European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance fluopicolide[1]

(Question No EFSA-Q-2009-309)

Issued on 4 June 2009

SUMMARY

Fluopicolide is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[2] the United Kingdom received an application from Bayer for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2005/778/EC[3].

Following the agreement with the EU-Commission EFSA will organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after 30 June 2002, the designated rapporteur Member State the United Kingdom made the report of its initial evaluation of the dossier on fluopicolide, hereafter referred to as the draft assessment report (DAR), available on 12 December 2005.

The peer review was initiated on 11 January 2006 by dispatching the draft assessment report for consultation to the Member States and the notifier. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in a written procedure in March 2007. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in November / December 2007 and in January 2009.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States in a written procedure in April 2009 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the notifier which comprise foliar spraying to vine grapes against downy mildew and to potatoes against late blight. Full details of the GAPs can be found in the attached end points.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance fluopicolide. *EFSA Scientific Report* (2009) 299. 1-158

[2] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19

[3] OJ No L 293. 9.11.2005

The representative formulated products for the evaluation were 'AE F053616 06 WG71 A1' or 'EXP 11074B', a water dispersible granule (WG), containing 44.4 g/kg fluopicolide and 666.7 g/kg fosetyl-aluminium and 'AE B066752 04 SC61 A1' or 'EXP 11120A', a suspension concentrate (SC), containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible. Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant and animal origin and environmental matrices. Since fluopicolide is not classified as acute toxic or very toxic, analytical methods for the determination of residues of fluopicolide in body fluids and/or tissues are not required.

In the mammalian metabolism studies, fluopicolide was moderately rapidly but incompletely absorbed orally (approximately 62 %) and widely distributed. There was no evidence of bioaccumulation, fluopicolide was extensively metabolised and rapidly excreted mainly via faeces.

The acute toxicity of fluopicolide in rats was low, either by the oral, dermal or inhalation route, no skin irritation and only slight irritation to the eyes were observed. Fluopicolide did not exhibit skin sensitisation potential. The liver was the main target organ of fluopicolide in short-term tests in rats, mice and dogs. A sub-acute NOAEL of 17.7 mg/kg bw/day was based on the 28-day rat study. The relevant short term NOAEL was 7.4 mg/kg bw/day from the 90-day dietary study in rat, based on haematological changes, clinical signs, liver and kidney toxicity at the next higher dose level of 109 mg/kg bw/day. As indicated in a mechanistic study, fluopicolide appears to be a phenobarbital-like inducer of liver enzymes. It is unlikely that fluopicolide presents a genotoxic hazard to humans. In a chronic rat study, effects on liver and kidneys were observed, but no tumour induction was found. Similarly, in a chronic study with mice, liver toxicity was observed. The increased incidence of hepatocellular adenomas seen at high dose was considered not relevant for human risk assessment based on mechanistic considerations. Accordingly, no classification for carcinogenicity was proposed. The relevant long term NOAEL was based on the mice study with a NOAEL of 7.9 mg/kg bw/day, which was supported by the rat NOAEL of 8.4 mg/kg bw/day.

In a two-generation study no effect on reproduction or fertility was seen. Premature delivery, effects on body weight (dams and pups) and reduced crown-rump lengths at maternally toxic doses were observed in developmental studies in rats and rabbits; the relevant developmental NOAEL was the dose level of 20 mg/kg bw/day from the rabbit study.

A series of fluopicolide metabolites were assessed for their toxicological relevance with the aid of toxicological studies conducted with M01[4], M02[5], M04[6], M05[7], M10[8] and M14[9]. Plant metabolites M04, M05, M08[10] and M09[11], were considered less toxic than the parent. The M01 metabolite may be considered of comparable toxicity as the parent, although slightly more acutely toxic. In principle, the ADI of the parent could have been applied, however, as

[4] M01 or BAM: 2,6-dichlorobenzamide
[5] M02: 3-chloro-5-(trifluoromethyl)pyridine-2-carboxylic acid
[6] M04: 2,6-dichloro-3-hydroxybenzamide
[7] M05: 3-(methylsulfinyl)-5-(trifluoromethyl)pyridine-2-carboxylic acid
[8] M10: 3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[9] M14: 3-(methylsulfonyl)-5-(trifluoromethyl)pyridin-2-ol
[10] M08: 3-chloro-5-(trifluoromethyl)pyridine-2-carboxamide
[11] M09: 3-chloro-5-(trifluoromethyl)pyridin-2-ol

an acceptable set of studies were conducted with M01 and considering that M01 is also a metabolite of another active substance, an acceptable daily intake (ADI) of 0.05 mg/kg bw/day was set for this metabolite as well as an acute reference dose (ARfD) of 0.3 mg/kg bw. The metabolites M01, M03[12], M05, M10, M11[13], M12[14], M13[15] and M14 were not considered relevant according to the guidance document on groundwater metabolites[16] even if they appear at levels above 0.1 µg/L in groundwater, however information is lacking on the metabolite M15[17], which was not peer-reviewed.

The acceptable daily intake (ADI) of fluopicolide was set at 0.08 mg/kg bw/day derived from the 78-week dietary study in mice and supported by the 2-year study in rats; a safety factor of 100 was applied. The acceptable operator exposure level (AOEL) was set at 0.05 mg/kg bw/day, derived from the 90-day rat study, corrected for limited oral absorption of 62 % and applying a safety factor of 100. The acute reference dose (ARfD) was set at 0.18 mg/kg bw, derived from the 28-day dietary rat study and the rabbit developmental study, applying a safety factor of 100.

For both representative preparations, the dermal absorption values were agreed at 0.24 % for the concentrate and 2.75 % for the in-use spray dilution. Considering only the fluopicolide component of these formulations, the level of operator exposure estimated at a maximum dose rate of 0.133 kg fluopicolide/ha in grapevines and 0.1 kg fluopicolide/ha in potatoes was below the AOEL for all scenarios proposed when gloves were used during mixing/loading and application and even when no personal protective equipment (PPE) was considered according to the German model and EUROPOEM. Estimated exposures for unprotected re-entry workers and bystanders were below the AOEL for both fluopicolide representative formulations.

Metabolism of fluopicolide was investigated in grapes, potatoes and lettuce. Metabolism was found to be moderate. Besides fluopicolide, its metabolites M-01, M-02 and M-06 were identified. With the exception of M-01 for which an ADI and an ARfD was set by the toxicology section, the metabolites were regarded as less toxic than the parent and/or were also found in the rat metabolism studies. It was decided to include M-01 in the residue definition for risk assessment for plant matrices. As the metabolite M-01 is not unique to fluopicolide it was not included in the residue definition for monitoring. A sufficient number of residue trials on grapes and potatoes supporting the notified GAPs have been submitted to propose MRLs for these crops.

Metabolism in rotational crops was found to be similar, but more extensive as in primary crops. Additionally identified metabolites were M-04, M-05, M-08 and M-09. On the basis of the results of field studies on rotational crops, no quantifiable levels of fluopicolide are expected in consumable crop parts.

Metabolism studies on lactating diary and laying hens showed a low transfer into tissues, milk and eggs. Metabolism was extensive, mainly by hydroxylation followed by conjugation. The only hydrolysis product identified was metabolite M-01, which was included in the residue definition for risk assessment because of its toxicological potential. Dietary burden

[12] M03: 2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl](hydroxy)methyl}benzamide
[13] M11: 6-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[14] M12: 4-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[15] M13: 3-chloro-4-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid; 3-chloro-6-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid
[16] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.
[17] M15: 3,5-dichloro-4-[3-chloro-5-trifluoromethylpyridine-2-yl-methyl)carbamoyl]benzene sulfonic acid

calculations showed only significant intake of fluopicolide residues for cattle. On the basis of available feeding studies on lactating cows, no quantifiable residues are expected in products of bovine.

Chronic and acute dietary intake calculations showed that an exceedance of ADI or ARfD is not expected for intake of crops after treatment with fluopicolide according to the notified GAPs. The level of 0.75 µg/L is expected to be exceeded in groundwater by metabolites M-01, M-05, M-10 and M-11. A consumer risk assessment for the consumption of drinking water for these metabolites showed that an exceedance of the relevant reference values is not expected after chronic or acute intake of fluopicolide through drinking water.

Fluopicolide is of high to very high persistence in soil ($DT_{50\ lab\ 20\ ºC}$ = 194 d – 411 d) under aerobic conditions at 20 ºC. In soil fluopicolide forms the metabolite M-03. This compound breaks down to M-01 and M-02. The metabolite M-03 is of low persistence ($DT_{50\ lab\ 20\ ºC}$ = 2.2 – 5.0 d) in soils at acidic pH and of very low persistence ($DT_{50\ lab\ 20\ ºC}$ < 5h) in soils at neutral or slightly alkaline pH and may be considered an intermediate in the formation of M-01 and M-02. M-01 is of very high persistence in soil ($DT_{50\ lab\ 20\ ºC}$ = 557 – 1831 d) and M-02 is of low persistence ($DT_{50\ lab\ 20\ ºC}$ = 3.2 – 4.6 d). No other metabolites were detected in significant amounts in the laboratory soil studies. Extent of degradation in sterilized and non sterilized samples was in the same range, indicating little contribution of microbiological degradation. M-01 was shown to be very stable in the two soils where it was investigated. Degradation of M-02 produced an extensive number of pyridine derivatives. Some of them were identified and characterized: M-10, M-05, M-14, M-11/12 and M-13. M-05 and M-10 are moderate to high persistent (M-05: $DT_{50\ lab\ 20\ ºC}$ = 31 -130 d; M-10: 22 – 253 d), M-14 is low persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 5- 8 d). RMS considered that values obtained for half lives metabolites M-11/12 ($DT_{50\ lab\ 20\ ºC}$ = 38.5 – 86.1 d), M-13 ($DT_{50\ lab\ 20\ ºC}$ = 10.3 – 43.0 d), and M-10 ($DT_{50\ lab\ 20\ ºC}$ = 4.5 – 307 d) were not robust due to low and variable levels of these metabolites but acceptable to be used in groundwater modelling.

Fluopicolide was very stable under dark anaerobic conditions and only metabolites M-01 and M-02 were identified at minor amounts.

Photolysis degradation occurs to some extend but no new metabolites are identified in the available studies. On the absence of further data, the meeting considered that photolysis may contribute to some extend to the degradation of fluopicolide under natural conditions in EU and that the applicant should update their estimate of photolytic half life at 40 – 45 ºN latitude.

