	0 1	Method: 00782/M001
				0.125	250	0.050	18.06.2001 (7 days)	65	Tuber Tuber	<0.01 <0.01	<0.01 <u>≤0.01</u>	<0.01 <u>≤0.01</u>	3 7	LOQ = 0.01 mg/kg
				0.125	250	0.050	25.06.2001	71	Tuber	<u>0.013</u>	<0.01	<0.01	14	
Report No 01R283 Trial No 01R283-2 France, South (69380 Chazay D'Azergues)	Potato / Bintje	1. 20.04.2001 2. Not reported 3. 20.08.2001	Spray, flat-fan	0.125	300	0.042	31.07.2001 (6 days)	45	Tuber Tuber	<0.01 0.017	<0.01 <0.01	<0.01 <0.01	0 1	Method: 00782/M001
				0.125	300	0.042	06.08.2001 (7 days)	47	Tuber Tuber	<0.01 <u>0.013</u>	<0.01 <u>≤0.01</u>	<0.01 <u>≤0.01</u>	3 7	LOQ = 0.01 mg/kg
				0.125	300	0.042	13.08.2001	48	Tuber	<0.01	<0.01	<0.01	14	

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 01R283 Trial No 01R283-3 Italy (44040 San Carlo)	Potato / Kennebec	1. 15.03.2001 2. 01.05.2001 to 15.06.2001 3. 27.08.2001	Spray, flat-fan	0.125 0.125 0.125	350 350 350	0.036 0.036 0.036	06.08.2001 (7 days) 13.08.2001 (7 days) 20.08.2001	46 47 48	Tuber Tuber Tuber Tuber Tuber	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 01R283 Trial No 01R283-4 Spain (41310 Brenes, Sevilla)	Potato / Espunta	1. 02.02.2001 2. 15.04.2001 to 28.04.2001 3. 21.05.2001	Spray, flat-fan	0.125 0.125 0.125	300 300 300	0.042 0.042 0.042	30.04.2001 (7 days) 07.05.2001 (7 days) 14.05.2001	43 45 47	Tuber Tuber Tuber Tuber Tuber	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 01R283 Trial No 01R283-5 Spain (46230 Alginet, Valencia))	Potato / Monalisa	1. 20.03.2001 2. 01.06.2001 to 10.06.2001 3. 12.06.2001	Spray, flat-fan	0.125 0.125 0.125	300 300 300	0.042 0.042 0.042	22.05.2001 (7 days) 29.05.2001 (7 days) 05.06.2001	45 65 67	Tuber Tuber Tuber Tuber Tuber	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 7 14	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/05-[redacted] 2003 (M-231883-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	Germany, France (north), UK	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (95 g/L)	Other active ingredients in the formulation:	-
Formulation type (e.g. WG):	SE		
Commercial product name:	AE C638206 00 SE10 A303	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 02R282 Trial No 02R282-1 Germany (04808 Falkenhain)	Potato / Princess	1. 18.4.2002 2. 22.06.2002 to 02.07.2002 3. 05.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	300 300 300 300	0.033 0.033 0.033 0.033	08.07.2002 (7 days) 15.07.2002 (7 days) 22.07.2002 (7 days) 29.07.2002	69 85 89 91	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R282 Trial No 02R282-2 United Kingdom (CB7 4UP, Cambridgeshire)	Potato / Maris Piper	1. 26.4.2002 2. 25.06.2002 to 25.07.2002 3. 22.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	302 302 302 302	0.033 0.033 0.033 0.033	25.07.2002 (7 days) 01.08.2002 (7 days) 08.08.2002 (7 days) 15.08.2002	46 47 47 48	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 02R282 Trial No 02R282-3 France, North (80700 Cremery)	Potato / Bintje	1. 24.4.2002 2. 14.07.2002 to 30.07.2002 3. 18.09.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	21.08.2002 (8 days) 29.08.2002 (7 days) 05.09.2002 (6 days) 11.09.2002	91 93 95 97	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R282 Trial No 02R282-4 France, North (02400 Lucy le Bocage)	Potato / Bintje	1. 15.4.2002 2. 15.06.2002 to 15.07.2002 3. 31.08.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	08.08.2002 (6 days) 14.08.2002 (6 days) 20.08.2002 (6 days) 26.08.2002	47 48 48 48	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/06-[redacted], 2003 (M-231939-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South), Italy, Spain	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (95 g/L)	Other active ingredients in the formulation:	-
Formulation type (e.g. WG):	SE		
Commercial product name:	AE C638206 00 SE10 A303	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days)	Growth stage at last sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)		(a)	FLC	M-01	M-02	(d)	(e)
Report No 02R283 Trial No 02R283-1 France, South (69380 Chazay d'Azergues)	Potato / Bintje	1. 16.04.2002 2. 05.06.2002 to 15.06.2002 3. 24.07.2002	Spray flat-fan	0.100	300	0.033	26.06.2002 (8 days)	44	Tubers	<0.01	<0.01	<0.01	0	Method: 00782/M001 LOQ = 0.01 mg/kg
				0.100	300	0.033	04.07.2002 (6 days)	45	Tubers	<0.01	<0.01	<0.01	7	
				0.100	300	0.033	10.07.2002 (7 days)	46						
				0.100	300	0.033	17.07.2002	91						

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 02R283 Trial No 02R283-2 France, South (47400 Gontaud-de-Nogaret)	Potato / Charlotte	1. 10.03.2002 2. 01.06.2002 to 18.06.2002 3. 09.07.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	250 250 250 250	0.040 0.040 0.040 0.040	11.06.2002 (7 days) 18.06.2002 (7 days) 25.06.2002 (7 days) 02.07.2002	73 81 91 95	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R283 Trial No 02R283-3 Italy (70056 Molfetta)	Potato / Spunta Olandese	1. 08.02.2002 2. 25.05.2002 to 05.06.2002 3. 13.06.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	500 500 500 500	0.020 0.020 0.020 0.020	16.05.2002 (7 days) 23.05.2002 (7 days) 30.05.2002 (7 days) 06.06.2002	35 39 91 93	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg
Report No 02R283 Trial No 02R283-4 Spain (41310 Brenes, Sevilla)	Potato / Spunta	1. 16.01.2002 2. N/A 3. 20.05.2002	Spray, flat-fan	0.100 0.100 0.100 0.100	300 300 300 300	0.033 0.033 0.033 0.033	22.04.2002 (7 days) 29.04.2002 (7 days) 06.05.2002 (7 days) 13.05.2002	44 45 46 47	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/07 - [redacted], 2004 (M-236086-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	Germany, the Netherlands and the United Kingdom	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (64.7 g/L) and propamocarb hydrochloride (634.0 g/L)	Other active ingredients in the formulation:	propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	AE B066752 04 SC61 A1 (688 SC)	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)		(a)	PLC	M-01	M-02	(d)	(e)
Report No RA-2604/03 Trial No R 2003 01 23/5 United Kingdom (NR14 7DV Norwich)	Potato / Spey	1. 2003-04-02 2. 2003-07-02 to 2003-07-31 3. 2003-07-30	Spray flat-fan	0.10 0.10 0.10 0.10	400 400 400 400	0.025 0.025 0.025 0.025	2003-07-02 (7 days) 2003-07-09 (7 days) 2003-07-16 (7 days) 2003-07-23	51-59 51-59 51-69 45-47[1]	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2604/03 Trial No R 2003 1008/0 Germany (D-51399 Burscheid)	Potato Cilena	1. 2003-04-25 2. 2003-06-17 to 2003-07-24 3. 2003-08-15	Spray flat-fan	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-07-28 (7 days) 2003-08-04 (7 days) 2003-08-11 (7 days) 2003-08-18	75 79-81 83 89	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA-2604/03 Trial No R 2003 1009/9 Germany (D-40789 Monheim)	Potato / Agria	1. 2003-05-15 2. 2003-06-30 3. 2003-07-17	Spray, flat-fan	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-07-28 (7 days) 2003-08-04 (7 days) 2003-08-11 (8 days) 2003-08-19	75 79 81 85	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2604/03 Trial No R 2003 101 0/2 Netherlands (NL-1681NBZwaagdijk-Oost)	Potato / Agria	1. 2003-04-18 2. No data 3. 2003-09-20	Spray, flat-fan	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-08-25 (8 days) 2003-09-02 (7 days) 2003-09-09 (7 days) 2003-09-16	81 81 83 85	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/08- [redacted], 2004 (M-237282-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	Italy, Spain, Greece, France (South)	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (64.7 g/L) and propamocarb hydrochloride (634.0 g/L)	Other active ingredients in the formulation:	propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	AE B06G752 04 SC61 A1 (688 SC)	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate			Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
				kg a.s./ha	Water (L/ha)	kg a.s./hL				EEC	M-01	M-02		
	(a)	(b)					(c)		(a)				(d)	(e)
Report No RA-2605/03 Trial No R 2003 01 24/3 Italy (I-70056 Molfetta)	Potato / Spunta	1. 2003-03-20 2. 2003-05-20 to 2003-05-30 3. 2003-06-1 to 2003-06-30	Spraying	0.10	500	0.020	2003-05-20 (7 days)	41	Tubers	<0.01	<0.01	<0.01	0	Method: 00782/M004 LOQ = 0.01 mg/kg
				0.10	500	0.020	2003-05-27 (7 days)	43	Tubers	<0.01	<0.01	<0.01	7	
				0.10	500	0.020	2003-06-03 (7 days)	45						
				0.10	500	0.020	2003-06-10	48						

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA-2605/03 Trial No R 2003 101 1/0 Greece (GR-32200 Ypato-Thiva)	Potato / Spunta	1. 2003-08-18 2. 2003-10-15 to 2003-10-25 3. 2003-11-30	Spraying	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-10-27 (7 days) 2003-11-03 (7 days) 2003-11-10 (7 days) 2003-11-17	89 89 89 91	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2605/03 Trial No R 2003 101 2/9 Spain (E-46230 Alginet)	Potato / Safrane	1. 2003-01-29 2. 2003-05-01 to 2003-05-20 3. 2003-06-01 to 2003-06-15	Spraying	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-05-09 (7 days) 2003-05-16 (7 days) 2003-05-23 (7 days) 2003-05-30	40 43 46 47	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2605/03 Trial No R 2003 101 3/7 France, South (F-82600 Mas Grenier)	Potato / Lisetta	1. 2003-03-22 2. 2003-05-30 to 2003-06-15 3. 2003-07-01	Spraying	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2003-06-03 (7 days) 2003-06-10 (7 days) 2003-06-17 (7 days) 2003-06-24	42-51 44-53 46 48	Tubers Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	0 7	Method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/09-[redacted], 2010 (M-398344-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (North), Germany, Belgium and the Netherlands	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and propamocarb-hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb-hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	SC 687.5	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)		(a)	FEC	M-01	M-02	(d)	(e)
Report No 10-2121 Trial No 10-2121-01 France, North (78410 Bouafle)	Potato / Amandine	1. 2010-04-21 2. 2010-06-22 to 2010-07-02 3. 2010-08-16 to 2010-08-30	Spray	0.10	600	0.017	2010-07-06 (7 days)	70	Tuber	<0.01	<0.01	<0.01	-0	Method: 01209
				0.10	600	0.017	2010-07-13 (7 days)	73	Tuber	<0.01	<0.01	<0.01	0	
				0.10	600	0.017	2010-07-20 (7 days)	79	Tuber	<0.01	<0.01	<0.01	7	LOQ = 0.01 mg/kg
				0.10	600	0.017	2010-07-27	91	Tuber	<0.01	<0.01	<0.01	14	
									Tuber				21	
Report No 10-2121 Trial No 10-2121-02 Germany (D-49377 Langförden)	Potato / Belana	1. 2010-04-28 2. 2010-07-09 to 2010-07-16 3. 2010-08-20 to 2010-08-30	Spray	0.10	300	0.033	2010-07-09 (7 days)	61	Tuber	<0.01	<0.01	<0.01	-0	Method: 01209
				0.10	300	0.033	2010-07-16 (7 days)	69	Tuber	<0.01	<0.01	<0.01	0	
				0.10	300	0.033	2010-07-23 (7 days)	71	Tuber	<0.01	<0.01	<0.01	7	LOQ = 0.01 mg/kg
				0.10	300	0.033	2010-07-30	75	Tuber	<0.01	<0.01	<0.01	14	
									Tuber				21	