Dissipation of fluopicolide under field conditions has been investigated in a number of field dissipation studies in Germany (3 studies, 3 sites), Spain, Southern France and Northern France. One of the studies performed in Germany and the studies performed in France were prolonged over some seasons to investigate the potential for accumulation of fluopicolide residues. Dissipation in most of the cases was better described by a biphasic model. Three soil dissipation and accumulation studies were conducted by the applicant in Germany (one site, 5 years), Northern France (one site, 4 years) and Southern France (one site, 4 years). The expert meeting agreed with the RMS and confirmed the initial evaluation that indicates that the plateau has not been reached in some of the studies.

For PEC soil calculations, the PRAPeR 37 expert meeting agreed using a SFO DT_{50} = 290 d for fluopicolide and a SFO DT_{50} = 315 d for M01 since they result in DT_{90} corresponding approximately to the worst case observed in the field studies. Potential for accumulation of fluopicolide and the metabolite M-01 was confirmed by the PEC soil calculation (plateau are

reached for the parent after 7 years in potatoes and after 9 years in vines and for the metabolite M-01 after 5 years in potatoes and 6 years in vines).

Fluopicolide exhibits medium mobility in soil (K_{Foc} = 172 – 580 mL / g). M-01 and M-02 are very high mobile in soil (M-01: K_{Foc} = 31 - 51 mL / g; M-02: K_{Foc} = 1.1 – 10.5 mL / g). The metabolite M-03 is high mobile in acidic soil (K_{Foc} = 82 - 133 mL / g). Finally the metabolites M-05 and M-10 are very high mobile in soil (M-05: K_{Foc} = 11 - 49 mL / g; M-10: K_{Foc} = 0 – 10.66 mL / g).

A three years lysimeter study was performed in Germany. Due to the fact that fluopicoline was only labelled at the pyridine ring, no information on the potential leaching of M-01 was obtained from these experiments. A number of metabolites not previously identified in the laboratory degradation in soil studies were identified in the leachate of these lysimeter studies: M-05 (max. annual average concentration = 0.9 μg / L), M-10 (max. annual average concentration = 0.83 μg / L), M-11/12 (max. annual average concentration = 0.55 / 0.36 μg / L), M-13 (max. annual average concentration = 0.14 μg / L), M-14 (max. annual average concentration = 0.19 μg / L), M-15 (max. annual average concentration = 0.095 μg / L), M-16 (max. annual average concentration = 0.08 μg / L), M54 (max. annual average concentration = 0.03 μg / L), P6A (max. annual average concentration = 0.03 μg / L), P6 (max. annual average concentration = 0.07 μg / L), M3 (max. annual average concentration = 0.04 μg / L) and M29 (max. annual average concentration = 0.09 μg / L)[18].

The mobility of the lysimeter metabolites M-14, M-11/12 and M-13 was assessed with the HPLC method. All these metabolites are very high mobile. Due to the high polarity of M-11/12 and M13, the results obtained were considered meaningless and a K_{oc} = 0 was assumed for the risk assessment. For M-14 was possible to estimate acceptable soil sorption parameters (K_{oc} = 19.2 mL / g).

A field leaching study in South West Germany is also available. Metabolite M-01 reached annual average concentrations up to 2.93 μg / L at 120 cm depth on the third year after application.

Fluopicolide and its metabolite M-01 may be considered stable to hydrolysis under most relevant environmental conditions. Hydrolysis M-03 was pH dependent with half lives between 45.5 h (pH 5.1) to 9 min (pH 8.1).

Aqueous photolysis is unlikely to be a significant route of degradation of fluopicolide in the natural aqueous environment.

Fluopicolide and M-01 compounds should be considered not readily biodegradable.

Degradation of fluopicolide in the water sediment systems was very limited. RMS calculated whole systems half lives for fluopicolide in both systems ($DT_{50\ whole\ system}$ = 873 – 1428 d). During the experiment, fluopicolide was partitioned to the sediment. At the equilibrium about 10 to 40 % AR remained as parent fluopicolide in the water phase. Only M-01 and M-02 were identified as degradation metabolites at low levels.

$PEC_{SW\ /\ SED}$ values were calculated by means of FOCUS SW. FOCUS Step 1-2 were calculated for fluopicolide and metabolites M-01, M-02 and M-03. FOCUS SW Step 3 values were also calculated for fluopicolide.

[18] Metabolites M54, P6A, P6, M3 and M29 were not characterized and their chemical identity remains unknown.

The potential of ground water contamination by fluopicolide and the metabolites M-03, M-01, M-02, M-05, M-10, M-11, M-12, M-14 and M-13 was assessed in the original dossier for the use in vines and potatoes with FOCUS PELMO 3.3.2. Further modelling with FOCUS PEARL has become available during the peer review. Fluopicolide and its metabolites M-03, M-01, M-05, M-10, M-11, M-12 and M-13 may exceed the limit of 0.1 μg / L annual average concentration at 1 m depth for at least one of the scenarios simulated. The metabolite M-01 also exceeded the limit of 0.75 μg / L in a number of scenarios. For the use in vines fluopicolide exceeds 0.1 μg / L annual average concentration at 1 m depth for more than half of the scenarios simulated.

In the lysimeter study, where potatoes were planted, annual average concentration of metabolites M-05, M-10, M-11, M-12, M-13 and M-15 at 1 m depth exceed the 0.1 μg / L trigger, in the case of M-05 and M-10 also the trigger of 0.75 μg / L was exceeded in at least one of the lysimeters in oneout of of the three years the experiment was performed. In the field leaching study metabolite M-01 reached an annual average concentration of 2.9 μg / L in the leachate at 120 cm depth the third year after the product was applied.

Since half life in the atmosphere is longer than 2 d and fluopicolide is sprayed, formation of aerosols and long range transport trough the atmosphere cannot be excluded.

It was concluded that the risk for birds and mammals was assessed as low for both evaluated uses, except for the long-term risk for mammals for the use in vines. Risk mitigation measures should be required at Member Stated level. The risk from secondary poisoning and from consumption of contaminated drinking water was assessed to be low for birds and mammals.

A potential high risk was identified for the aquatic organism for both evaluated uses, therefore risk mitigation measures were required. The risk for bioaccumulation in fish from fluopicolide is considered to be low. The risk for the relevant metabolites to aquatic organism was assessed as low.

The risk for bees, non-target arthropods, earthworms, other non-target macro-organisms, soil non-target micro-organism, non-target plants and biological methods for swage treatments, was assessed to be low.

Key words: fluopicolide, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC the United Kingdom received an application from Bayerfor inclusion of the active substance fluopicolide in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2005/778/EC

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State the United Kingdom submitted the report of its initial evaluation of the dossier on 12 December 2005 hereafter referred to as the draft assessment report (DAR), to the EFSA. This draft assessment report was distributed for consultation to the Member States and the notifier on 11 January 2006.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in a written procedure in March 2007 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised by the EFSA by the in November / December 2007 and in January 2009. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States in a written procedure in April 2009 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

Following the agreement between the EU Commission and EFSA regarding the peer review of new active substances, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a peer review report comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (revision 1-1, 02-04-2007),

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (revision 3-1, 25.05.2009).

Given the importance of the draft assessment report including its addendum (compiled version of February 2009 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Fluopicolide is the ISO common name for 2,6-dichloro-*N*-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl]benzamide (IUPAC).

Fluopicolide belongs to the class of benzamide fungicides or pyridine fungicides and its biochemical mode of action is currently not fully known. First assessments have shown that fluopicolide modifies the distribution of fungal spectrin-like proteins. It is effective against a wide range of Oomycete (Phycomycete) diseases including downy mildews (*Plasmopara, Pseudoperonospara, Peronospora, Bremia*), late blight (*Phytophthora*) and some *Pythium* species. Fluopicolide has protectant, antisporulant activity and potential for curative activity. Fluopicolide is redistributed *via* the xylem (acropetal systemic activity) and effective disease control can be achieved from foliar, seed and soil applications. Fluopicolide has contact activity on several stages of the development of *Plasmopara viticola* and *Phytophthora infestans* and is best used before infection of the leaves occurs.

The representative formulated products for the evaluation were 'AE F053616 06 WG71 A1' or 'EXP 11074B', a water dispersible granule (WG), containing 44.4 g/kg fluopicolide and 666.7 g/kg fosetyl-aluminium and 'AE B066752 04 SC61 A1' or 'EXP 11120A', a suspension concentrate (SC), containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride.

The representative uses evaluated comprise foliar spraying

-against downy mildew (*Plasmopara viticola)* in vine grapes, from growth stage of BBCH 53 up to growth stage of BBCH 77-81, in all EU countries, up to a maximum of three applications at a maximum individual application rate per spray of 133 g a.s./ha, with an interval of 10 to 14 days between applications.

-against late blight (*Phytophtora infestans*) in potatoes, from growth stage of BBCH 20 up to growth stage of BBCH 89-91, in all EU countries, up to a maximum of four applications at a maximum individual application rate per spray of 100 g a.s./ha, with an interval of 5 days between applications.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of fluopicolide is 970 g/kg. There is no FAO specification available.

The experts at the PRAPeR 36 meeting (November, 2007) agreed that once full scale manufacturing is in progress then new 5-batch data must be provided. The new 5-batch and QC data has been presented in the Addendum 2 to Volume 4 (December 2008). The revised proposed specification as given by the applicant was agreed by the experts at the PRAPeR 61 meeting (January, 2009). Toluene was considered relevant impurity with a maximum amount of 0.3% in the technical material.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of fluopicolide or the respective formulations.

The main data regarding the identity of fluopicolide and its physical and chemical properties are given in appendix 1.

Adequate analytical methods are available for the determination of fluopicolide in the technical material and in the representative formulations (HPLC-UV) as well as for the determination of the respective impurities in the technical material (HPLC-UV).

Sufficient test methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

Fluopicolide residues can be monitored in food/feed of plant origin by a modified version of the German modular multi-residue method DFG S19, with LOQs of 0.1 mg/kg, 0.02 mg/kg and 0.02 mg/kg for grape, wheat grain and potato respectively.

Residues of fluopicolide in food/feed of animal origin can be monitored by HPLC/MS/MS, with LOQs of 0.01 – 0.05 mg/kg (milk, meat, fat, liver and kidney). It should be mentioned that the method is able also to monitor residues of metabolites M-01 and M-02.

An HPLC/MS/MS method is available to monitor fluopicolide residues in soil with a LOQ of 0.005 mg/kg. It should be mentioned that the method can be used also for monitoring the metabolites M-01, M-02 and M-03 with LOQs of 0.005 mg/kg for each compound. Residues of fluopicolide and its M-01 and M-02 metabolites in surface and drinking water can be determined by HPLC/MS/MS with LOQs of 0.1 µg/l for each. Adequate methods (GC/ECD and GC/MS) are available to monitor residues of fluopicolide in air with a LOQ of 3 µg/m^3.

Since fluopicolide is not classified as acute toxic or very toxic, analytical methods for the determination of residues of fluopicolide in body fluids and/or tissues are not required.

2. Mammalian toxicity

Fluopicolide was discussed at the PRAPeR expert meeting on mammalian toxicology, PRAPeR 39, in December 2007 and PRAPeR 64, in January 2009.

The batches used in the toxicological studies were considered to represent adequately the technical specifications set for the pilot plant (as referred in the addendum 1 to volume 4); this was extended to the full scale manufacturing process as referred in the addendum 2 to volume 4 (please refer to section 1 on physical and chemical properties).

The experts agreed also that toluene is a relevant impurity and its maximum level should be 5 g/kg (0.5 %) in the technical specification.

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

In the rat, fluopicolide was absorbed moderately rapidly with maximum concentrations in the blood between 6-8 hours after application. The extent of oral absorption, based on biliary excretion, was approximately 62 % for pyridyl labelled fluopicolide. Fluopicolide was widely distributed into organs and tissues. The highest tissue residues were found in liver and kidneys and, to a lesser extent, in the spleen and blood. There was no evidence for accumulation of fluopicolide. The substance was rapidly and extensively excreted, mainly via faeces to an extent of approximately 95 % within 48 hours after oral ingestion. The biliary fraction amounted to approximately 52 % of pyridyl radiolabelled fluopicolide. Metabolism in the rat was extensive. Biotransformation observed included aromatic ring hydroxylation, hydrolysis, dealkylation, acetylation, oxidative N-dealkylation, glucuronidation, sulphatation

and conjugation with glutathione. The glutathione conjugates were further metabolised to cysteine conjugates which were then further transformed to mercapturic acids or S-methyl metabolites. The S-methyl metabolites were oxidised to sulphones and sulphoxides.

2.2. Acute toxicity

Fluopicolide was of low acute toxicity in rats by the oral (LD_{50} > 5000 mg/kg bw), the dermal (LD_{50} > 5000 mg/kg bw) and the inhalation route (LC_{50} > 5.16 mg/L air/4 h). Fluopicolide was not irritating to rabbit' skin and was transiently slightly irritating to the rabbit's eyes. Fluopicolide was not a skin sensitizer in guinea pigs in a Magnusson & Kligman test. Overall, no classification for acute effects is proposed for the active substance.

2.3. Short-term toxicity

The liver was the main target organ in short term tests with fluopicolide in all species tested. With rats, a 28-day and a 90-day dietary study and a 28-day dermal study were carried out. In the 28-day dietary study a NOAEL of 17.7 mg/kg bw/day was derived, based on reduced bodyweight gain in females, increased absolute and relative liver weights in males and histopathology findings in liver and kidney of both sexes at the LOAEL of 179 mg/kg bw/day. In the 90-day study the NOAEL was set at 7.4 mg/kg bw/day, based on changes in haematological and clinical parameters, increased relative organ weights (liver, kidney and spleen) and histopathological changes in liver and kidney at the next higher dose of 109 mg/kg bw/day. In the dermal study no treatment related findings could be observed up to the highest dose of 1000 mg/kg bw/day.

With mice, a 28-day and a 90-day dietary study were performed. In the 28-day study a NOAEL of 10.4 mg/kg bw/day was derived, based on increased liver weights and hepatocyte hypertrophy seen at a dose of 100 mg/kg bw/day. In the 90-day study also a NOAEL of 10.4 mg/kg bw/day was defined, based on reduced cholesterol levels at 37.8 mg/kg bw/day and clinical effects and liver effects observed at higher dose levels.

With dogs, a 28-day and a 90-day gavage study were reported. In the 28-day a NOAEL of 100 mg/kg bw/day was derived, based on increased cholesterol level associated with increased absolute and relative liver weights. Similarly also in the 90-day study liver effects were observed (pronounced increases in absolute and relative weight), based on which a NOAEL of 70 mg/kg bw/day was determined.

2.4. Genotoxicity

The genotoxic potential of fluopicolide was assessed *in vitro* in five bacterial assays in *Salmonella typhimurium* and *Escherichia coli*, a gene mutation test at the hypoxanthine-guanine phosphoribosyl transferase locus of Chinese hamster lung V79 cells (V79/HGPRT) and two clastogenicity tests in Chinese hamster lung V79 cells and human lymphocytes. *In vivo* three micronucleus tests in mouse bone marrow and an unscheduled DNA synthesis (UDS) in rat liver were carried out. Fluopicolide showed weak clastogenic properties in one *in vitro* test in Chinese hamster lung cells and very weak clastogenic potential in one *in vivo* micronucleus test at toxic doses. All other assays yielded clearly negative results. Based on the overall evidence it was considered unlikely that fluopicolide presents a genotoxic hazard to humans.

2.5. Long-term toxicity and carcinogenicity

A two-year combined carcinogenicity and toxicity study in rats and an 18-month carcinogenicity study in mice were reported in the DAR. In the rat study, no evidence for an oncogenic potential could be found and the systemic NOAEL was set at 8.4 mg/kg bw/day, based on histopathological changes in liver and kidneys observed at 31.5 mg/kg bw/day dose level.

The systemic NOAEL in the 18-month mouse study was set at 7.9 mg/kg bw/day, based on increased liver weights, liver pathology (enlarged liver, masses and nodules in the liver) and hypertrophy at higher doses. At the highest dose level (552 mg/kg bw/day) an increased incidence of hepatocellular adenomas was seen, but since the tumours occurred only at the maximum tolerate dose (MTD) and fluopicolide has been shown to be a phenobarbital like enzyme inducer (please refer to point 2.8: Further studies), this was not considered relevant for human risk assessment. At a meeting of experts (PRAPeR 39, December 2007), it was agreed that no classification for carcinogenicity was proposed for fluopicolide, taking also into account that no tumours were seen in rats.

2.6. Reproductive and developmental toxicity

Reproduction toxicity

Dietary administration of fluopicolide was well tolerated at all concentrations given in a two-generation toxicity study with rats. At the highest dose in the F_0 and F_1 generations effects on food intake and consequently bodyweight gain were observed, while fertility and reproductive performance remained unaffected. No adverse effects were observed in F_1 and F_2 litters. The NOAEL for reproductive toxicity was therefore set at 103.4 mg/kg bw/day (the highest dose applied), while the parental NOAEL and the NOAEL for the developing offspring were set at 25.5 mg/kg bw/day dose level.

Developmental toxicity

In a developmental toxicity study with rats, the NOAELs for both maternal and developmental toxicity were set at 60 mg/kg bw/day, based on decreased body weight in dams and reduction in weight and crown-rump lengths in foetuses at the next higher dose of 700 mg/kg bw/day.

The NOAEL for developmental and maternal toxicity in a developmental toxicity study with rabbits was 20 mg/kg bw/day, based on mortality, high incidence of premature delivery and reduction in body weight gain and food consumption in dams, and reduction in foetal weights and foetal crown-rump lengths at the dose level of 60 mg/kg bw/day.

2.7. Neurotoxicity

Fluopicolide does not belong to a chemical group known to induce neurotoxicity. Acute, short-term and chronic toxicity studies did not provide indications of neurotoxicity. An acute and a short term neurotoxicity study with rats were presented in the DAR. A NOAEL of 100 mg/kg bw was obtained in the acute study, based on reduced body temperature measured in the animals and excessive grooming observed in females at doses of 2000 mg/kg bw. In the 90-day study a NOAEL of 15 mg/kg bw/day was derived, based on histopathological findings (liver, kidneys) and impaired growth at the next higher dose. There was no sign of neurotoxicity found up to the highest dose tested of 781 mg/kg bw/day.

2.8. Further studies

Metabolites

Fluopicolide metabolites M01[19], M03[20], M05[21], M10[22], M11[23], M12[24], M13[25] and M15[26] were estimated to exceed potentially a level of 0.1 µg/L in groundwater according to fate and behaviour environmental models. Furthermore, M01, M05 and M10 may exceed the 0.75 µg/L threshold for consumer risk assessment according to these models.

The metabolites M01, M04[27], M05, M08[28] and M09[29] were assessed for their toxicological relevance as plant metabolites. Out of these metabolites, only M01 and M04 were found also in rat metabolism studies.

M01 (or BAM)

This metabolite was re-discussed at PRAPeR 64 (January 2009) based on the addendum 2 to the draft assessment report (December 2008). An almost full set of studies was submitted on M01, only a long-term mouse study and a developmental rat study were not available to complete the dossier.

Approximately 82 % and 13 % of an oral dose of metabolite M01 when given to rats were voided via the urine and the faeces respectively. No indication of bioaccumulation was seen. The metabolite M01 is further metabolised by hydroxylation and subsequent glucuronidation or sulphatation, followed by conjugation with glutathione. These conjugates were further degraded to form mercapturic acid or S-methyl metabolites.

The oral LD_{50} in rats was 500 mg/kg bw and consequently classification as **Xn; R22 "Harmful if swallowed"** was proposed. In a 90-day feeding study with rats a NOAEL of 14 mg/kg bw/day was derived, based on reduced food intake/body weight gain at higher dose levels. A 90-day dietary study in dogs, with limited acceptability, resulted in a NOAEL of 22.5 mg/kg bw/day.

In a battery of four *in vitro* and one *in vivo* mutagenicity tests, including a bacterial gene mutation assay performed with *Salmonella typhimurium*, V79/HGPRT gene locus assay, unscheduled DNA synthesis assay *in vitro* and a mouse micronucleus assay *in vivo,* negative results were obtained in all assays.

The liver was the main target organ upon long term exposure of rats to M01. In a two-years dietary study in rats a NOAEL was set at 5.7 mg/kg bw/day, based on liver histopathology. In this study a slightly increased incidence (of non-statistical significance) of hepatocellular adenomas was detected in females at 19 mg/kg bw/day, which was not considered relevant for human risk assessment by the experts at PRAPeR 39 (December 2007) and no

[19] M01 or BAM: 2,6-dichlorobenzamide
[20] M03: 2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl](hydroxy)methyl}benzamide
[21] M05: 3-(methylsulfinyl)-5-(trifluoromethyl)pyridine-2-carboxylic acid
[22] M10: 3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[23] M11: 6-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[24] M12: 4-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid
[25] M13: 3-chloro-4-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid; 3-chloro-6-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid
[26] M15: 3,5-dichloro-4-({[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}carbamoyl)benzenesulfonic acid
[27] M04: 2,6-dichloro-3-hydroxybenzamide
[28] M08: 3-chloro-5-(trifluoromethyl)pyridine-2-carboxamide
[29] M09: 3-chloro-5-(trifluoromethyl)pyridin-2-ol

classification for carcinogenicity was proposed. A two-year dog study resulted in a NOAEL of 4.5 mg/kg bw/day, based on decreased body weight and body weight gain at 12.5 mg/kg bw/day dose level.