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 10-2121 Trial No 10-2121-03 Belgium (6210 Frasnes-Lez-Gosselies)	Potato / Bintje	1. 2010-04-27 2. 2010-06-20 to 2010-07-05 3. 2010-08-09 to 2010-10-13	Spray	0.10 0.10 0.10 0.10	700 700 700 700	0.014 0.014 0.014 0.014	2010-07-12 (7 days) 2010-07-19 (7 days) 2010-07-26 (7 days) 2010-08-02	71 75 79 85	Tuber Tuber Tuber Tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	-0 0 7 14 21	Method: 01209 LOQ = 0.01 mg/kg
Report No 10-2121 Trial No 10-2121-04 Netherlands (1175 LD Lijden)	Potato / Frieslander	1. 2010-04-16 2. 2010-07-15 to 2010-07-31 3. 2010-08-05 to 2010-08-15	Spray	0.10 0.10 0.10 0.10	300 300 300 300	0.033 0.033 0.033 0.033	2010-07-08 (8 days) 2010-07-16 (7 days) 2010-07-23 (7 days) 2010-07-30	91 95 95 95	Tuber Tuber Tuber Tuber	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	-0 0 7 14 21	Method: 01209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/10 - [redacted] 2011 (M-401823-02-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	3
Country:	Germany, Netherlands, France (North and South), Italy, Spain	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and propamocarb-hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb-hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	SC 687.5	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days)	Growth stage at sampling (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)		(a)	FLC	M-01	M-02	(d)	(e)
Report No 09-2233 Trial No 09-2233-01 France, North (78410 Bouafle Ile-de-France)	Potato / Amandine	1. 2009-04-16 2. 2009-06-08 to 2009-07-06 3. 2009-08-10 to 2009-08-30	Spray	0.10	600	0.017	2009-07-01 (8 days)	70	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2009-07-09 (7 days)	79						
				0.10	600	0.017	2009-07-16 (5 days)	89						
				0.10	600	0.017	2009-07-21 (7 days)	91						
				0.10	600	0.017	2009-07-16 (5 days)	89	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2009-07-21 (7 days)	91						
				0.10	600	0.017	2009-07-28 (7 days)	93						
				0.10	600	0.017	2009-08-04	95						

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 09-2233 Trial No 09-2233-02 Germany (51399 Burscheid Nordrhein-Westfalen)	Potato / Laura	1. 2009-05-13 2. 2009-07-07 to 2009-07-18 3. 2009-09-01 to 2009-09-15	Spray	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2009-08-04 (7 days) 2009-08-11 (7 days) 2009-08-18 (7 days) 2009-08-25	73 75 81 91	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg
				0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2009-08-04 (7 days) 2009-08-11 (7 days) 2009-08-18 (7 days) 2009-08-25	73 75 81 91	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg
Report No 09-2233 Trial No 09-2233-03 Netherlands (1681 ND Zwaagdijk-Oost Noord-Holland)	Potato / Triumph	1. 2009-04-22 2. 2009-06-15 to 2009-07-15 3. 2009-08-09 to 2009-08-15	Spray	0.10 0.10 0.10 0.10	800 800 800 800	0.013 0.013 0.013 0.013	2009-07-01 (7 days) 2009-07-08 (7 days) 2009-07-15 (7 days) 2009-07-22	39 68 61 70	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg
				0.10 0.10 0.10 0.10	800 800 800 800	0.013 0.013 0.013 0.013	2009-07-15 (7 days) 2009-07-23 (7 days) 2009-07-29 (7 days) 2009-08-05	43 45 47 48	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg
Report No 09-2233 Trial No 09-2233-04 France, South (84210 Les	Potato / Agata	1. 2009-03-14 2. N/A 3. 2009-07-07 to 2009-07-21	Spray	0.10 0.10 0.10 0.10	800 800 800 800	0.013 0.013 0.013 0.013	2009-05-26 (7 days) 2009-06-02 (7 days) 2009-06-09 (7 days) 2009-06-16	29 31 35 39	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Valayans Provence-Cote D'azur)				0.10 0.10 0.10 0.10	800 800 800 800	0.013 0.013 0.013 0.013	2009-06-09 (7 days) 2009-06-16 (7 days) 2009-06-23 (7 days) 2009-06-30	35 35 91 48	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg
Report No 09-2233 Trial No 09-2233-05 Spain (08520 Llerona - Les Franqueses del Valles Cataluña)	Potato / Red Pontiac	1. 2009-08-10 2. 2009-09-15 to 2009-10-05 3. 2009-10-25 to 2009-11-13	Spray	0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2009-09-30 (8 days) 2009-10-08 (7 days) 2009-10-15 (8 days) 2009-10-23 (7 days)	62 69 70 47	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg
				0.10 0.10 0.10 0.10	600 600 600 600	0.017 0.017 0.017 0.017	2009-10-15 (8 days) 2009-10-23 (7 days) 2009-10-30 (7 days) 2009-11-06	70 47 48 49	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg
Report No 09-2233 Trial No 09-2233-06 Italy (40128 Bologna Emilia - Romagna)	Potato / Agata	1. 2009-03-17 2. 2009-06-01 to 2009-06-20 3. 2009-07-20 to 2009-07-31	Spray	0.10 0.10 0.10 0.10	500 500 500 500	0.020 0.020 0.020 0.020	2009-06-19 (6 days) 2009-06-25 (8 days) 2009-07-03 (6 days) 2009-07-09	45 47 48 48	Tuber	<0.01	<0.01	<0.01	7	Plot T1 Method: 01209 LOQ = 0.01 mg/kg
				0.10 0.10 0.10 0.10	500 500 500 500	0.020 0.020 0.020 0.020	2009-07-03 (6 days) 2009-07-09 (8 days) 2009-07-17 (7 days) 2009-07-24	48 48 48 49	Tuber	<0.01	<0.01	<0.01	7	Plot T2 Method: 01209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.2/11-[redacted], 2011 (M-420098-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Potato	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	4
Country:	Germany and France (South)	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and propamocarb-hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb-hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	SC 687.5	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application (interval in days) (c)	Growth stage at sampling (BBCH) (a)	Portion analysed (a)	Residues (mg/kg) FIC	M-01	M-02	PHI (d)	Remarks (e)
Report No IF-10/01635342 Trial No 10-DE-007 Germany (Pöpsel Schnetiage Nr 1 49624 Löningen)	Potato / Premiere	1. 12.04.2010 2. 22.06.2010 to 05.07.2010 3. 05.08.2010	Spray	0.096	900	0.011	25.05.2010 (0 days)	13	Tubers	<0.01	<0.01	<0.01	69	Plot T1 00782/M004 LOQ = 0.01 mg/kg
				0.106	900	0.012	01.06.2010	17						
				0.093	900	0.010	07.06.2010 (7 days)	51	Tubers	<0.01	<0.01	<0.01	56	Plot T2 00782/M004 LOQ = 0.01 mg/kg
				0.098	900	0.011	14.06.2010	55						
				0.095	900	0.011	22.06.2010 (6 days)	60	Tubers	<0.01	<0.01	<0.01	42	Plot T3 00782/M004 LOQ = 0.01 mg/kg
				0.095	900	0.011	28.06.2010	62						
				0.098	900	0.011	05.07.2010 (8 days)	69	Tubers	<0.01	<0.01	<0.01	27	Plot T4 00782/M004 LOQ = 0.01 mg/kg
				0.095	900	0.011	13.07.2010	71						

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

				0.100 0.098	900 900	0.011 0.011	13.07.2010 (7 days) 20.07.2010	71 45	Tubers	<0.01	<0.01	<0.01	20	Plot T5 00782/M004 LOQ = 0.01 mg/kg
				0.106 0.106	900 900	0.012 0.012	20.07.2010 (7 days) 27.07.2010	45 47	Tubers	<0.01	<0.01	<0.01	11	Plot T6 00782/M004 LOQ = 0.01 mg/kg
				0.104 0.098	900 900	0.012 0.011	27.07.2010 (6 days) 02.08.2010	47 45	Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	-0 7	Plot T7 00782/M004 LOQ = 0.01 mg/kg
Report No IF-10/01635342 Trial No 10-DE-008 Germany (Johannes Sassen-Stolle Stoiles Weg 2 27801 Dötlingen)	Potato / Donald	1. 21.04.2010 2. 30.06.2010 to 08.07.2010 3. 19.08.2010	Spray	0.098 0.102	900 900	0.011 0.011	02.06.2010 (7 days) 09.06.2010	16 24	Tubers	<0.01	<0.01	<0.01	71	Plot T1 00782/M004 LOQ = 0.01 mg/kg
				0.107 0.095	900 900	0.012 0.011	17.06.2010 (7 days) 24.06.2010	31 51	Tubers	<0.01	<0.01	<0.01	56	Plot T2 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.093	900 900	0.011 0.010	30.06.2010 (8 days) 08.07.2010	60 69	Tubers	<0.01	<0.01	<0.01	42	Plot T3 00782/M004 LOQ = 0.01 mg/kg
				0.098 0.104	900 900	0.011 0.012	13.07.2010 (7 days) 20.07.2010	71 43	Tubers	<0.01	<0.01	<0.01	30	Plot T4 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.098	900 900	0.011 0.011	20.07.2010 (10 days) 30.07.2010	43 45	Tubers	<0.01	<0.01	<0.01	20	Plot T5 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