In a multigeneration study, no effect on reproductive/fertility parameters was observed, the NOAEL for reproduction was the highest dose tested of 13.5 mg/kg bw/day. The NOAEL for parental and offspring's toxicity was 7.5 mg/kg bw/day, based on reduced body weight in offspring and in dams at 13.5 mg/kg bw/day. In a developmental toxicity study in rabbits, the NOAEL for maternal toxicity was 30 mg/kg bw/day, based on maternal deaths, body weight loss and increased incidence of abortions at 90 mg/kg bw/day. The developmental NOAEL was also 30 mg/kg bw/day, based on reduction in foetal birth weight at 90 mg/kg bw/day.

The experts decided to set reference values for the metabolite itself once the set of data was considered adequate and this metabolite is common to several active substances (e.g. dichlobenil[30]), instead of using the reference values of fluopicolide. **The acceptable daily intake (ADI) for M01 was set at 0.05 mg/kg bw/day** based on the long term (two-year) rat and dog studies performed with M01 and a safety factor of 100. **The acute reference dose (ARfD) was set at 0.3 mg/kg bw**, based on the developmental toxicity study in rabbits and the same safety factor of 100.

M02[31]

When given orally to rats, M02 is absorbed almost completely (87 % of a given dose), excreted rapidly and mainly unchanged via the urine (about 78.5 % of the dose) and to a much lesser extent (6.6 %) voided with the faeces. Consequently, it has only a low potential for bioaccumulation.

The oral LD_{50} of M02 in rats was > 2000 mg/kg bw.

In three *in vitro* assays including bacterial gene mutation assay in *Salmonella typhimurium* and *Escherichia coli*, chromosome aberrations in human lymphocytes and V79/HGPRT gene locus assay, no evidence for genotoxicity was found related to M02 treatment.

The NOAEL derived from a 28-day study in rats was 1574 mg/kg bw/day, the highest dose tested.

M04

The oral LD_{50} of M04 in rats exceeded 2000 mg/kg bw.

M04 was negative in a battery of three *in vitro* and two *in vivo* genotoxicity tests including bacterial gene mutation assay in *Salmonella typhimurium*, chromosome aberrations in human lymphocytes and V79/HGPRT gene locus assay *in vitro*, and a mouse micronucleus assay and an unscheduled DNA synthesis assay in rat hepatocytes *in vivo*.

In a 28-day dietary study in rats, a NOAEL of 159.2 mg/kg bw/day was defined, based on effects on liver and kidneys seen at 1775 mg/kg bw/day.

[30] The reference values for M01 were based on studies submitted in the original fluopicolide DAR, toxicological data submitted in the US for dichlobenil which, initially, were not submitted in Europe for neither fluopicolide nor dichlobenil dossier, but were reported in the addendum 2 to the fluopicolide DAR.

[31] M02: 3-chloro-5-(trifluoromethyl)pyridine-2-carboxylic acid

M05

The oral LD_{50} of M05 in rats exceeded 2000 mg/kg bw.

M05 was negative in three *in vitro* genotoxicity tests including bacterial gene mutation assay in *Salmonella typhimurium*, chromosome aberrations in human lymphocytes and V79/HGPRT gene locus assay.

In a 28-day dietary study in rats, a NOAEL of 152 mg/kg bw/day was determined, based on reduced body weight gain and kidney degeneration observed in animals treated at 1495 mg/kg bw/day.

M10

The oral LD_{50} of M10 in rats exceeded 2000 mg/kg bw.

M10 did not exert genotoxic activities in a bacterial gene mutation assay in *Salmonella typhimurium* and a chromosome aberrations test in human lymphocytes, but mutagenic activity was seen in a V79/HGPRT gene locus assay both with and without metabolic activation. However, a mouse micronucleus assay and an unscheduled DNA synthesis assay in rat hepatocytes *in vivo* gave both negative results showing that, overall, M10 does not appear as a genotoxic compound.

The NOAEL of M10 in a 28-day dietary study in rats was 163.8 mg/kg bw/day, based on clinical signs of diarrhoea at 1748.2 mg/kg bw/day.

M14[32]

M14 was not genotoxic in a battery of three *in vitro* and two *in vivo* tests including bacterial gene mutation assay in *Salmonella typhimurium*, chromosome aberrations in human lymphocytes and V79/HGPRT gene locus assay *in vitro*, and a mouse bone marrow micronucleus assay and an unscheduled DNA synthesis assay in rat hepatocytes *in vivo*.

Groundwater metabolites

Metabolites M01, M03, M05, M10, M11, M12, M13 and M14 were discussed for their relevance as groundwater metabolites.

According to the guidance document on groundwater metabolites[33], M01 was not considered relevant even if it occurs in groundwater at levels above 0.1 µg/L, however, a consumer risk assessment has to be carried out with the ADI/ARfD set by the experts (see above).

M03 is a transient intermediate of fluopicolide, forming M01 and M02 in the rat metabolism. Any concern was considered as covered by the negative genotoxicity tests with the parent compound, M01 and M02.

Metabolites, M05, M10 and M14 were considered not relevant, based on the available data and metabolites M11, M12, M13 (no measured data presented) based on their structural similarity with M10 and M14. No toxicological information is available on the metabolite

[32] M14: 3-(methylsulfonyl)-5-(trifluoromethyl)pyridin-2-ol

[33] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

M15, this metabolite is structurally closely related to the parent compound and metabolites M06, M07, M16 and M18 which are rat's metabolites. On this basis, the RMS did not consider M15 as a metabolite of concern during the written procedure. However, its relevance was not considered by the meetings of experts and therefore, a data requirement is proposed by EFSA.

Plant metabolites

Metabolites M04, M05, M08 and M09 were considered less toxic than the parent; for M08 and M09 this conclusion was based on their similarity to M02. Only M01 may be considered as slightly more toxic and has got its own reference values.

Mechanistic studies

A 28-day dietary study with mice indicated that fluopicolide is a phenobarbital-like inducer of liver enzymes (P-450, BROD, PROD), strongly suggesting that the liver tumours observed in mice are attributable to a mechanism considered as not being relevant for humans.

2.9. Medical data

Fluopicolide is a new active substance. At the date of the submission of the dossier, there were no reported incidents of adverse reactions during the pilot scale manufacture or the formulation of fluopicolide.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

ADI

As proposed by the rapporteur Member State in the draft assessment report, **the ADI was set at 0.08 mg/kg bw/day** based on the NOAEL of 7.9 mg/kg bw/day derived from the 78-week dietary study in mice, supported by the 2-year dietary study in rats with a NOAEL of 8.4 mg/kg bw/day. A safety factor of 100 was applied.

AOEL

As proposed by the rapporteur Member State in the DAR, **the AOEL was set at 0.05 mg/kg bw/day** based on the NOAEL of 7.4 mg/kg bw/day derived from the 90-day rat study, corrected for the low oral absorption of 62 % with pyridyl-labelled fluopicolide, and applying a safety factor of 100.

ARfD

The experts at PRAPeR 39 agreed with the rapporteur Member State proposal in the DAR. **The ARfD was set at 0.18 mg/kg bw** based on the NOAEL of 17.7 mg/kg bw/day found in the 28-day dietary rat study, and applying a safety factor of 100; this value was further supported by the rabbit developmental toxicity study presenting a NOAEL of 20 mg/kg bw/day.

2.11. Dermal absorption

Dermal absorption values have been determined for the Suspension Concentrate EXP11120A and were 0.24 % for the undiluted and 2.75 % for the in-use spray dilution. The values were based on an *in vivo* dermal penetration study with rats and a comparative *in vitro* dermal penetration study using rat and human skin. The experts considered that these values could be extrapolated from the SC to the WG formulation.

2.12. Exposure to operators, workers and bystanders

The representative plant protection products are "EXP 11074B", a wettable granule (WG) formulation containing 44.4 g fluopicolide/kg and 666.7 g fosetyl-aluminium/kg, used as a horticultural fungicide on grapevines and "EXP 11120A", a suspension concentrate (SC) formulation containing 62.5 g fluopicolide/L and 625 g propamocarb hydrochloride/L used as an agricultural fungicide on potatoes.

EFSA note: The assessment below has only considered the fluopicolide component of the formulations. Since there is no agreed procedure for performing combined assessments for more than one a.s., combined exposure to fluopicolide and fosetyl-aluminium or propamocarb hydrochloride has to be taken into account at Member State level. Consequently, the risk assessment for both combi-formulations cannot be concluded for the operators, workers and bystanders exposure.

Operator exposure

The operator exposure estimates were calculated using the German model[34] and the UK Predictive Operator Exposure Model (POEM)[35]. As the UK POEM data are derived from studies conducted on fruit trees only, additional estimates have been made by the rapporteur Member State using the EUROPOEM database[36] which contains some exposure data relating specifically to spraying grapevines.

EXP 11074B (WG formulation) - grapevines

According to the representative uses, the maximum applied dose is 0.133 kg fluopicolide/ha on grapevines (3.0 kg EXP 11074B/ha) in a spray volume of 100-1500 L/ha; application by tractor-mounted/trailed broadcast air-assisted sprayer or hand-held sprayer are proposed up to three applications per year, with intervals of 10-14 days between applications.

[34] BBA (1992). Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products. Biologische Bundesanstalt für Land- und Forstwirtschaft, Bundesgesundheitsamt, und Industrieverband Agrar e.V. ISBN 3489-27700-7.

[35] PSD (1986). UK Scientific Subcommittee on Pesticides & British Agrochemicals Association, Joint Medical Panel; UK Predictive Operator Exposure Model (POEM): Estimation of Exposure and Absorption of Pesticides by Spray Operators. PSD (2003). UK Predictive Operator Exposure Model (POEM) version 3.

[36] EUROPOEM Project Group (1996). The development, maintenance and dissemination of a European predictive operator exposure model (EUROPOEM) database.

Estimated operator exposure presented as % of AOEL (0.05 mg/kg bw/day) in grapevines by tractor, application rate of 0.133 kg fluopicolide/ha

Tractor-mounted broadcast air-assisted sprayers (high crop)	No PPE	With PPE[(a)] during M/L	With PPE[(a)] during M/L & application	With PPE[(b)] during M/L & application
UK POEM *medium volume (100L/ha)*	113	112	79	-
UK POEM *high volume (500 L/ha)*	49	48	40	-
German model	11	10	10	2
EUROPOEM	28	27	26	19

[(a)] PPE: gloves; M/L: mixing and loading
[(b)] PPE: gloves (M/L & application), protective garment and sturdy footwear* (application)
* sturdy footwear is used only in the German model, not in the EUROPOEM

Estimated operator exposure presented as % of AOEL (0.05 mg/kg bw/day) in grapevines, hand-held, application rate of 0.133 kg fluopicolide/ha

Hand held equipment	No PPE	With PPE[(a)] during M/L	With PPE[(a)] during M/L & application	With PPE[(b)] during M/L & application
UK POEM *(based on low crop data)*	132	130	66	29
German model *(high crop)*	6	5	4	2

[(a)] PPE: gloves; M/L: mixing and loading
[(b)] PPE: gloves (M/L & application), protective garment and sturdy footwear* (application)
*sturdy footwear is used only in the German model, not in the POEM

EXP 11120A (SC formulation) – potatoes

According to the representative uses, the maximum applied dose is 0.1 kg fluopicolide/ha on potatoes (1.6 L EXP 11120A/ha) in a spray volume of 200-400 L/ha in Northern countries and 400-1000 L/ha in Southern countries; application by tractor-mounted/trailed or self-propelled field crop sprayer are proposed up to four applications *per* crop, with intervals of 7-10 days between applications.

Estimated operator exposure presented as % of AOEL (0.05 mg/kg bw/day) in potatoes by tractor, application rate of 0.1 kg fluopicolide/ha

Tractor-mounted/trailed field crop sprayers	No PPE	With PPE[(a)] during M/L	With PPE[(a)] during M/L & application	With PPE[(b)] during M/L & application
UK POEM	21	20	4	-
German model	4	3	3	0.3

[(a)] PPE: gloves; M/L: mixing and loading
[(b)] PPE: gloves (M/L & application), protective garment and sturdy footwear (application)

It was concluded from the above estimations that operator exposure to fluopicolide is below the AOEL for all scenarios proposed when gloves are used during mixing/loading and

application, and even when no personal protective equipment is considered according to the German model and EUROPOEM.

Worker exposure

Estimation of worker exposure was performed according to the German model for re-entry workers[37].

The following assumptions were used:

	EXP 11074B (WG formulation) - grapevines	**EXP 11120A (SC formulation) – potatoes**
Application rate (R) [kg fluopicolide/ha]	0.399 [(a)]	0.4 [(b)]
Initial dislodgeable foliar residue (DFR) [µg fluopicolide/cm^2 *per* kg fluopicolide/ha] [(c)]	3 x R	3 x R
Task-related transfer coefficient (TC) [cm^2/person/h]	4500	5000
Duration of task (A) [hours/day]	8	2

[(a)] based on the maximum total dose from three applications and assuming, as a worst case, no decline in residues following each application

[(b)] based on the maximum total dose of 6.4 L of EXP 11120A/ha/crop and assuming, as a worst case, no decline in residues following each application

[(c)] considering the default values in the EUROPOEM database

Assuming a worker body weight of 60 kg and a worst case dermal absorption of 2.75 % for fluopicolide in dry transferred foliar residues, systemic worker exposure was estimated to represent **40 % of the systemic AOEL** of 0.05 mg/kg bw/day for EXP 11074B used on grapevines and **11 % of the AOEL** for EXP11120A used on potatoes, when no personal protective equipment is considered.

Bystander exposure

The exposure for a bystander positioned 8 m downwind from the edge of the treatment area was estimated based on direct measurements of simulated bystander exposure for broadcast air-assisted sprayers in a UK study[38] for applications of EXP 11074B on grapevines, and on direct measurements in field crop sprayers[39] after the application of EXP 11120A on potatoes. Assuming a body weight of 60 kg, 2.75 % dermal absorption for the spray solution, 100 % absorption of potential inhalation and no exposure reduction from clothing, the resulting level of exposure to fluopicolide for unprotected bystanders was estimated to represent **5 % and 0.1 % of the AOEL for high crop and field crop respectively**.

The rapporteur Member State provided also a risk assessment for residential exposure to fluopicolide, which is not yet sufficiently recognized or agreed, but gave indications of a residential exposure level below the AOEL.

[37] Hoernicke E, *et al* (1998) Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflanzenschutzmitteln behandelten Kulturen. *Nachrichtenblatt des Deutschen Pflanzenschutzdienstes. Vol 50 (10) p.267.*

[38] Lloyd G.A., Cross J.V. *et al.* (1987). Orchard sprayers: comparative operator exposure and spray drift study (MAFF/ADAS).

[39] Lloyd G.A. and Bell G.J. (1983). Hydraulic nozzles: comparative spray drift study (MAFF/ADAS).

3. Residues

The active substance fluopicolide was discussed at the PRAPeR experts meetings for residues 40, round 8 in December 2007 and 65, round 13 in January 2009.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

To support the notified uses on grapes and potatoes, the metabolism was studied with [^{14}C] phenyl and pyridinyl ring labelled fluopicolide in lettuce, grapes and potatoes.

Grapes were treated with three foliar application at rates of 0.12–0.17 kg a.i./ha (representing approximately the dose rate of the notified cGAP) 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 (representing the notified seasonal application rate) and in additional trials at ten times the notified seasonal application rate. The growths stages at the time of applications were in line with the notified GAPs. Lettuce was treated with two foliar applications at a rate of 0.2 kg a.i./ha or as a soil drench treatment at a rate of 0.2 kg a.i./ha.

In all three 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 metabolites identified in primary crops were also found in the rat metabolism studies.

On the basis of the results of the metabolism studies on primary and rotational crops (see section 3.1.2) the RMS proposed in the DAR to include M-01 in the residue definition for risk assessment. The metabolite M-01 is not unique to fluopicolide, e.g. also dichlobenil is metabolised to M-01. (It is noted that in the DAR for dichlobenil the abreviasion BAM is used for this metabolite.) Therefore, it was proposed not to include M-01 in the residue definition for monitoring.

The PRAPeR 40 meeting decided to follow the proposal of the RMS. The decisions concerning residue definition for risk assessment and conversion factors taken during this meeting were made under the assumption that the toxicological end points of fluopicolide should be applied also for the risk assessment of M-01 and that M-02 and M-06 are less toxic than fluopicolide.

However, the PRAPeR 64 meeting set an ADI and an ARfD for M-01 which are different from those of fluopicolide. Therefore, the PRAPeR 65 meeting had to revise the conclusion of the PRAPeR 40 meeting. The available analytical method detects parent and metabolite M-01 separately. Therefore and taking into account the different toxicological end points for fluopicolide and M-01 the following residue definitions were proposed: for monitoring: fluopicolide only; for risk assessment: fluopicolide and M-01 separately.

A total of 19 residue trials carried out in Northern Europe and 20 trials carried out in Southern Europe in the years 2000 and 2001 were submitted to support the notified representative use on grapes. The samples were analysed for fluopicolide, M-01 and M-02. Whereas fluopicolide concentrations up to 1.2 mg/kg were found in the grapes, concentrations of M-01 and M-02 were maximal 0.05 and 0.06 mg/kg. It was noted during the peer review that all submitted residue trials were used for the assessment in the DAR although five of the residue trials from Northern Europe used four instead of maximal three applications. The PRAPeR 40 meeting decided that deleting these trails would not change the evaluation as the highest residue levels were found in trials from Southern Europe.

Thirteen residue trials were carried out in both Northern and Southern Europe in the years 2001 and 2002 were submitted to support the notified representative use on potatoes. The samples were analysed for fluopicolide, M-01 and M-02. Residue concentrations were below the LOQ (0.01 mg/kg) for all analytes in all trials with the exception of two trials carried out in Southern Europe where flupicolide residues of 0.01 mg/kg were analysed.

Submitted data on freezer storage stability showed that fluopicolide, M-01 and M-02 residues are stable in grapes, potatoes, cabbage and wheat grain for at least 30 months. Fluopicolide, M-01, M-04 and M-05 are stable in wheat straw for at least 18 months.

The effect of processing on the nature of residues was investigated in buffer solutions under conditions simulating pasteurisation, boiling and sterilisation. Fluopicolide was shown to be stable under these conditions.

Eight studies on the level of residues in processed grape commodities were submitted, six studies providing information on production of must, wine and pomace and two studies on the production of raisins. Residues of fluopicolide increased in pomace and raisins and decreased in must and wine during processing. Transfer factors have been calculated.
The PRAPeR 40 meeting noted that in the DAR for the evaluation of the processing studies no distinction was made between white wine, red wine and heated red wine although the production processes are very different. However, it was agreed that in the case of fluopicolide the type of process had very little influence on the transfer factors.

3.1.2. Succeeding and rotational crops

Confined rotational crop studies are available. [^{14}C] phenyl and pyridinyl ring labelled fluopicolide was applied to soil at a rate of 0.4 kg a.i./ha (notified seasonal application rate for potatoes). Lettuce, wheat and radish were planted after 29, 133 and 365 days of ageing. Translocation of radioactive residues was observed. In crops planted after 29 days of ageing TRR were max. 3 mg/kg in consumable parts and max. 14 mg/ in crop parts used for animal feed. Due to the relatively high stability of fluopicolide in soil, TRR found in crops after 365 days of ageing were still max. 0.6 mg/kg in consumable parts and max. 2 mg/kg in crop parts used for animal feed.

Metabolism 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.

From the metabolites identified in rotational crops, M-05, M-08 and M-09 were not found in the rat metabolism studies. However, they are regarded as less toxic as fluopicolide. Therefore, they were not included in the residue definition for risk assessment (see section 3.1.1).

Nine field trials on rotational crops have been submitted. After the harvest of potatoes which were treated with four foliar applications of fluopicolide at a rate of 0.1 kg a.i./ha (N rate), winter and spring wheat, beans and cabbage were planted into the soil after 28-227 days of ageing. Samples were analysed for fluopicolide, M-01 and M-02, wheat samples additionally for M-04 and M-05. Fluopicolide was below the LOQ (0.01 mg/kg) in crops harvested at maturity with the exception of wheat straw which contained up to 0.12 mg/kg. M-01 was found in quantifiable concentrations in cabbage (max. 0.04 mg/kg) and wheat straw (max. 0.03 mg/kg). Low levels (all below 0.1 mg/kg) of M-02, M-04 and M-05 were found in some samples of wheat grain and straw. On the basis of the residue trials on rotational crops, levels of fluopicolide (proposed residue definition for monitoring for plant matrices) below the LOQ are expected in crop parts intended for the human consumption.

3.2. Nature and magnitude of residues in livestock

For lactating diary cows dosed with [^{14}C] phenyl and pyridinyl ring labelled fluopicolide at 1 mg/kg feed (representing approximately 17 and 8 times the residue intake calculated based on DM for dairy and beef cattle respectively) and 10 mg/kg feed for 7 consecutive days the majority of the applied radioactivity was excreted. Transfer of radioactivity into milk and tissues was low. For the high dose group a residue plateau in milk of 0.01-0.02 mg/kg was reached after four days. In the low dose group TRR in milk and tissues were below the LOQ with the exception of kidney and liver (max. 0.09 mg/kg). The only identified radioactive component in milk, muscle and fat was fluopicolide. In liver and kidney fluopicolide, 3-hydroxy and 4-hydroxy fluopicolide (metabolites M-06 and M-07) and sulphates and glucuronides of hydroxy/dihydroxy fluopicolide were identified.