				0.107 0.106	900 900	0.012 0.012	30.07.2010 (6 days) 05.08.2010	45 47	Tubers	<0.01	<0.01	<0.01	14	Plot T6 00782/M004 LOQ = 0.01 mg/kg
				0.091 0.104	900 900	0.010 0.012	05.08.2010 (6 days) 11.08.2010	49 49	Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	-0 8	Plot T7 00782/M004 LOQ = 0.01 mg/kg
Report No IF-10/01635342 Trial No 10-FR-0Q9 France, South (N. Rey Barnague 47120 Duras)	Potato / Agata	1. 13.04.2010 2. 20.06.2010 to 01.07.2010 3. 16.07.2010	Spray	0.104 0.104	600 600	0.017 0.017	12.05.2010 (6 days) 20.05.2010	16 16	Tubers	<0.01	<0.01	<0.01	56	Plot T2 00782/M004 LOQ = 0.01 mg/kg
				0.104 0.104	600 600	0.017 0.017	27.05.2010 (6 days) 02.06.2010	19 19	Tubers	<0.01	<0.01	<0.01	43	Plot T3 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.104	600 600	0.017 0.017	10.06.2010 (7 days) 17.06.2010	19 19	Tubers	<0.01	<0.01	<0.01	28	Plot T4 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.099	600 600	0.017 0.017	17.06.2010 (7 days) 24.06.2010	19 47	Tubers	<0.01	<0.01	<0.01	21	Plot T5 00782/M004 LOQ = 0.01 mg/kg
				0.104 0.105	600 600	0.017 0.018	24.06.2010 (7 days) 01.07.2010	47 47	Tubers	<0.01	<0.01	<0.01	14	Plot T6 00782/M004 LOQ = 0.01 mg/kg
				0.105 0.103	600 600	0.018 0.017	01.07.2010 (7 days) 08.07.2010	47 48	Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	-0 7	Plot T7 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No IF-10/01635342 Trial No 10-FR-010 France, South (Sari Allix Avenue de Pierroton 33127 St Jean D'lllac)	Potato / Agata	1. 27.07.2010 2. 13.10.2010 to 20.10.2010 3. 15.11.2010	Spray	0.102 0.107	1300 1300	0.008 0.008	24.08.2010 (8 days) 01.09.2010	16 17	Tubers	<0.01	<0.01	<0.01	70	Plot T1 00782/M004 LOQ = 0.01 mg/kg
				0.107 0.102	800 800	0.013 0.013	08.09.2010 (7 days) 15.09.2010	19 39	Tubers	<0.01	<0.01	<0.01	56	Plot T2 00782/M004 LOQ = 0.01 mg/kg
				0.107 0.093	800 800	0.013 0.012	22.09.2010 (6 days) 28.09.2010	40 43	Tubers	<0.01	<0.01	<0.01	43	Plot T3 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.107	800 800	0.013 0.013	06.10.2010 (7 days) 13.10.2010	43 46	Tubers	<0.01	<0.01	<0.01	28	Plot T4 00782/M004 LOQ = 0.01 mg/kg
				0.102 0.093	800 800	0.013 0.012	13.10.2010 (7 days) 20.10.2010	46 47	Tubers	<0.01	<0.01	<0.01	21	Plot T5 00782/M004 LOQ = 0.01 mg/kg
				0.093 0.098	800 800	0.012 0.012	20.10.2010 (7 days) 27.10.2010	47 49	Tubers	<0.01	<0.01	<0.01	14	Plot T6 00782/M004 LOQ = 0.01 mg/kg
				0.098 0.093	800 800	0.012 0.012	27.10.2010 (7 days) 03.11.2010	49 49	Tubers	<0.01 <0.01	<0.01 <0.01	<0.01 <0.01	-0 7	Plot T7 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/01 - [redacted], 2013 (M-465360-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	4
Country:	Italy, Spain Greece, Germany, Portugal	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No RA- 12-2059 Trial No 12-2059-01 Germany (67125 Dannstadt-Schauernheim)	Lettuce / Rondai Lollo Rosso	1. 2012-05-16 2. N/A 3. 2012-06-11 to 2012-06-29	Spray Applicator, flat-fan	0.10	500	0.020	2012-05-30 (7 days)	16	Head	0.23	<0.01	<0.01	-0	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10	500	0.020	2012-06-06 (8 days)	18	Head	0.54 0.075	0.014 <0.01	<0.01 <0.01	7 14	
				0.10	500	0.020	2012-06-06	47						
				0.10	500	0.020	2012-06-06 (8 days)	18	Head Head	0.17 0.63	<0.01 0.011	<0.01 <0.01	-0 7	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	500	0.020	2012-06-14	47	Head	0.088	<0.01	<0.01	14	
				0.10	500	0.020	2012-06-14	37	Head Head	0.72 0.14	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA- 12-2059 Trial No 12-2059-02 Germany (42799 Leichlingen)	Lettuce / Aleppo lollo bionda	1. 2012-05-10 2. N/A 3. 2012-06-25 to 2012-07-06	Spray Applicator, flat-fan	0.10 0.10 0.10	300 300 300	0.033 0.033 0.033	2012-06-05 (7 days) 2012-06-12 (7 days) 2012-06-19	41 44 47	Head Head Head	0.45 0.28 0.065	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	300 300	0.033 0.033	2012-06-12 (7 days) 2012-06-19	44 47	Head Head	0.38 0.28 0.085	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	300	0.033	2012-06-19	47	Head Head	0.21 0.043	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-03 Belgium (6210 Villers-Perwin)	Lettuce / Klausia Lettuce Oakleaf	1. 2012-08-13 2. N/A 3. 2012-09-25 to 2012-10-05	Spray Applicator, flat-fan	0.10 0.10 0.10	650 650 650	0.015 0.015 0.015	2012-09-04 (8 days) 2012-09-12 (7 days) 2012-09-19	41 44 48	Head Head Head	1.4 1.8 1.3	0.011 0.014 0.015	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	650 650	0.015 0.015	2012-09-12 (7 days) 2012-09-19	44 48	Head Head Head	0.67 0.87 0.64	<0.01 <0.01 0.012	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	650	0.015	2012-09-19	48	Head Head	0.48 0.33	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-04 France - North	Lettuce / Quelio type loose leaf	1. 2012-05-03 2. N/A 3. 2012-06-19 to 2012-06-28	Spray Applicator, flat-fan	0.10 0.10 0.10	600 600 600	0.017 0.017 0.017	2012-05-30 (7 days) 2012-06-06 (7 days) 2012-06-13	19 33 37	Head Head Head	0.35 0.22 0.027	<0.01 0.015 <0.01	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

(95000 Cergy)				0.10 0.10	600 600	0.017 0.017	2012-06-06 (7 days) 2012-06-13	33 37	Head Head Head	0.31 <u>0.19</u> 0.024	<0.01 <u>0.013</u> <0.01	<0.01 <u><0.01</u> <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2012-06-13	37	Head Head	<u>0.10</u> 0.020	<u><0.01</u> <0.01	<u><0.01</u> <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-05 France - South (13103 St étienne du gres)	Lettuce / Kiribati Lettuce leaf	1. 2012-03-27 2. N/A 3. 2012-05-20 to 2012-05-30	Spray Applicator, flat-fan	0.10 0.10 0.10	600 600 600	0.017 0.017 0.017	2012-05-02 (7 days) 2012-05-09 (7 days) 2012-05-16	46 48 49	Head Head Head Head	0.73 0.36 0.11 0.48	0.029 0.018 0.015 0.015	<0.01 <0.01 <0.01 <0.01	-0 7 14 -0	Plot T1 Method: 1209 LOQ = 0.01 mg/kg Plot T2
				0.10	600	0.017	2012-05-09 (7 days)	48	Head Head	0.28	0.012	<u><0.01</u>	7	Method: 1209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2012-05-16	49	Head	0.072	<0.01	<0.01	14	
				0.10	600	0.017	2012-05-16	49	Head Head	<u>0.13</u> 0.036	<u><0.01</u> <0.01	<u><0.01</u> <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-06 France - South (31200 Toulouse)	Lettuce / Bellino Loose leaf	1. 2012-05-16 2. N/A 3. 2012-06-27 to 2012-06-27	Spray Applicator, flat-fan	0.10 0.10 0.10	1000 1000 1000	0.010 0.010 0.010	2012-06-06 (7 days) 2012-06-13 (7 days) 2012-06-20	33 45 47	Head Head Head	3.1 0.55 0.12	0.013 0.020 0.027	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10	1000	0.010	2012-06-13 (7 days)	45	Head Head	2.9 <u>0.68</u>	0.010 0.018	<0.01 <u><0.01</u>	-0 7	Plot T2 Method: 1209
				0.10	1000	0.010	2012-06-20	47	Head	0.14	<u>0.020</u>	<0.01	14	LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

				0.10	1000	0.010	2012-06-20	47	Head Head	0.52 0.16	0.012 0.014	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-07 Italy (76123 Andria)	Lettuce / Vulsini Oak leaf red lettuce	1. 2012-05-04 2. N/A 3. 2012-07-10 to 2012-07-25	Spray Applicator, flat-fan	0.10 0.10 0.10	700 700 700	0.014 0.014 0.014	2012-06-22 (7 days) 2012-06-29 (7 days) 2012-07-06	35 36 38	Head Head Head Head	0.67 0.55 1.2 1.6	<0.01 <0.01 0.035 0.028	<0.01 <0.01 0.015 0.012	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	700 700	0.014 0.014	2012-06-29 (7 days) 2012-07-06	46 48	Head Head Head	0.66 0.62 1.6	<0.01 <0.01 0.028	<0.01 <0.01 0.012	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	700	0.014	2012-07-06	48	Head Head	0.62 1.6	<0.01 0.024	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2059 Trial No 12-2059-08 Spain (46230 Alginet)	Lettuce / Rivero Loose leaf variety	1. 2012-04-12 2. N/A 3. 2012-06-03 to 2012-06-23	Spray Applicator, flat-fan	0.10 0.10 0.10	600 600 800	0.017 0.015 0.013	2012-05-14 (9 days) 2012-05-23 (7 days) 2012-05-30	44 46 49	Head Head Head	0.71 0.78 0.63	<0.01 0.012 0.017	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	600 800	0.017 0.013	2012-05-23 (7 days) 2012-05-30	46 49	Head Head Head	0.51 0.99 0.53	<0.01 0.012 0.014	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	800	0.013	2012-05-30	49	Head Head	0.62 0.33	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/02 - [redacted], 2013 (M-465694-04-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	5
Country:	Germany, France, Italy Belgium, Portugal, Greece	Indoor/outdoor:	Indoor (greenhouse)
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No RA- 12-2060 Trial No 12-2060-01 Germany (42799 Leichlingen)	Lettuce / Quelio lollo bionda loose leaf variety	1. 2012-06-02 2. N/A 3. 2012-07-01 to 2012-07-15	Spray Applicator flat-fan	0.10	300	0.033	2012-06-19 (7 days)	44	Head Head	1.7 1.4	<0.01 <0.01	<0.01 <0.01	-0 7	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10	300	0.033	2012-06-26 (7 days)	46	Head	0.25	<0.01	<0.01	14	
				0.10	300	0.033	2012-07-03	48						
				0.10	300	0.033	2012-06-26 (7 days)	46	Head Head	1.5 1.4	<0.01 <0.01	<0.01 <0.01	-0 7	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	300	0.033	2012-07-03	48	Head	0.27	<0.01	<0.01	14	
				0.10	300	0.033	2012-07-03	48	Head Head	0.91 0.14	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method:

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

														1209 LOQ 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-02 France - North (37230 Fondettes)	Lettuce / Feska Lollo rosso loose leaf variety	1. 2012-03-20 2. N/A 3. 2012-04-25 to 2012-05-15	Spray Applicator, flat-fan	0.10 0.10 0.10	600 600 600	0.017 0.017 0.017	2012-04-06 (7 days) 2012-04-13 (7 days) 2012-04-20	43 45 47	Head Head Head	1.4 4.1 0.68	0.010 0.024 0.017	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	600 600	0.017 0.017	2012-04-13 (7 days) 2012-04-20	45 47	Head Head	0.59 4.6 1.1	<0.01 0.021 0.018	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2012-04-20	47	Head Head	3.3 1.5	<0.01 0.011	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-03 Italy (44042 Cento)	Lettuce / lollo rossa red variety loose leaf variety	1. 2012-04-26 2. N/A 3. 2012-05-18 to 2012-06-11	Spray Applicator, flat-fan	0.10 0.10 0.10	600 600 600	0.017 0.017 0.017	2012-05-07 (7 days) 2012-05-14 (7 days) 2012-05-21	16 41 45	Head Head Head	0.30 0.54 0.14	0.015 0.022 0.014	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	600 600	0.017 0.017	2012-05-14 (7 days) 2012-05-21	41 45	Head Head Head	0.27 0.69 0.30	<0.01 0.014 <0.01	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
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(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

				0.10	600	0.017	2012-05-21	45	Head Head	0.74 0.20	0.010 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-04 Netherlands (2988 DA Ridderkerk)	Lettuce / Lollo Bionda loose leaf variety (summer)	1. 2012-06-04 2. N/A 3. 2012-07-09 / 2012-07-16	Spray Applicator, flat-fan	0.10 0.10 0.10	300 300 300	0.033 0.033 0.033	2012-06-18 (7 days) 2012-06-25 (7 days) 2012-07-02	43 45 48	Head Head Head Head Head Head	0.60 0.54 0.31 0.47 0.45 0.21	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	-0 7 14 -0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	300 300	0.033 0.033	2012-06-25 (7 days) 2012-07-02	45 48	Head Head Head Head	0.41 0.10	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-05 Netherlands (2988 CG Ridderkerk)	Lettuce / Lollo Bionda loose leaf variety (summer)	1. 2012-06-04 2. N/A 3. 2012-07-09 to 2012-07-16	Spray Applicator, flat-fan	0.10 0.10 0.10	300 300 300	0.033 0.033 0.033	2012-06-18 (7 days) 2012-06-25 (7 days) 2012-07-02	43 45 48	Head Head Head Head Head Head	0.32 0.29 0.10 0.31 0.25 0.10	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01 <0.01 <0.01	-0 7 14 -0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg Plot T2 Method: 1209

(a) According to EEC and Codex class classification
(b) Only if relevant
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(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

														LOQ = 0.01 mg/kg
				0.108	325	0.033	2012-07-02	48	Head Head	0.19 0.11	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-06 Belgium (6210 Villers-Perwin)	Lettuce / Klausia oak leaf lettuce loose leaf variety	1. 2012-03-12 2. N/A 3. 2012-05-10 to 2012-05-25	Spray Applicator, flat-fan	0.10 0.10 0.10	650 650 650	0.015 0.015 0.015	2012-04-03 (7 days) 2012-04-10 (7 days) 2012-04-17	16 32 42	Head Head Head Head Head Head	3.8 2.6 0.57	0.024 0.022 0.018	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	650 650	0.015 0.015	2012-04-10 (7 days) 2012-04-17	32 42	Head Head Head	2.8 2.1 0.49	0.010 0.015 0.014	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	650	0.015	2012-04-17	42	Head Head	0.73 0.22	<0.01 0.010	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-07 Portugal (2040-535 Malaqueijo)	Lettuce / Invicta loose leaf variety	1. 2012-08-27 2. N/A 3. 2012-01-01 to 2012-12-31	Spray Applicator, flat-fan	0.10 0.10 0.10	400 400 500	0.025 0.025 0.020	2012-09-07 (7 days) 2012-09-14 (7 days) 2012-09-21	15 18 37	Head Head Head Head Head Head	0.39 0.74 0.18	0.030 0.028 0.034	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10	400	0.025	2012-09-14 (7 days)	18	Head Head	0.24 0.65	0.013 0.020	<0.01 <0.01	-0 7	Plot T2 Method:

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(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

				0.10	500	0.020	2012-09-21	37	Head	0.18	0.032	<0.01	14	1209 LOQ 0.01 mg/kg
				0.10	500	0.020	2012-09-21	18	Head Head	0.54 0.19	0.011 0.010	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg
Report No RA- 12-2060 Trial No 12-2060-08 Greece (GR - 60100 Aronas, Katerini)	Lettuce / Manchester Type lollo rosso loose leaf variety	1. 2012-10-28 2. N/A 3. 2012-11-30 to 2013-02-28	Spray Applicator, flat-fan	0.10 0.10 0.10	500 500 500	0.020 0.020 0.020	2012-11-12 (7 days) 2012-11-19 (7 days) 2012-11-26	14 16 19	Head Head Head	7.3 5.8 3.8	0.010 0.012 0.011	<0.01 <0.01 <0.01	-0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10 0.10	500 500 500	0.020 0.020 0.020	2012-11-19 (7 days) 2012-11-26	16 19	Head Head Head	5.8 5.0 3.1	<0.01 0.010 0.010	<0.01 <0.01 <0.01	-0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	500	0.020	2012-11-26	19	Head Head	3.3 1.6	<0.01 <0.01	<0.01 <0.01	7 14	Plot T3 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/03 - [redacted], 2015 (M-525304-02-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	4
Country:	Belgium, Germany, Netherlands, France (North), Spain, Italy and Portugal	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH) (a)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 14-2083 Trial No 14-2083-01 Belgium (6210 Villers-Perwin)	Lettuce / Sansula, Oakleaf variety Loose leaf variety	1. 2014-08-06 2. N/A 3. 2014-09-10 to 2014-09-25	Spray Applicator, flat-fan	0.10	600	0.017	2014-08-21 (6 days)	19 41	Head Head	0.49 2.1	0.013 0.015	<0.01 <0.01	-0 0	Plot T1 Method: 1209
				0.10	600	0.017	2014-08-27 (7 days)	44	Head	0.76	0.013	<0.01	7	LOQ = 0.01 mg/kg
				0.10	600	0.017	2014-09-03		Head	0.31	0.016	<0.01	14	
				0.10	600	0.017	2014-08-27 (7 days)	41 44	Head Head	0.42 1.7	0.010 0.012	<0.01 <0.01	-0 0	Plot T2 Method: 1209
				0.10	600	0.017	2014-09-03		Head Head	<u>0.73</u> 0.24	<u>0.012</u> 0.011	<u><0.01</u> <0.01	7 14	LOQ = 0.01 mg/kg
Report No 14-2083 Trial No	Lettuce /	1. 2014-05-13 2. N/A	Spray Applicator, flat-fan	0.10	600	0.017	2014-05-28 (7 days)	19 43	Head Head	0.20 1.8	<0.01 0.010	<0.01 <0.01	-0 0	Plot T1 Method: 1209
				0.10	600	0.017	2014-06-04	46	Head	0.27	0.012	<0.01	7	

(a) According to EEC and Codex class classification
(b) Only if relevant
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(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

14-2083-02 Germany (67125 Dannstadt-Schauernheim)	Cavernet, Lollo Rosso Loose leaf variety	3. 2014-06-10 to 2014-06-30		0.10	600	0.017	(7 days) 2014-06-11		Head	0.044	<0.01	<0.01	14	LOQ = 0.01 mg/kg
				0.10	600	0.017	2014-06-04 (7 days)	45	Head	0.46	<0.01	<0.01	-0	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.10	600	0.017	2014-06-11	46	Head	1.5	<0.01	<0.01	0	
									Head	0.19	<0.01	<0.01	7	
									Head	0.020	<0.01	<0.01	14	
Report No 14-2083 Trial No 14-2083-03 Netherlands (1681 ND Zwaagdijk)	Lettuce / Loka, Lollo Rossa Loose leaf variety	1. 2014-05-22 2. N/A 3. 2014-06-29 to 2014-07-06	Spray Applicator, flat-fan	0.10	500	0.020	2014-06-11 (7 days)	42	Head	2.0	0.034	<0.01	-0	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
								45	Head	4.9	0.029	<0.01	0	
				0.106	531	0.020	2014-06-18 (7 days)	47	Head	0.50	0.013	<0.01	7	
									Head	0.043	<0.01	<0.01	14	
				0.10	500	0.020	2014-06-25							
				0.10	500	0.020	2014-06-18 (7 days)	45	Head	1.3	0.025	<0.01	-0	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
								47	Head	3.6	0.030 (1)	<0.01	0	
				0.10	500	0.020	2014-06-25		Head	0.36	0.010	<0.01	7	
									Head	0.048	<0.01	<0.01	14	
Report No 14-2083 Trial No 14-2083-04 France - North (37130 Lignières de Touraine)	Lettuce / Kiribati Loose leaf variety	1. 2014-05-15 2. N/A 3. 2014-06-20 to 2014-07-10	Spray Applicator, flat-fan	0.10	600	0.017	2014-06-06 (7 days)	44	Head	0.61	0.012	<0.01	-0	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
								47	Head	2.4	0.012	<0.01	0	
				0.10	600	0.017	2014-06-13 (7 days)	48	Head	0.094	<0.01	<0.01	7	
									Head	<0.01	<0.01	<0.01	14	
				0.10	600	0.017	2014-06-20							
				0.10	600	0.017	2014-06-13 (7 days)	47	Head	0.83	<0.01	<0.01	-0	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
								48	Head	2.4	<0.01	<0.01	0	
				0.10	600	0.017	2014-06-20		Head	0.17	<0.01	<0.01	7	
									Head	<0.01	<0.01	<0.01	14	
Report No 14-2083	Lettuce / Paladin	1. 2014-04-15 2. N/A		0.10	750	0.013	2014-05-06 (8 days)	42	Head	0.72	<0.01	<0.01	-0	Plot T1 Method:
								46	Head	1.8	<0.01	<0.01	0	

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(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Trial No 14-2083-05 Spain (46230 Alginet)	Loose leaf variety	3. 2014-05-25 to 2014-06-15	Spray Applicator, flat-fan	0.10 0.10	750 750	0.013 0.013	2014-05-14 (6 days) 2014-05-20	48	Head Head	0.42 0.11	<0.01 <0.01	<0.01 <0.01	7 14	1209 LOQ = 0.01 mg/kg
				0.10 0.10	750 750	0.013 0.013	2014-05-14 (6 days) 2014-05-20	46 48	Head Head Head Head	0.72 2.1 0.49 0.21	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	-0 0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
Report No 14-2083 Trial No 14-2083-06 Italy (95100 C.da Pigno; Catania)	Lettuce / Nauplus - Canasta Loose leaf variety	1. 2014-05-16 2. N/A 3. 2014-06-22 to 2014-07-12	Spray Applicator, flat-fan	0.115 0.10 0.10	690 600 600	0.017 0.017 0.017	2014-06-09 (7 days) 2014-06-16 (7 days) 2014-06-23	18 46 47	Head Head Head Head	0.43 1.6 0.51 0.37	<0.01 <0.01 <0.01 0.010	<0.01 <0.01 <0.01 <0.01	-0 0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	600 600	0.017 0.017	2014-06-16 (7 days) 2014-06-23	46 47	Head Head Head Head	0.56 1.7 0.76 0.28	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	-0 0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
Report No 14-2083 Trial No 14-2083-07 Italy (70044 Polignano a mare)	Lettuce / Sirmai Red oak leaf lettuce Loose leaf variety	1. 2014-10-09 2. N/A 3. 2014-12-01 to 2014-12-31	Spray Applicator, flat-fan	0.10 0.10	700 700	0.014 0.014	2014-11-21 (7 days) 2014-11-28 (7 days) 2014-12-05	46 47 48	Head Head Head Head	0.17 4.4 2.0 0.99	0.012 0.012 0.014 0.016	<0.01 <0.01 <0.01 <0.01	-0 0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	700 700	0.014 0.014	2014-11-28 (7 days) 2014-12-05	47 48	Head Head Head Head	1.0 4.0 1.9 1.1	<0.01 <0.01 0.010 0.014	<0.01 <0.01 <0.01 <0.01	-0 0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
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(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 14-2083 Trial No 14-2083-08 Portugal (2590-409 Sapataria Casal Cochim)	Lettuce / Kilomas Loose leaf variety	1. 2014-07-29 2. N/A 3. 2014-09-10 to 2014-09-18	Spray Applicator, flat-fan	0.10 0.10 0.10	500 500 500	0.020 0.020 0.020	2014-08-20 (7 days) 2014-08-27 (7 days) 2014-09-03	19 41 44 41	Head Head Head Head	0.87 2.0 0.32 0.063	<0.01 <0.01 <0.01 <0.01	<0.01 <0.01 <0.01 <0.01	0 0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.10 0.10	500 500	0.020 0.020	2014-08-27 (7 days) 2014-09-03	41 44 41	Head Head Head	0.63 2.0 0.20	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	0 0 7	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
										0.042	<0.01	<0.01	14	

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/04-[redacted], 2018 (M-612853-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South) and Italy	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) Fl	M-01	M-02	PHI (d)	Remarks (e)
Report No 16-2087 Trial No 16-2087-01 France, South (31200 Toulouse)	Lettuce / Kiribati RZ Oak leaf variety	1. 2016-04-26 2. N/A 3. 2016-06-15 to 2016-06-25	Spray applicator (flat-fan)	0.100	800	0.0125	2016-05-24 (9 days)	41	Head	1.4	0.025	<0.01	-0	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.100	800	0.0125	2016-06-02 (6 days)	45 47	Head Head	4.3 1.1	0.029 0.034	<0.01 <0.01	0 7	
				0.125	1056	0.0125	2016-06-08		Head	0.36	0.033	<0.01	14	
				0.100	800	0.0125	2016-06-03 (6 days)	45 47	Head Head	1.5 3.4	0.014 0.015	<0.01 <0.01	-0 0	Plot T2 Method: 1209 LOQ = 0.01 mg/kg
				0.100	800	0.0125	2016-06-08		Head Head	<u>0.76</u> 0.17	<u>0.021</u> 0.017	<u><0.01</u> <0.01	7 14	