Laying hens were dosed with [^{14}C] phenyl and pyridinyl ring labelled fluopicolide at 1 mg/kg feed (representing approximately 50 times the intake calculated based on DM for poultry) and 10 mg/ kg feed for 14 days. The majority of TRR were excreted, with less than 0.2% found in eggs and 0.3% in tissues. For the high dose group TRR reached a plateau after 8 days. In the low dose group radioactive residue in egg yolk did not exceed 0.02 mg/kg and in egg white did not exceed 0.01 mg/kg. TRR in tissues were below 0.01 mg/kg, with the exception of liver (max. 0.13 mg/kg). Fluopicolide was only identified in in eggs and fat. Further identified radioactive components in different poultry matrices were M-01, M-07, sulphate of hydroxy/dihydroxy fluopicolide and a methyl sulphone conjugate of fluopicolide.

Based on the results of the metabolism studies on livestock, the RMS suggested including metabolite M-01 in the residue definition for risk assessment. The PRAPeR 65 meeting proposed the following residue definitions for monitoring: fluopicolide only; for risk assessment: fluopicolide and M-01 separately. (For further details see discussions concerning the residue definitions in plant matrices, section 3.1.1).

The RMS carried out intake calculations for domestic animals on the basis of the highest and median residues levels for fluopicolide and M-01 in cereal grain and straw, field bean and potatoes. For dairy cattle, beef cattle, pigs and chicken, theoretical maximum daily intakes of 0.06, 0.12, 0.04 and 0.02 mg/kg feed (DM) and theoretical mean daily intakes of 0.04, 0.04, 0.02 and 0.02 mg/kg feed (DM) were calculated.

Feeding studies for lactating cows dosed at 0.5 (8 N for dairy cows 4N for beef cattle based on DM), 1.5, and 5 mg/kg feed were submitted. Samples of milk and tissues were analysed for fluopicolide and its metabolites M-01 and M-02. Residues were below LOQ for all analytes in all samples from the low dose group with the exception of milk where up to 0.02 mg fluopicolide/kg was found. Therefore, no quantifiable residues are expected in cattle fed with crops after treatment with fluopicolide according to the notified GAPs.

No feeding studies are required for poultry.

Data on freezer storage stability showed that fluopicolide, M-01 and M-02 residues are stable in milk for at least 2 months, in fat and muscle for at least four months and in liver and kidney for at least 9 months.

3.3. Consumer risk assessment

The RMS provided a consumer risk assessment for chronic exposure in the list of end points (not peer reviewed) taking into account the ADI of 0.08 mg/kg bw/day for fluopicolide and the ADI of 0.05 mg/kg for M-01. For the WHO model the maximum estimated daily intake (TMDI) was below 2% of the ADI for the WHO European diet for fluopicolide and M-01 (not including intake of water). A calculation carried out with the EFSA PRAPeR model (EFSA PRIMO rev. 2) showed the French diet for the general population (TMDI = 11% ADI for fluopicolide and M-01 not including intake of water) as the most critical models for the chronic intake.

A calculation of the chronic exposure was carried out by EFSA after the PRAPeR 65 meeting using the EFSA PRAPeR model (EFSA PRIMO rev. 2). For fluopicolide (ADI of 0.08 mg/kg) for intake of table and wine grapes (proposed MRL of 2 mg/kg), potatoes (proposed MRL of 0.02 mg/kg) and rotational crops (other root and tuber vegetables, leaf vegetables and herbs, head and leaf brassica and cereals, all at the LOQ of 0.01 mg) a maximal TMDI of 10% of ADI was calculated for the French diet for the general population. For M-01 (ADI of 0.05 mg/kg) for intake of table and wine grapes (proposed HR of 0.05 mg/kg), potatoes (proposed LOQ of 0.01 mg/kg) and rotational crops (for leaf vegetables, head and leaf brassica and herbs at the highest residue level for cabbage of 0.04 mg/kg, for other root and tuber vegetables and cereals at the LOQ of 0.01 mg) a maximal TMDI of 0.6% of ADI was calculated for the WHO cluster B.

Since the level of 0.75 µg/L is expected to be exceeded in groundwater by metabolites M-01, M-05, M-10 and for one scenario also for M-11, a consumer risk assessment for the consumption of drinking water was performed. For M-05, M-10 and M-11, which are regarded as less toxic as fluopicolide, the ADI of fluopicolide was used as a worst case estimation.

Calculations for M-01 using the UK model provided by the RMS in addendum 3 (February 2009) (not peer-reviewed) showed that NEDIs for diverse consumer groups for intake of grape, wine, potatoes, cabbage, wheat, barley rye, oats and drinking water were below 4% of the ADI. For the metabolites M-05, M-10 and M-11 the chronic exposure was less than 1% of the ADI of fluopicolide.

EFSA made an assessment following the WHO guideline for drinking water quality (not peer-reviewed). For an adult of 60 kg consuming 2L/day, a child of 10 kg consuming 1L/day and an infant of 5 kg consuming 0.75 L/day the estimated daily intake of metabolite M-01 is 0.00022, 0.00067 and 0.0010 mg/kg bw/day, respectively, accounting for 0.5, 1.3 and 2.0% of the ADI of M-01. The estimated daily intakes of the sum of metabolites M-05, M-10 and

M-11 is 0.00008, 0.00025 and 0.00038 mg/kg bw/day, respectively, accounting for 0.1, 0.3 and 0.5% of the ADI of fluopicolide.

The acute exposure is not expected to exceed the ARfDs for fluopicolide and M-01. NESTIs for fluopicolide for consumer/intake combinations calculated by EFSA (not peer-reviewed) with the EFSA PRAPeR model (EFSA PRIMO rev. 2) on the basis of the proposed MRLs are maximal 73% of the ARfD (for intake of grapes by children). NESTIs for M-01 are maximal 1% (for intake of scarole or table grapes by children).

No high consumption data for drinking water for the acute risk assessment are available. It is assumed that they are higher than the mean consumption used for the chronic risk assessment. However, as the ARfD for fluopicolide and M-01 are likewise higher than the ADIs, the acute intake of residues though drinking water are also expected to be well below the ARfDs.

3.4. Proposed MRLs

In accordance with the proposed residue definition for monitoring (fluopicolide alone) the following MRLs were proposed by the RMS in the DAR:

Grapes (table and wine)	2 mg/kg
Potatoes	0.02* mg/kg

The LOQ of the method used for the residue trials on potatoes was 0.01 mg/kg. The LOQ of the analytical method for monitoring submitted by the notifier is 0.02 mg/kg. As residues up to 0.01 mg/kg were found in potatoes and the risk assessment for the consumer based on the proposed MRLs does not lead to an exceedance of ADI and ARfD respectively (see section 3.3) the RMS proposed to set an MRL of 0.02 mg/kg for potatoes.

In rotational crops, residues of parent fluopicolide were below LOQ (0.01 mg/kg) in samples of consumable crop parts. Therefore, in accordance with the proposed residue definition for monitoring (fluopicolide alone) it is not necessary to propose MRLs for rotational crops at the moment.

MRLs for food of animal origin are not required for the notified representative uses (refer to chapter 3.2 above).

4. Environmental fate and behaviour

Fate and behaviour in the environment of fluopicolide was discussed in the meeting of experts PRAPeR 37 (December 2007) on basis of the DAR (November 2005) and addendum 1 (B8, B9, received in EFSA 20th of November 2007).[40] This addendum 1 was supplemented before the meeting with another document, also named addendum 1 (received in EFSA 21st of November 2007)[and renamed as addendum 2 (November 2007) in the final addendum], that provided additional information related to open points 4.8 and 4.1. After the meeting of experts RMS produced the addendum 2 (December 2008) that was discussed in the meeting of experts PRAPeR 62 (January 2009).

[40] This addendum with some minor changes was merged by the RMS with the addendums for the other sections in another addendum 1 (received in EFSA 26th of November 2007).

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

The route of degradation of fluopicolide (labelled either in the benzoyl or the pyridine ring) under dark aerobic conditions was investigated in two studies with a total of three soils (pH 5.7 – 7.5, OC 1.6 – 3.5, clay 6 – 29 %) at 20 or 25 ºC. In another study, degradation was investigated only with product labelled in the benzoyl ring in two additional soils (pH 4.9 - 7.4, OC 0.7 – 0.9, clay 2.9 – 21 %).

Degradation of fluopicolide was very limited (more than 50 % AR remained as parent fluopicolide after 120 d). Degradation occurs through hydroxylation in the bridge carbon to form transformation product **M-03** (max. 10.6 % AR after 120 d). This compound breaks down to **M-01** (max. 40.2 % after 369 d) and **M-02** (max. 7.3 % after 42 d; max. 9.7 % wt / wt in field studies corresponding to a 16 % of applied parent on molar basis). No other metabolites were detected in significant amounts in these studies. Mineralization was negligible (< 3 % AR after 120 d) and unextracted residues were formed up to 22.6 % AR after 369 d. In one soil, degradation was also investigated under sterilized conditions. Extend of degradation in sterilized and non sterilized samples were in the same range, indicating little contribution of microbiological degradation to the initial dissipation of fluopicolide.
The route of degradation in soil under aerobic conditions of metabolites M-03 (only labelled in the benzoyl ring; four soils: pH 4.9 – 7.2, OC 1.1 – 3.2 %, clay 4 – 16 %), M01 (two soils: pH 4.8 – 7.7, OC 0.9 – 5.6 %, clay 6 -10 %) and M-02 (three soils: pH 5.4 -7.5, OC 1.1- 2.6 %, clay 3.8 – 22.8 %) was also investigated in separated studies. The only product identified from the degradation of M-03 labelled in the benzoyl ring is M-01 (max. 95 % AR after 1 d in neutral or slightly alkaline soils; max. 94 % AR after 120 d in acidic soils). Mineralization was negligible in this study (< 0.5 % AR at the end of the experiments 1d or 120 d). M-01 was shown to be very stable in the two soils where it was applied (more than 80 % AR remained as parent M-01 after 180 d). Only very minor uncharacterized metabolites were found (< 0.5 % AR). Unextractable residues and CO_2 reached maximum levels of 5.12 % AR and 8.23 % AR respectively. Degradation of M-02 produced an extensive number of pyridine derivatives. Some of them were identified and characterized: M-10 (max. 5 % AR after 14 d), M-05 (max. 18 % AR after 14 d), M-14 (max. 1.6 % AR after 62 d), M-11/12 (max. 6.5 % AR after 62 d) and M-13 (max. 4.4 % AR after 14 d). In a study performed to investigate the rate of degradation of M-05 it was observed that this metabolite may be a precursor of M-14 (max. 10.4 % after 29 d) and of another unidentified metabolite (max. 25.5 % AR after 135 d).