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 16-2087 Trial No 16-2087-02 Italy (95100 C.da Pigno; Catania)	Lettuce / Ribai Oak leaf variety	1. 2016-04-14 2. N/A 3. 2016-05-25 to 2016-06-03	Spray applicator (flat-fan)	0.100 0.100 0.100	400 600 600	0.025 0.017 0.017	2016-05-06 (7 days) 2016-05-13 (7 days) 2016-05-20	43 44 46	Head Head Head Head	1.9 4.8 1.8 0.22	0.033 0.039 0.047 0.022	<0.01 <0.01 <0.01 <0.01	0 0 7 14	Plot T1 Method: 1209 LOQ = 0.01 mg/kg
				0.100 0.100	600 600	0.017 0.017	2016-05-13 (7 days) 2016-05-20	44 47	Head Head Head Head	1.3 4.0 1.2 0.21	0.012 0.015 <u>0.028</u> 0.011	<0.01 <0.01 <u><0.01</u> <0.01	0 0 7 14	Plot T2 Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/05 - [redacted], 2018 (M-612854-02-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South), Italy, Portugal and Greece	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 16-2179 Trial No 16-2179-01 France, South (13103 St Etienne du Gres)	Lettuce / Kiribati Oak leaf variety	1. 2016-03-23 2. N/A 3. 2016-05-10 to 2016-05-25	Spray applicator (flat-fan)	0.10	600	0.017	2016-05-02	47	Head Head Head	2.2 <u>0.73</u> 0.15	<0.01 <u>0.014</u> <0.01	<0.01 <u><0.01</u> <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg
Report No 16-2179 Trial No 16-2179-02 Italy (85024 Lavello)	Lettuce / Freestar Oak leaf variety	1. 2016-04-29 2. N/A 3. 2016-07-01 to 2016-07-15	Spray applicator (flat-fan)	0.10	600	0.017	2016-06-24	48	Head Head Head	0.94 <u>0.099</u> 0.058	<0.01 <u><0.01</u> <0.01	<0.01 <u><0.01</u> <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 16-2179 Trial No 16-2179-03 Italy (93012 C.da Mignehi; Gela)	Lettuce / Ribai Oak leaf variety	1. 2016-04-14 2. N/A 3. 2016-05-27 to 2016-06-02	Spray applicator (flat-fan)	0.10	800	0.0125	2016-05-17	44	Head Head Head	2.5 1.2 0.50	<0.01 <u>0.011</u> 0.011	<0.01 <u><0.01</u> <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg
Report No 16-2179 Trial No 16-2179-04 Portugal (2590-409-Sapataria Sobral Monte Agraço)	Lettuce / Radia Oak leaf variety	1. 2016-08-11 2. N/A 3. 2016-09-26 to 2016-10-10	Spray applicator (flat-fan)	0.10	500	0.02	2016-09-12	46	Head Head Head	1.4 <u>0.092</u> 0.047	<0.01 <u><0.01</u> <0.01	0.016 <u>0.016</u> <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg
Report No 16-2179 Trial No 16-2179-05 Greece (GR - 601 00 Aronas, Katerini - Pieria)	Lettuce / Exotine (EX DIP 9410) Oak leaf variety	1. 2016-09-19 2. N/A 3. 2016-11-13 to 2016-12-23	Spray applicator (flat-fan)	0.10	600	0.017	2016-11-04	47	Head Head Head	2.0 <u>1.2</u> 0.97	<0.01 <0.01 <u>0.011</u>	<0.01 <u><0.01</u> <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/06 - [redacted], 2018 (M-613148-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (North), Germany, Netherlands and Belgium	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (l/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 16-2095 Trial No 16-2095-01 France, North (37130 Lignières de Touraine)	Lettuce / Kiribati Oak leaf variety	1. 2016-04-13 2. N/A 3. 2016-06-01 to 2016-06-20	Spray applicator (flat-fan)	0.10	600	0.0167	2016-05-19	44	Head Head Head	6.2 0.87 0.059	<0.01 0.012 <0.01	<0.01 <0.01 <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg
Report No 16-2095 Trial No 16-2095-03 Germany (67125 Dannstadt-Schauernheim)	Lettuce / Kisheri Oak leaf variety	1. 2016-05-20 2. N/A 3. 2016-07-04 to 2016-07-18	Spray applicator (flat-fan)	0.10	600	0.0167	2016-06-20	47	Head Head Head	2.5 0.17 0.044	<0.01 0.015 0.013	<0.01 <0.01 <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 16-2095 Trial No 16-2095-04 Netherlands (1756 CE Anna Paulowna)	Lettuce / Mathix (red) Oak leaf variety	1. 2016-05-24 2. N/A 3. 2016-06-22 to 2016-06-25	Spray applicator (flat-fan)	0.10	400	0.0250	2016-06-10	44	Head Head Head	4.8 0.96 0.25	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg
Report No 16-2095 Trial No 16-2095-5 Belgium (06221 Saint-Amand)	Lettuce / Sansula Oak leaf variety	1. 2016-06-10 2. N/A 3. 2016-07-13 to 2016-07-27	Spray applicator (flat-fan)	0.10	750	0.0133	2016-06-29	45	Head Head Head	3.1 0.37 0.14	<0.01 0.014 0.015	<0.01 <0.01 <0.01	0 7 14	Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/07 - [redacted], 2011 (M-404524-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	1
Country:	France (North) and Germany	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application, (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 09-2217 Trial No 09-2217-01 France, North (80320 Puzeaux Picardie)	Lettuce / Madras	1. 2009-04-29 2. N/A 3. 2009-06-22 to 2009-06-26	Knapsack sprayer / Spraying boom	0.10 0.10 	300 300 	0.033 0.033 	2009-06-03 (7 days) 2009-06-10 	43 45 	Head Head Head Head Head Head Head	0.97 10 0.07 <u>0.03</u> <0.01 <0.01	0.01 0.02 0.05 <u><0.01</u> <0.01 <0.01	<0.01 <0.01 <0.01 <u><0.01</u> <0.01 <0.01	-0 0 3 7 14 21	Method: 1209 LOQ = 0.01 mg/kg
Report No 09-2217 Trial No 09-2217-02 Germany (40764 Langenfeld-Reusrath Nordrhein-Westfalen)	Lettuce / Argentinas	1. 2009-04-25 2. N/A 3. 2009-06-08 to 2009-06-18	Knapsack sprayer / Spraying boom	0.10 0.10 	300 300 	0.033 0.033 	2009-05-20 (7 days) 2009-05-27 	41 43 	Head Head Head Head Head Head Head	0.52 2.3 1.2 <u>0.52</u> 0.08 <0.01	<0.01 <0.01 <0.01 <u><0.01</u> <0.01 <0.01	<0.01 <0.01 <0.01 <u><0.01</u> <0.01 <0.01	-0 0 3 7 14 21	Method: 1209 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.3/08 - [redacted], 2018 (M-612891-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Lettuce	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	1
Country:	United Kingdom	Indoor/outdoor:	Outdoor
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) HPLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 16-2210 Trial No 16-2210-01 United Kingdom (IP31 2NG Pakenham, Bury St Edmunds)	Lettuce / Kiribati Oak Leaf Variety	1. 2016-07-07 2. N/A 3. 2016-08-15 to 2016-09-05	Knapsack sprayer / Spraying boom	0.10	350	0.029	2016-08-10	48	Head Head Head	1.8 1.0 0.38	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	0 6 13	Method: 1209/M001 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.4/01 - [redacted] 2006 (M-281542-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Cucumber	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	4
Country:	Italy, Spain Greece, Germany, Portugal	Indoor/outdoor:	Indoor (greenhouse)
Content of active ingredient (nominal):	Fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application (interval in days)	Growth stage at treatment (BBCH)	Portion analysed	Residues (mg/kg)			PHI	Remarks
	(a)	(b)					(c)			ELC	M-01	M-02	(d)	(e)
Report No RA-2162/05 Trial No R 2005 0834/4 Italy (I-97017 Santa Croce Camerina, Sicilia)	Cucumber / Solverde	1. 2005-09-21 2. 2005-10-05 to 2005-12-15 3. 2005-10-20 to 2005-12-30	Knapsack Sprayer, spraying boom	0.1188 0.1188 0.1188	1425 1425 1425	0.008 0.008 0.008	2005-10-26 (7 days) 2005-11-02 (7 days) 2005-11-09	71 72 89	Fruit Fruit	0.04 0.04	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA-2162/05 Trial No R 2005 0861/1 Italy (I-70056 Molfetta, Bari, Puglia)	Cucumber / Locale di Polignano	1. 2005-02-27 2. 2005-04-20 to 2005-06-30 3. 2005-05-15 to 2005-07-31	Knapsack Sprayer / spraying boom	0.0938 0.1250 0.1250	1125 1500 1500	0.008 0.008 0.008	2005-10-26 (7 days) 2005-11-02 (7 days) 2005-11-09	71 72 89	Fruit Fruit	0.03 0.02	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2162/05 Trial No R 2005 0863/8 Spain (E-04738 Puebla ae Vicar, Andalucia)	Cucumber / Argos	1. 2005-03-19 2. 2005-04-10 to 2005-05-24 3. 2005-05-10 to 2005-07-15	Knapsack Sprayer / spraying boom	0.1250 0.1250 0.1250	1500 1500 1500	0.008 0.008 0.008	2005-05-09 (7 days) 2005-05-16 (7 days) 2005-05-23	72 73 74	Fruit Fruit	0.06 0.04	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2162/05 Trial No R 2005 0864/6 Spain (E-11540 Sanlucar de Barrameda, Monte Algaida, Andalucia)	Cucumber / Alanis F1 Hibrido	1. 2005-02-10 2. 2005-03-20 to 2005-05-30 3. 2005-04-18 to 2005-06-30	Knapsack Sprayer / spraying boom	0.1040 0.1000 0.1125	975 1200 1350	0.011 0.008 0.008	2005-04-20 (7 days) 2005-04-27 (6 days) 2005-05-03	72 81 89	Fruit Fruit	0.04 0.03	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA-2162/05 Trial No R 2005 0865/4 Greece (GR-57006 Vasilika, Northern Greece - Macedonia)	Cucumber / Z14	1. 2005-08-14 2. 2005-09-01 to 2005-10-26 3. 2005-09-25 to 2005-11-10	Knapsack Sprayer / spraying boom	0.0906 0.1125 0.1250	1087.5 1350 1500	0.008 0.008 0.008	2005-09-13 (7 days) 2005-09-20 (7 days) 2005-09-27	65 68 83	Fruit Fruit	0.12 0.09	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2162/05 Trial No R 2005 0866/2 Germany (D-42799 Leichlingen, Nordrhein-Westfalen)	Cucumber / Aramon	1. 2005-06-05 2. 2005-06-20 to 2005-08-20 3. 2005-07-10 to 2005-09-15	Knapsack Sprayer / spraying boom	0.1000 0.1250 0.1250	1200 1500 1500	0.008 0.008 0.008	2005-06-29 (7 days) 2005-07-06 (7 days) 2005-07-13	69 71 72	Fruit Fruit	0.05 0.03	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg
Report No RA-2162/05 Trial No R 2005 0867/0 Germany (D-42799 Leichlingen, Nordrhein-Westfalen)	Cucumber / Indira	1. 2005-04-28 2. 2005-05-12 to 2005-08-15 3. 2005-06-10 to 2005-08-30	Knapsack Sprayer / spraying boom	0.1125 0.1250 0.1250	1350 1500 1500	0.008 0.008 0.008	2005-05-30 (7 days) 2005-06-06 (7 days) 2005-06-13	71 72 73	Fruit Fruit	0.03 0.02	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No RA-2162/05 Trial No R 2005 0868/9 Portugal (P-2560 Torres Vedras, Ribatejo e Oeste)	Cucumber / Caman	1. 2005-03-30 2. 2005-04-04 to 2005-05-20 3. 2005-05-16 to 2005-06-25	Knapsack Sprayer / spraying boom	0.0625 0.0831 0.1250	750 997.5 1500	0.008 0.008 0.008	2005-05-05 (7 days) 2005-05-12 (7 days) 2005-05-19	73 77 87	Fruit Fruit	0.09 0.08	<0.01 <0.01	<0.01 <0.01	0 1	Analytical method 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.4/02 - [redacted], 2008 (M-307724-01-2)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Cucumber	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	1
Country:	Italy	Indoor/outdoor:	Indoor (greenhouse)
Content of active ingredient (nominal):	fluopicolide (62.5 g/L) and Propamocarb hydrochloride (625 g/L)	Other active ingredients in the formulation:	Propamocarb hydrochloride
Formulation type (e.g. WG):	SC		
Commercial product name:	687.5 SC	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate kg a.s./ha	Water (L/ha)	kg a.s./hL	Dates of application (interval in days) (c)	Growth stage at treatment (BBCH)	Portion analysed (a)	Residues (mg/kg) HLC	M-01	M-02	PHI (d)	Remarks (e)
Report No RA-2162/05 Trial No R 2007 0333/3 Italy (I-70056 Molfetta, BA, Puglia)	Cucumber / Sarig	1. 2007-03-25 2. 2007-04-20 to 2007-06-20 3. 2007-05-15 to 2007-07-10	Knapsack Sprayer spraying boom	0.1250 0.1250 0.1250	1500 1500 1500	0.008 0.008 0.008	2007-05-21 (7 days) 2007-05-28 (7 days) 2007-06-04	77 83 86	Fruit Fruit	0.03 0.02	<0.01 <0.01	0.01 <0.01	0 1	Analytical method: 00782/M004 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.5/01 - [redacted] 2010 (M-390353-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Oilseed rape	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (North), Germany and The Netherlands	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)	Other active ingredients in the formulation:	Clothianidin and fluoxastrobin
Formulation type (e.g. WG):	FS		
Commercial product name:	FS 510	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate			Dates of application, (interval in days) (c)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg)			PHI (d)	Remarks (e)
				g a.s./ha	Water (L/ha)	g a.s./kg seed				EEC	M-01	M-02		
Report No 08-2217 Trial No 08-2217-01 Germany (D-51399 Burscheid)	Winter rape / Exocett	1. 2008-08-29 2. 2009-04-10 to 2009-04-30 3. 2009-07-14	Seed treatment	90	-	1.5	-	00 89	Seed (treated) Seed	1500 <0.01	<0.2 <0.01	<0.2 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg
Report No 08-2217 Trial No 08-2217-02 Netherlands (NL-9687 Nieuw Beerta)	Winter rape / Exocett	1. 2008-08-28 2. 2009-04-15 to 2009-05-15 3. 2009-07-27 to 2009-08-03	Seed treatment	9	-	1.5	-	00 89	Seed (treated) Seed	1500 <0.01	<0.2 <0.01	<0.2 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 08-2217 Trial No 08-2217-03 France, North (F-37310 Chambourg sur Indre)	Winter rape / Exocett	1. 2008-09-02 2. 2009-04-14 to 2009-05-05 3. 2009-07-03 to 2009-07-09	Seed treatment	8.4	-	1.4	-	00 19 89 89	Seed (treated) Green material Seed Rest of plant	1400 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg
Report No 08-2217 Trial No 08-2217-04 Germany (D-53913 Swistal-Miel)	Winter rape / Exocett	1. 2008-09-05 2. N/A 3. 2009-07-20 to 2009-07-30	Seed treatment	10.8	-	1.6	-	00 19 89 89	Seed (treated) Green material Seed Rest of plant	1600 0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.5/02 - [redacted] 2010 (M-390357-01-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Oilseed rape	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	2
Country:	France (South), Spain	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)	Other active ingredients in the formulation:	Clothianidin and fluoxastrobin
Formulation type (e.g. WG):	FS		
Commercial product name:	FS 510	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate g a.s./ha	Water (L/ha)	g a.s./kg seed	Dates of application, (interval in days) (c)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg) FLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 08-2218 Trial No 08-2218-01 Spain (E-17185 Vilobi d'Onyar)	Winter rape / Exocett	1. 2008-10-16 2. 2009-04-01 to 2009-04-28 3. 2009-06-15 to 2009-06-27	Seed treatment	10.8	-	1.8	-	00 89	Seed (treated) Seed	1800 <0.01	<0.2 <0.01	<0.2 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg
Report No 08-2218 Trial No 08-2218-02 France (F-31620 Villineuve les Bouloc)	Winter rape / Exocett	1. 2008-09-03 2. 2009-03-25 to 2009-05-08 3. 2009-06-25 to 2009-07-01	Seed treatment	10.8	-	1.8	-	00 89	Seed (treated) Seed	1800 <0.01	<0.2 <0.01	<0.2 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Report No 08-2218 Trial No 08-2218-03 Spain (E-41310 Brenes, Sevilla)	Winter rape / Exocett	1. 2008-10-30 2. 2009-03-20 to 2009-04-20 3. 2009-05-15 to 2009-06-20	Seed treatment	9.6	-	1.6	-	00 19 89 89	Seed (treated) Green material Seed Rest of plant	1600 <0.01 <0.01 0.01	<0.2 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg
Report No 08-2218 Trial No 08-2218-04 France (F-69480 Amberieux)	Winter rape / Exocett	1. 2008-09-16 2. 2009-04-10 to 2009-05-06 3. 2009-06-29 to 2009-07-05	Seed treatment	10.2	-	1.7	-	00 19 89 89	Seed (treated) Green material Seed Rest of plant	1700 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	<0.2 <0.01 <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg

(a) According to EEC and Codex class classification
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (underline label PHI)
(e) Remarks may include; climatic conditions, reference to analytical methods and LOQ

Reference	**CA 6.3.5/03 - [redacted] 2010 (M-396237-02-1)**		
Active ingredient:	Fluopicolide	Producer of commercial product:	Bayer CropScience AG
Crop/Crop group:	Oilseed rape	Submission date:	-
Responsible body for reporting:	Bayer CropScience AG	Pages:	1
Country:	Germany, Poland	Indoor/outdoor:	outdoor
Content of active ingredient (nominal):	clothianidin (300 g/L), fluopicolide (120 g/L) and fluoxastrobin (90 g/L)	Other active ingredients in the formulation:	Clothianidin and fluoxastrobin
Formulation type (e.g. WG):	FS		
Commercial product name:	FS 510	Residues calculated as:	Fluopicolide, Metabolite M-01 and Metabolite M-02

1	2	3	4	5			6	7	8	9			10	11
Report No Trial No Location (inc postcode)	Crop Variety (a)	Dates of… 1. Sowing/planting 2. Flowering 3. Harvest (b)	Method of application	Application rate g a.s./ha	Water (L/ha)	g a.s./kg seed	Dates of application, (interval in days) (c)	Growth stage at sampling (BBCH)	Portion analysed (a)	Residues (mg/kg) PLC	M-01	M-02	PHI (d)	Remarks (e)
Report No 09-2225 Trial No 09-2225-01 Germany (21739 Dollern Lower-Saxony)	Winter rape / Senator	1. 2009-04-23 2. 2009-07-15 to 2009-08-15 3. 2009-09-17	Seed treatment	9.1		1.52		00 19 89	Seed (treated) Green material Seed	1523 <0.01 <0.01	- <0.01 <0.01	- <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg
Report No 09-2225 Trial No 08-09-2225-02 Poland (64-560 Ostrorog Wielkopolska)	Winter rape / Senator	1. 2009-04-16 2. 2009-06-03 to 2009-06-20 3. 2009-08-28	Seed treatment	8.6		1.43		00 19 89	Seed (treated) Green material Seed	1433 0.02 <0.01	- <0.01 <0.01	- <0.01 <0.01	-	Analytical method: 00782/M005 LOQ = 0.01 mg/kg

(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Either growth stage description or BBCH Code
G greenhouse F field
(e) Days after last application (Label pre-harvest interval, PHI, underline)
(f) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
(g) Study reference
* prior to last treatment
(h) Formulation type
(i) Application method
(j) Method information
(k) LOQ
** residue in control
(l) Method validation
(m) Storage (max)
! based on date of analysis
P based on production date
no data available

APPENDIX 3 - PRIMo model

The consumer risk assessments for fluopicolide and M-01 were completed using the EFSA PRIMo 3.1 calculator.

In the case of the TMDI (theoretical maximum daily intake) calculation for fluopicolide, the proposed MRL values for each commodity (as given within Table 6.7.2-1). The output of the TMDI (relevant to chronic consumer exposure) is given within Figure A3- 1.

NEDI (national estimated daily intake) and NESTI (national estimate of short-term intake) calculations were also undertaken for both fluopicolide and M-01. These calculations are representative of the chronic and acute exposures for consumers. The inputs for these calculations were based on several sources:

- Supervised residue trials data for the treated (primary) commodities (refer to section CA 6.3).
- Data from the residues in succeeding crops studies (refer to section CA 6.6).
- The STMR and HR values reported for the commodities listed within Table B.1.2.1 and Table B.1.2.2. of the Article 12 MRL review report for fluopicolide (EFSA Journal 2019;17(7):5748).

The highest residue values from each of these sources was used as input within the respective calculations for fluopicolide and M-01. Consolidated tables of the input values are given within Table A3- 1 (for fluopicolide) and Table A3- 2 (for M-01). The output of the NEDI and NESTI calculations are presented within Figure A3- 2 (for fluopicolide) and Figure A3- 3 (for M-01).

Conclusions on the results of the consumer risk assessment for fluopicolide and M-01 are provided within section CA 6.9 of this document.

Table A3- 1 Input values for the fluopicolide NEDI and NESTI calculations

Commodity / commodity group(s)	Input value (mg/kg)		Comment / source
	STMR-RAC	HR-RAC	
Citrus fruit	0.01	0.01	No data – set at LOQ
Tree nuts	0.01	0.01	No data – set at LOQ
Pome fruit	0.01	0.01	No data – set at LOQ
Stone fruit	0.01	0.01	No data – set at LOQ
Table grapes	0.36	1.20	EFSA Article 12 report
Wine grapes	0.36	1.20	EFSA Article 12 report
Strawberries	0.03	0.04	Rotational crop data (CA 6.6.2)
Blackberries	0.52	1.10	EFSA Article 12 report
Cane fruit	0.01	0.01	No data – set at LOQ
Other small fruit / berries	0.01	0.01	No data – set at LOQ
Miscellaneous fruit	0.01	0.01	No data – set at LOQ
Root and tuber vegetables	0.11	0.13	Rotational crop data (CA 6.6.2)
Carrots	0.11	0.13	Rotational crop data (CA 6.6.2)
Celeriac	0.11	0.13	Rotational crop data (CA 6.6.2)
Horseradish	0.11	0.13	Rotational crop data (CA 6.6.2)
Jerusalem artichokes	0.11	0.13	Rotational crop data (CA 6.6.2)
Parsnips	0.11	0.13	Rotational crop data (CA 6.6.2)
Parsley roots	0.11	0.13	Rotational crop data (CA 6.6.2)
Radishes	0.11	0.13	Rotational crop data (CA 6.6.2)
Salsifies	0.11	0.13	Rotational crop data (CA 6.6.2)
Swedes	0.11	0.13	Rotational crop data (CA 6.6.2)
Turnips	0.11	0.13	Rotational crop data (CA 6.6.2)
Garlic	0.03	0.21	EFSA Article 12 report
Onions	0.03	0.21	EFSA Article 12 report
Shallots	0.03	0.21	EFSA Article 12 report

Commodity / commodity group(s)	Input value (mg/kg)		Comment / source
	STMR-RAC	HR-RAC	
Spring onions	0.25	0.82	EFSA Article 12 report
Tomatoes	0.12	0.23	EFSA Article 12 report
Sweet / bell peppers	0.13	0.52	EFSA Article 12 report
Cucumbers	0.04	0.09	Primary crop data (CA 6.3.4)
Gherkins	0.04	0.09	Extrapolation from cucumber primary data
Courgettes	0.04	0.09	Extrapolation from cucumber primary data
Melons	0.03	0.04	Rotational crop data (CA 6.6.2)
Pumpkins	0.03	0.04	Rotational crop data (CA 6.6.2)
Watermelons	0.03	0.04	Rotational crop data (CA 6.6.2)
Sweet corn	0.030	0.040	Rotational crop data (CA 6.6.2)
Broccoli	0.01	0.11	EFSA Article 12 report
Cauliflower	0.01	0.11	EFSA Article 12 report
Brussels sprouts	0.04	0.13	EFSA Article 12 report
Head cabbage	0.02	0.18	EFSA Article 12 report
Chinese cabbages	0.75	0.84	EFSA Article 12 report
Kales	0.75	0.84	EFSA Article 12 report
Kohlrabies	0.01	0.02	EFSA Article 12 report
Lamb's lettuce	0.40	4.30	EFSA Article 12 report
Lettuce	0.69	3.40	EFSA Article 12 report
Escaroles / endives	0.10	1.20	EFSA Article 12 report
Cresses, spouts, shoots	0.40	4.30	EFSA Article 12 report
Land cresses	0.40	4.30	EFSA Article 12 report
Roman rocket	0.40	3.10	EFSA Article 12 report
Red mustards	0.40	4.30	EFSA Article 12 report
Baby leaf crops	0.40	4.30	EFSA Article 12 report
Spinaches	0.40	3.10	EFSA Article 12 report
Purslanes	0.40	3.10	EFSA Article 12 report
Chards/ beet leaves	0.40	3.10	EFSA Article 12 report
Chervil	1.09	4.90	EFSA Article 12 report
Chives	1.09	4.90	EFSA Article 12 report
Celery leaves	1.09	4.90	EFSA Article 12 report
Parsley	1.09	4.90	EFSA Article 12 report
Sage	1.09	4.90	EFSA Article 12 report
Rosemary	1.09	4.90	EFSA Article 12 report
Thyme	1.09	4.90	EFSA Article 12 report
Basil and edible flowers	1.09	4.90	EFSA Article 12 report
Bay leaves	1.09	4.90	EFSA Article 12 report
Tarragon	1.09	4.90	EFSA Article 12 report
Legume vegetables	0.01	0.01	Rotational crop data (CA 6.6.2)
Leeks	0.25	0.82	EFSA Article 12 report
Stem veg. (except leeks)	0.04	0.11	Rotational crop data (CA 6.6.2)
Fungi	0.01	0.01	No data – set at LOQ
Pulses	0.01	0.01	Rotational crop data (CA 6.6.2)
Rapeseed	0.03	0.05	Rotational crop data (CA 6.6.2)
Oilseeds / oil fruit	0.03	0.05	Rotational crop data (CA 6.6.2)
Cereal grains	0.09	0.13	Rotational crop data (CA 6.6.2)
Herbal infusions from dried flowers and dried leaves	0.06	1.02	Rotational crop data (CA 6.6.2)
Herbal infusions from roots	0.80	4.96	EFSA Article 12 report
Spices, seeds, fruit, bark, buds, aril, stigma	0.05	0.10	Rotational crop data (CA 6.6.2)
Spices rhizome	0.11	0.13	Rotational crop data (CA 6.6.2)
Hops	0.05	0.08	EFSA Article 12 report

Commodity / commodity group(s)	Input value (mg/kg)		Comment / source
	STMR-RAC	HR-RAC	
Sugar beet roots	0.11	0.13	Rotational crop data (CA 6.6.2)
Sugar cane	0.04	0.11	Rotational crop data (CA 6.6.2)
Chicory	0.11	0.13	Rotational crop data (CA 6.6.2)
Other sugar plants	0.11	0.13	Rotational crop data (CA 6.6.2)
Livestock meat	0.02	0.02	EFSA Article 12 report -set at LOQ
Livestock fat	0.05	0.05	EFSA Article 12 report -set at LOQ
Livestock liver	0.05	0.05	EFSA Article 12 report -set at LOQ
Livestock kidney	0.05	0.05	EFSA Article 12 report -set at LOQ
Milk	0.01	0.01	EFSA Article 12 report -set at LOQ
Birds eggs	0.01	0.01	EFSA Article 12 report -set at LOQ
Honey	0.05	0.05	Default MRL for honey

Table A3- 2 Input values for the M-01 NEDI and NESTI calculations

Commodity / commodity group(s)	Input value (mg/kg)		Comment / source
	STMR-RAC	HR-RAC	
Citrus fruit	0.01	0.01	No data – set at LOQ
Tree nuts	0.01	0.01	No data – set at LOQ
Pome fruit	0.01	0.01	No data – set at LOQ
Stone fruit	0.01	0.01	No data – set at LOQ
Table grapes	0.015	0.05	EFSA Article 12 report
Wine grapes	0.015	0.05	EFSA Article 12 report
Strawberry	0.03	0.045	Rotational crop data (CA 6.6.2)
Blackberries	0.01	0.01	EFSA Article 12 report
Cane fruit	0.01	0.01	No data – set at LOQ
Other small fruit / berries	0.01	0.01	No data – set at LOQ
Miscellaneous fruit	0.01	0.01	No data – set at LOQ
Root and tuber crops	0.02	0.07	Rotational crop data (CA 6.6.2)
Bulb vegetables	0.01	0.07	Rotational crop data (CA 6.6.2)
Solancea	0.03	0.045	Rotational crop data (CA 6.6.2)
Cucurbits	0.02	0.08	Rotational crop data (CA 6.6.2)
Sweetcorn	0.03	0.045	Rotational crop data (CA 6.6.2)
Broccoli	0.02	0.05	EFSA Article 12 report
Cauliflowers	0.02	0.05	EFSA Article 12 report
Brussels sprouts	0.02	0.05	EFSA Article 12 report
Head cabbages	0.02	0.05	EFSA Article 12 report
Chinese cabbages	0.03	0.06	EFSA Article 12 report
Kales	0.03	0.06	EFSA Article 12 report
Kohlrabi	0.02	0.05	EFSA Article 12 report
Leaf vegetables and herbs	0.08	0.26	Rotational crop data (CA 6.6.2)
Stem vegetables	0.01	0.07	Rotational crop data (CA 6.6.2)
Pulses	0.01	0.02	Rotational crop data (CA 6.6.2)
Oilseeds and oilfruits	0.08	0.25	Rotational crop data (CA 6.6.2)
Cereal grain	0.02	0.09	Rotational crop data (CA 6.6.2)
Herbal infusions from flowers	0.01	0.04	EFSA Article 12 report
Herbal infusions from leaves and herbs	0.01	0.04	EFSA Article 12 report
Herbal infusions from roots	0.40	2.48	EFSA Article 12 report
Hops	0.07	0.12	EFSA Article 12 report
Bark spices	0.08	0.26	Rotational crop data (CA 6.6.2)
Bud spices	0.08	0.26	Rotational crop data (CA 6.6.2)
Flower pistil spices	0.08	0.26	Rotational crop data (CA 6.6.2)

Commodity / commodity group(s)	Input value (mg/kg)		Comment / source
	STMR-RAC	HR-RAC	
Spices rhizome	0.02	0.07	Rotational crop data (CA 6.6.2)
Sugar beet roots	0.01	0.01	EFSA Article 12 report
Livestock muscle	0.02	0.02	EFSA Article 12 report
Livestock fat	0.05	0.05	EFSA Article 12 report
Livestock kidney	0.05	0.05	EFSA Article 12 report
Livestock liver	0.05	0.05	EFSA Article 12 report
Milk	0.01	0.01	EFSA Article 12 report
Bird eggs	0.02	0.02	EFSA Article 12 report
Honey	0.01	0.01	EFSA Article 12 report

Figure A3- 1. Theoretical maximum daily intake (TMDI) for fluopicolide using EFSA PRIMo 3.1

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Fluopicolide

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0.08	ARfD (mg/kg bw):	0.15
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2019	Year of evaluation:	2019

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments: The ADI is based on the NOAEL obtained for M-05 (AE 1344122) from the rat 28-day study (0.25 mg/kg bw/d) with an additional safety factor of 2 applied.

In the absence of and ARfD value, the acute dietary intake assessment for consumers has been completed using the calculated ADI for M-05 (AE 1344122).

Normal mode

Chronic risk assessment: JMPR methodology (EDI/TMDI)

No of diets exceeding the ADI: –

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
	26%	NL toddler	21.20	5%	Spinaches	4%	Table grapes	3%	Maize/corn		
	21%	GEMS/Food G06	16.51	4%	Tomatoes	3%	Wheat	3%	Table grapes		
	17%	GEMS/Food G10	13.58	4%	Lettuces	2%	Tomatoes	1%	Wheat		
	17%	GEMS/Food G07	13.35	4%	Wine grapes	2%	Lettuces	2%	Wheat		
	17%	GEMS/Food G08	13.28	3%	Wine grapes	2%	Lettuces	2%	Wheat		
	16%	NL child	12.51	3%	Sugar beet roots	3%	Table grapes	2%	Spinaches		
	16%	DE child	12.45	3%	Table grapes	2%	Wheat	2%	Spinaches		
	15%	GEMS/Food G11	12.34	3%	Wine grapes	1%	Potatoes	1%	Wheat		
	15%	PT general	12.04	6%	Wine grapes	2%	Potatoes	1%	Wheat		
	15%	IE adult	11.84	3%	Wine grapes	1%	Sweet potatoes	1.0%	Lettuces		
	15%	GEMS/Food G15	11.79	3%	Wine grapes	2%	Wheat	1%	Tomatoes		
	15%	RO general	11.77	4%	Wine grapes	2%	Tomatoes	2%	Wheat		
	13%	SE general	10.50	5%	Lettuces	2%	Potatoes	1%	Wheat		
	13%	IT adult	10.41	4%	Lettuces	2%	Other lettuce and other salad plants	2%	Wheat		
	13%	IT toddler	10.10	3%	Lettuces	2%	Wheat	2%	Tomatoes		
	12%	FR child 3 15 yr	9.94	2%	Wheat	1%	Sugar beet roots	1%	Other lettuce and other salad plant		
	12%	ES adult	9.85	6%	Lettuces	1%	Wine grapes	1.0%	Tomatoes		
	12%	FR adult	9.81	6%	Wine grapes	2%	Other lettuce and other salad plants	0.8%	Wheat		
	12%	ES child	9.30	5%	Lettuces	2%	Wheat	1%	Tomatoes		
	11%	DE women 14-50 yr	8.98	2%	Wine grapes	2%	Sugar beet roots	1%	Lettuces		
	11%	DK child	8.69	2%	Rye	2%	Wheat	2%	Lettuces		
	11%	DE general	8.44	1%	Wine grapes	2%	Sugar beet roots	1%	Lettuces		
	10%	NL general	8.33	1%	Wine grapes	1%	Spinaches	1%	Sugar beet roots		
	10%	FR toddler 1 3 yr	7.69	1%	Spinaches	1%	Wheat	1%	Sugar beet roots		
	8%	UK vegetarian	6.58	2%	Wine grapes	2%	Lettuces	0.8%	Tomatoes		
	8%	UK toddler	6.39	1%	Wheat	1%	Potatoes	1%	Sugar beet roots		
	8%	FI 3 yr	6.10	2%	Potatoes	0.7%	Tomatoes	0.6%	Cucumbers		
	7%	UK adult	5.96	3%	Wine grapes	1%	Lettuces	0.6%	Wheat		
	7%	FR infant	5.85	2%	Spinaches	0.7%	Potatoes	0.7%	Cauliflowers		
	7%	DK adult	5.59	2%	Wine grapes	1%	Lettuces	0.6%	Tomatoes		
	7%	UK infant	5.43	1%	Potatoes	1.0%	Wheat	1.0%	Milk: Cattle		
	7%	FI 6 yr	5.22	1%	Potatoes	0.9%	Lettuces	0.5%	Tomatoes		
	5%	FI adult	4.34	2%	Lettuces	0.8%	Wine grapes	0.7%	Tomatoes		
	5%	PL general	3.91	1%	Potatoes	1%	Tomatoes	0.8%	Table grapes		
	4%	LT adult	3.55	1%	Potatoes	0.8%	Tomatoes	0.7%	Lettuces		
	2%	IE child	1.94	0.4%	Wheat	0.2%	Potatoes	0.2%	Broccoli		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Fluopicolide is unlikely to present a public health concern.

Figure A3- 2 Results of the NEDI and NESTI calculations for fluopicolide

European Food Safety Authority
EFSA PRIMo revision 3.1; 2019/03/19

Fluopicolide

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0.08	ARfD (mg/kg bw):	0.18
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2019	Year of evaluation:	2019

Input values

Details - chronic risk assessment | Supplementary results chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments: The ADI is based on the NOAEL obtained for M-05 (AE 1344122) from the rat 28-day study (0.25 mg/kg bw/d) with an additional safety factor of 3 applied.

In the absence of and ARfD value, the acute dietary intake assessment for consumers has been completed using the calculated ADI for M-05 (AE 1344122).