Degradation of fluopicolide was also investigated (labelled either at the benzoyl or pyridine ring) under dark anaerobic conditions in one soil (pH 7.4, OC 2.2 %, clay 11 %). Fluopicolide was very stable under these conditions and only metabolites M-01 and M-02 were identified at minor amounts.

Photolytic degradation of fluopicolide (labelled in the pyridine ring) was investigated following application to soil thin layers (pH 7.4, OC 2.1 %, clay 17 %) irradiated with a Xenon lamp claiming to simulate a sunny day in Scotland (latitude 55 ºN). Photolysis degradation occurs to some extend but no new metabolites are identified in these studies. During the peer review the applicant was required to provide further information on the effect of photolysis at other latitudes. The cases presented by the applicant implied challenging the actual measurements of natural irradiation in Scotland performed by the laboratory doing the study and how it related to the actual irradiation applied to the system tested. However, no

amendment to the original GLP report was presented. Theses cases were discussed in the meeting of experts PRAPeR 37 and PRAPeR 62 and were considered not acceptable. A data requirement for a transparent assessment of the contract laboratory's comparison of the light energy used in the experiment and how it related to natural conditions and an updated of the GLP report with the new calculations was identified. On the absence of this report the meeting considered that photolysis may contribute to some extend to the degradation of fluopicolide under natural conditions in EU and that the applicant should update their estimate of photolytic half life at latitudes of 40 – 45 ºN.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

Rate of degradation of fluopicolide was calculated with data obtained in the route studies and in an additional study performed in one soil (pH 5.6, OC 3.3 % , clay 31 %) under aerobic conditions at 20 ºC. Fluopicolide is high to very high persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 194 d – 411 d) in soil under aerobic conditions at 20 ºC. A slower degradation rate observed at 10 ºC degradation ($DT_{50\ lab\ 10ºC}$ = 667 d). M-03 is low persistent ($DT_{50\ lab\ 20\ ºC}$ = 2.2 – 5.0 d) at acidic pH and very low persistent ($DT_{50\ lab\ 20\ ºC}$ < 5h) at neutral or slightly alkaline pH and may be considered and intermediate in the formation of M-01 and M-02. M-01 is very high persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 557 – 1831 d) and M-02 is low persistent ($DT_{50\ lab\ 20\ ºC}$ = 3.2 – 4.6 d).

Further studies are available to investigate the rate of degradation of metabolites M-05, M-10 and M-14 in three soils (pH 5.4 – 7.5, OC 1.1 – 2.6 %, clay 4 - 23 %) under dark aerobic conditions. M-05 and M-10 are moderate to high persistent (M-05: $DT_{50\ lab\ 20\ ºC}$ = 31 -130 d; M-10: 24 – 253 d), M-14 is low persistent in soil ($DT_{50\ lab\ 20\ ºC}$ = 5- 8 d).

A kinetic evaluation of data obtained with the degradation study of metabolite M-02 was performed with Model Maker in order to obtain the degradation and formation parameters of some metabolites for use in the subsequent risk assessment. In this analysis initial concentration of M-02 was fixed to 100 % to improve the fitting of the metabolites. For M-02 and M-05 the half lives obtained were in the range of the ones previously calculated. RMS considered that values obtained for metabolites M-11/12 ($DT_{50\ lab\ 20\ ºC}$ = 38.5 – 86.1 d), M-13 ($DT_{50\ lab\ 20\ ºC}$ = 10.3 – 43.0 d), and M-10 ($DT_{50\ lab\ 20\ ºC}$ = 4.5 – 307 d) were not robust due to low and variable levels of these metabolites but acceptable to be used in groundwater modelling. The meeting of experts PRAPeR 37 dicussed on the formation fraction derived for metabolite M14 from this study. The meeting agreed that averaging formation fractions of 0 accounting for the experiments were the metabolite is not detected, is not appropriate and that a formation fraction of 0.384 should be used when modelling the fate of this metabolite.

Photolysis may contribute to some extend to the degradation of fluopicolide under natural conditions in EU (see above section).

Dissipation of fluopicolide under field conditions has been investigated in a number of field dissipation studies in Germany (3 studies, 3 sites), Spain, Southern France and Northern France. One of the studies performed in Germany and the studies performed in France were prolonged over some seasons to investigate the potential for accumulation of fluopicolide residues. In all the field studies the product was sprayed at late spring or early summer on the bare soil surface, that was not cultivated and maintained free of vegetation during the duration of the study. Dissipation in most of the cases was better described by a biphasic model. The potential influence of the milder extraction method employed on the field dissipation studies in relation of the laboratory ones was discussed in the meeting of experts

PRAPeR 37. The fact that a fraction of the parent compound could have not been quantified in these studies was considered by the experts. The experts agreed that the "non quantified" fraction could correspond to the fraction of parent compound non equilibrium adsorbed to the soil. Therefore, an analysis of the decline assuming non equilibrium adsorption (as the one presented by the applicant for ground water modelling and summarized by the RMS in addendum 1) could, eventually, be double counting this phenomenon. The PRAPeR 37 meeting therefore discounted the applicants proposed method of refining the groundwater assessment using non-equilibrium adsorption assumptions. The applicant calculated most of the degradation rates using a "hockey stick" model. However, RMS recalculated half lives by means of first order kinetics. Acceptable fitting ($r^2 > 0.85$) was obtained for only two sites (DT_{50} = 173.9 d, 186.9 d). The meeting of experts considered acceptable the "hockey stick" fitting of the non normalized data calculated by the applicant and presented in the supplement to addendum 1 (named as addendum 2 (November 2007) in the final addendum) by the RMS (DT_{50} = 99.1 – 171.9; DT_{90} = 691.1 – 1184.4 d). For two sites, RMS also calculated acceptable first order half lives for the metabolite M-01 (DT_{50} = 119.9; 315 d). A kinetic evaluation of the field dissipation studies with a multicompartmental model was presented by the applicant to obtain DT_{50} values normalised to standard laboratory conditions. The modelling exercise was developed in a three tiered approach. For the last tier PEARL leaching model was used to do reverse modelling to determine the rates of the metabolites taking into account their leaching potential. This allowed to derive first order degradation half lives for the parent fluopicolide ($DT_{50\ field\ norm}$ =77 – 223.6 d) and metabolites M-01 ($DT_{50\ field\ norm\ 20\ ^oC}$ = 73 d – 256.7 d) and M-03 ($DT_{50\ field\ norm}$ = 55.5 d, only data from one site available). It was considered that no reliable field half life could be derived for M-02.

Three soil dissipation and accumulation studies were conducted by the applicant in Germany (one site, 5 years), Northern France (one site, 4 years) and Southern France (one site, 4 years). As for the field dissipation studies, product was sprayed on bare soils that were maintained free from vegetation. RMS considers results of the study in Southern France inconclusive with respect to the potential accumulation of fluopicolide. For the study in Northern France the RMS considers that the residues (fluopicolide and M-01) in this site did not reach a plateau by the study end. With respect to the study performed in Germany, a peak plateau occurring after three years is observed. Also a tendency of accumulation of metabolite M-01 was observed with maximum residues measured 123 d after the fourth application. The applicant disagreed with the conclusion of the RMS with respect to the fact that plateau has not been reached in some of the soil accumulation studies. A position paper was submitted and evaluated by the RMS in addendum 1. The meeting of experts agreed with the RMS and confirmed the initial evaluation that indicates that the plateau has not been reached in some of the studies.

The meeting of experts discussed different potential explanations for the biphasic behaviour observed in the field dissipation and field accumulation studies. The meeting agreed that it may be due to different causes: photolysis at the start of the study, deficient homogeneization, time dependent adsorption among others. Overall, the meeting agreed that the behaviour could not be attributed to a single reason. The meeting agreed that the field studies could be used to derive half lives for the FOCUS exposure modelling. However, the meeting did not agreed in the interpretation proposed by the applicant intended to explain the biphasic behaviour solely based on a time dependent adsorption.

PEC in soil for uses in potatoes and vines were calculated by the applicant for fluopicolide and metabolite M-01 using FOCUS-PELMO (v. 3.3.2) and FOCUS GW scenarios Thiva and Hamburg. Degradation parameters derived from the field studies were employed (90th

percentile half life). For potatoes it was assumed that the product was only applied once every two years and an incorporation depth of 20 cm was assumed. For vines the incorporation depth was assumed to be 10 cm. In principle, the RMS did not agreed on the use of 90th percentile DT_{50} in combination of FOCUS GW modelling for the calculation of PEC in soil. The meeting of experts (PRAPeR 37) supported and confirmed the RMS position. RMS recalculated PEC soil using the same assumptions made by the applicant worst case half lives and standard first order kinetic without the use of leaching models and scenarios. For the risk assessment worst case results were selected (either from the applicant or the RMS). The experts meeting agreed in using the PEC soil for potatoes derived by the applicant, since it resulted to be more conservative. Potential for accumulation of fluopicolide and metabolite M-01 was confirmed by these calculations (plateau are reached for the parent after 7 yr in potatoes and after 9 years in vines and for the metabolite M-01 after 5 yr in potatoes and 6 yr in vines). Maximum PEC soil for metabolites M-02 and M-03 were calculated by the RMS assuming retention in the top 5 cm layer. The meeting of experts (PRAPeR 37) agreed in using a SFO DT_{50} = 290 d for fluopicolide and a SFO DT_{50} = 315 d for M01 since they result in DT_{90}'s corresponding approximately to the worst case DT_{50} observed in the field studies.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Adsorption / desorption of fluopicolide (four studies, nine soils) metabolites M-01 (one study, five soils), M-02 (one study, three soils), M03 (two studies, five soils), M-05 (one study, three soils) and M-10 in soil was investigated by batch adsorption / desorption experiments. Fluopicolide exhibits medium mobility in soil (K_{Foc} = 172 – 580 mL / g), however it seems two be high mobile in subsoil (K_{Foc} = 83 – 106 mL / g; only two experiments available with soils from two different horizons of the same site). M-01 and M-02 are very high mobile in soil (M-01: K_{Foc} = 31 - 51 mL / g; M-02: K_{Foc} = 1.1 – 10.5 mL / g). Due to the instability at neutral or alkaline pH, for M-03 it was only possible to obtain reliable results in acidic soils (three of the five soils tested). Metabolite M-03 is high mobile in soil (K_{Foc} = 82 - 133 mL / g). Finally metabolites M-05 and M-10 exhibit very high mobility in soil (M-05: K_{Foc} = 11 - 49 mL / g; M-10: K_{Foc} = 0 – 10.66 mL / g).