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
6%	NL toddler	5.18	1%	Milk: Cattle	0.8%	Maize/corn	0.7%	Sugar beet roots		
4%	NL child	3.31	0.8%	Sugar beet roots	0.6%	Milk: Cattle	0.5%	Potatoes		
4%	GEMS/Food G06	2.94	0.8%	Wheat	0.5%	Tomatoes	0.5%	Table grapes		
3%	DE child	2.69	0.6%	Table grapes	0.5%	Milk: Cattle	0.5%	Wheat		
3%	GEMS/Food G07	2.60	0.7%	Wine grapes	0.5%	Potatoes	0.5%	Wheat		
3%	PT general	2.58	1%	Wine grapes	0.5%	Potatoes	0.4%	Wheat		
3%	RO general	2.58	0.8%	Wine grapes	0.6%	Wheat	0.5%	Potatoes		
3%	GEMS/Food G08	2.54	0.8%	Potatoes	0.5%	Wine grapes	0.5%	Wheat		
3%	GEMS/Food G11	2.53	0.5%	Potatoes	0.5%	Wine grapes	0.4%	Wheat		
3%	GEMS/Food G10	2.47	0.4%	Wheat	0.4%	Potatoes	0.3%	Lettuces		
3%	GEMS/Food G15	2.45	0.5%	Wheat	0.5%	Potatoes	0.5%	Wine grapes		
3%	FR child 3 15 yr	2.44	0.6%	Milk: Cattle	0.5%	Wheat	0.5%	Sugar beet roots		
3%	IE adult	2.33	0.8%	Wine grapes	0.5%	Sweet potatoes	0.3%	Potatoes		
3%	DK child	2.15	0.6%	Rye	0.5%	Wheat	0.3%	Potatoes		
3%	FR toddler 2 3 yr	2.12	0.7%	Milk: Cattle	0.4%	Sugar beet roots	0.3%	Wheat		
3%	SE general	2.10	0.6%	Potatoes	0.4%	Wheat	0.3%	Lettuces		
3%	UK infant	2.08	1.0%	Milk: Cattle	0.4%	Potatoes	0.3%	Wheat		
3%	DE women 14-50 yr	2.03	0.6%	Sugar beet roots	0.4%	Wine grapes	0.3%	Milk: Cattle		
2%	UK toddler	1.99	0.5%	Milk: Cattle	0.5%	Potatoes	0.4%	Wheat		
2%	DE general	1.97	0.6%	Sugar beet roots	0.4%	Wine grapes	0.3%	Milk: Cattle		
2%	NL general	1.93	0.4%	Sugar beet roots	0.3%	Potatoes	0.3%	Wine grapes		
2%	FR adult	1.75	1%	Wine grapes	0.3%	Wheat	0.1%	Milk: Cattle		
2%	ES child	1.71	0.5%	Wheat	0.4%	Lettuces	0.3%	Milk: Cattle		
2%	IT toddler	1.51	0.7%	Wheat	0.3%	Lettuces	0.2%	Tomatoes		
2%	ES adult	1.39	0.5%	Lettuces	0.3%	Wheat	0.2%	Wine grapes		
2%	FR 3 yr	1.28	0.6%	Potatoes	0.1%	Wheat	0.1%	Carrots		
2%	IT adult	1.26	0.5%	Wheat	0.3%	Lettuces	0.2%	Tomatoes		
2%	FR infant	1.25	0.4%	Milk: Cattle	0.3%	Potatoes	0.2%	Sugar beet roots		
1%	UK vegetarian	1.14	0.4%	Wine grapes	0.2%	Wheat	0.2%	Potatoes		
1%	UK adult	1.13	0.5%	Wine grapes	0.2%	Potatoes	0.2%	Wheat		
1%	DK adult	1.12	0.4%	Wine grapes	0.2%	Potatoes	0.1%	Milk: Cattle		
1%	FI 6 yr	1.07	0.3%	Potatoes	0.1%	Wheat	0.1%	Carrots		
1%	LT adult	0.93	0.4%	Potatoes	0.1%	Rye	0.1%	Wheat		
1.0%	FI adult	0.79	0.2%	Potatoes	0.1%	Coffee beans	0.1%	Wine grapes		
1.0%	PL general	0.79	0.5%	Potatoes	0.1%	Table grapes	0.1%	Tomatoes		
0.5%	IE child	0.37	0.1%	Wheat	0.1%	Milk: Cattle	0.1%	Potatoes		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) is below the ADI.
The long-term intake of residues of fluopicolide is unlikely to present a public health concern.

Figure A3- 3 Results of the NEDI and NESTI calculations for M-01

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

M-01

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0.05	ARfD (mg/kg bw):	0.3
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2019	Year of evaluation:	2019

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
5%	NL toddler	2.39	2%	Milk: Cattle	0.3%	Maize/corn	0.2%	Apples		
2%	NL child	1.25	0.9%	Milk: Cattle	0.2%	Sugar beet roots	0.2%	Wheat		
2%	UK infant	1.14	2%	Milk: Cattle	0.1%	Potatoes	0.1%	Wheat		
2%	DE child	1.04	0.8%	Milk: Cattle	0.2%	Apples	0.2%	Wheat		
2%	FR toddler 2 3 yr	1.02	1%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes		
2%	GEMS/Food G11	1.02	0.6%	Soyabeans	0.3%	Milk: Cattle	0.2%	Potatoes		
2%	FR child 3 15 yr	1.01	0.9%	Milk: Cattle	0.2%	Wheat	0.1%	Sugar beet roots		
2%	GEMS/Food G10	0.98	0.5%	Soyabeans	0.2%	Milk: Cattle	0.2%	Wheat		
2%	GEMS/Food G08	0.94	0.3%	Soyabeans	0.2%	Milk: Cattle	0.2%	Wheat		
2%	GEMS/Food G07	0.91	0.3%	Soyabeans	0.3%	Milk: Cattle	0.2%	Wheat		
2%	GEMS/Food G15	0.88	0.3%	Milk: Cattle	0.3%	Soyabeans	0.2%	Wheat		
2%	GEMS/Food G06	0.87	0.3%	Wheat	0.2%	Tomatoes	0.2%	Soyabeans		
2%	UK toddler	0.80	0.8%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes		
2%	DK child	0.78	0.5%	Milk: Cattle	0.2%	Rye	0.2%	Wheat		
2%	RO general	0.76	0.5%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes		
1%	ES child	0.73	0.5%	Milk: Cattle	0.2%	Wheat	0.1%	Olives for oil production		
1%	SE general	0.72	0.5%	Milk: Cattle	0.2%	Bovine: Muscle/meat	0.2%	Potatoes		
1%	IE adult	0.62	0.2%	Milk: Cattle	0.1%	Sweet potatoes	0.1%	Wheat		
1%	DE women 14-50 yr	0.61	0.5%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Wheat		
1%	DE general	0.60	0.5%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Wheat		
1%	NL general	0.60	0.3%	Milk: Cattle	0.1%	Potatoes	0.1%	Wheat		
1%	FR infant	0.56	0.7%	Milk: Cattle	0.1%	Potatoes	0.0%	Carrots		
0.9%	ES adult	0.44	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Lettuces		
0.9%	PT general	0.43	0.2%	Potatoes	0.2%	Wheat	0.1%	Wine grapes		
0.8%	FR adult	0.38	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Wine grapes		
0.7%	IT toddler	0.35	0.3%	Wheat	0.1%	Tomatoes	0.1%	Other cereals		
0.6%	FI 3 yr	0.32	0.2%	Potatoes	0.0%	Wheat	0.0%	Cucumbers		
0.6%	LT adult	0.32	0.2%	Milk: Cattle	0.1%	Potatoes	0.0%	Rye		
0.6%	DK adult	0.31	0.2%	Milk: Cattle	0.1%	Potatoes	0.0%	Wheat		
0.6%	IT adult	0.28	0.2%	Wheat	0.1%	Tomatoes	0.1%	Lettuces		
0.5%	UK vegetarian	0.27	0.1%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes		
0.5%	FI adult	0.25	0.2%	Coffee beans	0.0%	Potatoes	0.0%	Tomatoes		
0.5%	FI 6 yr	0.25	0.2%	Potatoes	0.0%	Wheat	0.0%	Cucumbers		
0.5%	UK adult	0.25	0.1%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes		
0.3%	PL general	0.17	0.1%	Potatoes	0.1%	Tomatoes	0.0%	Apples		
0.3%	IE child	0.16	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes		

Conclusion

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of M-01 is unlikely to present a public health concern.

Acute risk assessment /children	Acute risk assessment / adults / general population	Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults	Hide IESTI new calculations	Show IESTI new calculations

The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

IESTI new calculations:
The calculation is performed with the MRL and the peeling/processing factor (PF), taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.
Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI new Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI new Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI (children)

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Melons	0 / 0.08	12
4%	Potatoes	0 / 0.07	11
3%	Escaroles/broad-leaved	0 / 0.26	10
3%	Witloofs/Belgian endives	0 / 0.26	10
3%	Lettuces	0 / 0.26	9.9
3%	Watermelons	0 / 0.08	9.8
2%	Spinaches	0 / 0.26	5.9
2%	Cucumbers	0 / 0.08	5.2
1%	Carrots	0 / 0.07	4.4
1%	Leeks	0 / 0.07	4.1
1%	Chards/beet leaves	0 / 0.26	4.1
1%	Beetroots	0 / 0.07	4.0
1%	Celeriacs/turnip rooted	0 / 0.07	3.9
1%	Courgettes	0 / 0.08	3.7
1%	Table grapes	0 / 0.05	3.6

Expand/collapse list

IESTI (adults)

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Escaroles/broad-leaved	0 / 0.26	5.2
2%	Chards/beet leaves	0 / 0.26	4.9
2%	Witloofs/Belgian endives	0 / 0.26	4.8
1%	Watermelons	0 / 0.08	3.2
1%	Lettuces	0 / 0.26	3.2
1%	Melons	0 / 0.08	3.1
0.8%	Swedes/rutabagas	0 / 0.07	2.4
0.7%	Cucumbers	0 / 0.08	2.2
0.7%	Head cabbages	0 / 0.05	2.1
0.7%	Potatoes	0 / 0.07	2.1
0.7%	Yams	0 / 0.07	2.0
0.6%	Courgettes	0 / 0.08	1.9
0.6%	Table grapes	0 / 0.05	1.7
0.5%	Beetroots	0 / 0.07	1.6
0.5%	Valerian root	0 / 2.48	1.5

IESTI new (children)

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)

IESTI new (adults)

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Total number of commodities found exceeding the ARfD/ADI in children and adult diets (IESTI new calculation)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI (children)

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
8%	Witloofs / boiled	0 / 0.26	23
6%	Escaroles/broad-leaved er	0 / 0.26	17
3%	Chards/beet leaves / boile	0 / 0.26	8.1
2%	Pumpkins / boiled	0 / 0.08	7.1
2%	Potatoes / fried	0 / 0.07	6.5
1%	Leeks / boiled	0 / 0.07	4.0
1%	Broccoli / boiled	0 / 0.05	3.9
1%	Spinaches / frozen; boiled	0 / 0.26	3.6
1%	Turnips / boiled	0 / 0.07	3.6
1%	Parsnips / boiled	0 / 0.07	3.5
1%	Sweet potatoes / boiled	0 / 0.07	3.5
1%	Cauliflowers / boiled	0 / 0.05	3.5
1%	Florence fennels / boiled	0 / 0.07	3.2
1%	Beetroots / boiled	0 / 0.07	3.1
0.9%	Courgettes / boiled	0 / 0.08	2.8

Expand/collapse list

IESTI (adults)

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Escaroles/broad-leaved	0 / 0.26	5.3
2%	Witloofs / boiled	0 / 0.26	4.8
1%	Pumpkins / boiled	0 / 0.08	4.4
1%	Chards/beet leaves /	0 / 0.26	3.3
0.9%	Beetroots / boiled	0 / 0.07	2.7
0.8%	Celeries / boiled	0 / 0.07	2.4
0.7%	Spinaches / frozen; boiled	0 / 0.26	2.2
0.7%	Cauliflowers / boiled	0 / 0.05	2.1
0.6%	Courgettes / boiled	0 / 0.08	1.8
0.5%	Parsnips / boiled	0 / 0.07	1.5
0.5%	Florence fennels / boiled	0 / 0.07	1.4
0.4%	Turnips / boiled	0 / 0.07	1.3
0.4%	Cassava roots / boiled	0 / 0.07	1.3
0.4%	Celeriacs / boiled	0 / 0.07	1.3
0.4%	Leeks / boiled	0 / 0.07	1.2

IESTI new (children)

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!

IESTI new (adults)

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!
#NUM!	#NUM!	#NUM!	#NUM!

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of M-01 is unlikely to present a public health risk.

For processed commodities, no exceedance of the ARfD/ADI was identified.