Mobility of lysimeter metabolites M-14, M-11/12 and M-13 was assessed by the HPLC method. All these metabolites exhibit very high mobility. Due to the high polarity of M-11/12 and M13 the results obtained were considered meaningless and a K_{oc} = 0 was assumed for the risk assessment. For M-14, it was possible to estimate acceptable soil sorption parameters (K_{oc} = 19.2 mL / g).

A three years lysimeter study with two square lysimeters was performed in Germany. Pyridine labelled fluopicolide was applied at 400 g a.s on cultivated lysimeters. For one lysimeter the product was applied first year only and for the second lysimeter the product was applied first and second year. Due to the fact that fluopicoline was only labelled at the pyridine ring no information on the potential leaching of M-01 was obtained from these experiments. A maximum of 6.35 % AR was found in the leachate after three years. The parent compound fluopicolide was found in the first two leachate samples of the first year in one of the lysimeters (0.76 μg / L, 0.18 μg / L). These observations were believed to be explained by fast flow transport in macropores in this lysimeter. A number of metabolites not previously identified in the laboratory degradation in soil studies were identified in the leachate of these lysimeters: **M-05** (max. annual average concentration = 0.9 μg / L), **M-10** (max. annual average concentration = 0.83 μg / L), **M-11/12** (max. annual average

concentration = 0.55 / 0.36 μg / L), **M-13** (max. annual average concentration = 0.14 μg / L), **M-14** (max. annual average concentration = 0.19 μg / L), **M-15** (max. annual average concentration = 0.095 μg / L), M-16 (max. annual average concentration = 0.08 μg / L), M54 (max. annual average concentration = 0.03 μg / L), P6A (max. annual average concentration = 0.03 μg / L), P6 (max. annual average concentration = 0.07 μg / L), M3 (max. annual average concentration = 0.04 μg / L) and M29 (max. annual average concentration = 0.09 μg / L)[41].

A field leaching study in South West Germany is also available. A suspo-emulsion formulated fluopicolide was applied to lettuce (grow stage BBCH 14-19) at a rate equivalent to 400 g / ha split in four applications between May and October 2000. Suction samplers were placed at 30, 50, 85, 120 and 150 cm depth and samples of soil and water were collected for 3 years. Succeeding crops were oilseed rape (2001 and 2002) and winter wheat (2002). Flupicolide and metabolites M-03, M-02 and M-01 were analysed by LC/MS-MS (LOQ = 0.075 μg / L per analyte). Annual average concentration of fluopicolide and metabolite M-02 in the leachate were below 0.1 μg / L at depths higher than 85 cm or 30 cm respectively. Annual average concentration of metabolite M-03 was below LOQ at all the sampling depths. However, metabolite **M-01** reached annual average concentrations up to 2.93 μg / L at 120 cm depth on the third year after application.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Hydrolysis of fluopicolide and its soil metabolite M-01 was investigated in sterile buffer aqueous solutions (pH 5, 7 and 9) at 25 ºC. Additionally, hydrolysis of metabolite M-01 was also investigated at 50 ºC. Fluopicolide and its metabolite M-01 may be considered stable to hydrolysis under most relevant environmental conditions. Hydrolysis of soil metabolite M-03 was also investigated in sterile buffer solutions (ph 5.1, 6.1, 7.1 and 8.1) at 20 ºC. Hydrolysis M-03 was pH dependent with half lives between 45.5 h (pH 5.1) to 9 min (pH 8.1).

Aqueous photolysis of fluopicolide was investigated in three separated studies at 25 ºC with benzoyl labelled (two studies; one in sterile pH 7 buffer and the other with natural water) or pyridine labelled fluopicolide (in sterile pH 7 buffer). Artificial light (Xenon filtered lamp) simulating summer at latitudes between 35º and 38º N was used in these studies. One of the studies show a slightly contribution of aqueous photolysis to the degradation of fluopicolide; however, the other two studies indicated that the contribution of photolysis is actually negligible. It may be concluded that aqueous photolysis is unlikely to be a significant route of degradation of fluopicolide in the natural aqueous environment. An aqueous photolysis study at 25 ºC with artificial light simulating natural light intensity in Plainsboro, New Jersey (USA) is also available for metabolite M-01. It was concluded that there is no photolytic degradation of M-01 under these conditions.

Readily biodegradability studies are available for fluopicolide and its metabolite M-01. Both compounds should be considered not readily biodegradable.

A water / sediment study in two systems (pH water: 8.2, pH sediment: 6.5-6.6, OC sediment: 0.5 – 5.3 %) was performed to investigate the dissipation of fluopicolide (both benzoyl and pyridine labelled compounds were used) in the water environment. Degradation of

[41] Metabolites M54, P6A, P6, M3 and M29 were not characterized and their chemical identity remains unknown.

fluopicolide in the water sediment systems was very limited; 68.5 to 80.1 % AR remained as parent fluopicolide at the end of the experiments after 365 d. RMS calculated whole systems half lives for fluopicolide in both systems ($DT_{50\ whole\ system}$ = 873 – 1428 d). During the experiment, fluopicolide was partitioned to the sediment. The equilibrium was reached after about 30 d. At the equilibrium about 10 to 40 % AR remained as parent fluopicolide in the water phase. Only M-01 and M-02 were identified as degradation metabolites at low levels (M-01: max. in water 18.2 % AR, max. in sediment 3.9 % AR; M-02: max. in water 7.4 % AR, max in sediment 0.8 % AR). Unextractable sediment residue amounted up to a maximum of 10.3 % AR after 180 d and mineralization at the end of the study was negligible (max. 2.8 % AR after 365 d).

Inverse modelling using surface water model TOXSWA 1.2 was used in an attempt to determine degradation half lives for fluopicolide in water and sediment phases. However, a high correlation among these two parameters prevented the determination of separated degradation rate for the water and sediment phases. Therefore, the inverse modelling was used to obtain new estimations of the whole system degradation parameters ($DT_{50\ whole\ system}$ = 710.1 – 921.42 d). These are the values that were used for the calculation of the geometric mean used in the FOCUS SW modelling exercise. These half lives are slightly shorter than the ones calculated by the RMS but the difference is not considered to influence the outcome of the assessment performed for the representative uses.

In a separated modelling exercise, TopFit was used to derive whole system half lives for fluopicolide, M-01 and M-02 from the available water / sediment studies. However, due to the limited number of data and low levels of metabolites it was only possible to obtain reliable parameters for parent fluopicolide ($DT_{50\ whole\ system}$ = 686.4 – 897.1 d), these estimations are slightly shorter than the previous ones made by the RMS and the applicant with TOXSWA.

$PEC_{SW\ /\ SED}$ were calculated by means of FOCUS SW. FOCUS Step 1-2 were calculated for fluopicolide and metabolites M-01, M-02 and M-03. FOCUS SW Step 3 values were also calculated for fluopicolide.

4.2.2. Potential for ground water contamination of the active substance, their metabolites, degradation or reaction products

Potential of ground water contamination by fluopicolide and metabolites M-03, M-01, M-02, M-05, M-10, M-11, M-12, M-14 and M-13 was assessed in the original dossier for the use in vines and potatoes with FOCUS PELMO 3.3.2. The interception factor used for vines was slightly too high for the first application. For potatoes, application was assumed to occur once every three years. This was not fully in agreement with the proposed GAP where no restriction is proposed and even application every year is not excluded. Furthermore, this was not consistent with PEC soil calculations where application every two years was assumed. Degradation rates of fluopicolide and metabolites M-03 and M-01 are derived from field studies. Since the metabolite M-01 shows very high mobility in soil, some doubts arose during the peer review about whether the half life derived from field dissipation studies could actually represent a reliable degradation half life. The PRAPeR 37 expert meeting discussed this issue an agreed that the use of field data to derive degradation half lives is not recommended for compounds highly mobile such us M01. However, in this case they noted that a correction to account on the substance that could have been leach to deeper layers had been done and that no significant impact in the exposure assessment would be expected by

using a more adequate degradation half life. Degradation parameters for M-02, M-05, M-10, M-11, M-12, M-14 and M-13 were taken from laboratory aerobic degradation studies.

In these calculations, for vines, the 0.1 μg / L limit for the predicted 80th percentile annual concentration at 1m depth, was exceeded by fluopicolide (two of seven scenarios), M-03 (one of seven scenarios), M-01 (seven of seven scenarios; trigger of 0.75 μg / L exceeded in the seven scenarios; 1.75 – 4.61 μg / L), M-05 (seven of seven scenarios), M-10 (seven of seven scenarios), M-11 (seven of seven scenarios), M-12 (seven of seven scenarios), M-13 (one of seven scenarios).

For potatoes (applied only once every three years), the 0.1 μg / L limit for the predicted 80th percentile annual concentration at 1m depth was exceeded by M-01 (eight of nine scenarios; trigger of 0.75 μg / L exceeded in six scenarios; 1.22 – 2.00 μg / L), M-05 (three of nine scenarios), M-10 (two of nine scenarios), M-11 (three of nine scenarios), M-12 (two of nine scenarios), M-13 (one of nine scenarios).

Before the PRAPeR 37 expert meeting a new PELMO modelling based on a GAP for potatoes with applications every two years was presented in addendum 1. In this calculation, the 0.1 μg / L trigger for the predicted 80th percentile annual concentration at 1m depth was exceeded by M-01 (eight of nine scenarios; trigger of 0.75 μg / L exceeded in seven scenarios; 0.83 – 3.15 μg / L), M-05 (three of nine scenarios), M-10 (five of nine scenarios), M-11 (four of nine scenarios), M-12 (three of nine scenarios), M-13 (one of nine scenarios). Additionally, calculations for application every year are available in addendum 1 and may be considered by MSs for situations were applications may occur every year . In this worst case GAP, concentrations of M01 are still below 01 μg / L for one scenario and the level of 10 μg / L is not exceeded in any of the scenarios for any of the compounds under consideration.

Calculations produced with a second FOCUS GW modelling were required during the peer review, following the EFSA PPR panel opinion on comparability of FOCUS GW models.[42] The applicant submitted a new modelling exercise based on PEARL that deviated considerably from standard approaches in the processing of field data by assuming time dependent adsorption [see addendum 1 (November 2007)]. As already discussed in the previous sections, the meeting of experts (PRAPeR 37) did not find the use of this approach supported or justified by available experimental evidence. Therefore, new FOCUS PEARL GW calculations for potato and vines were provided before the meeting PRAPeR 62 in addendum 2 (December 2008). For potatoes applied every two years, the 0.1 μg / L trigger for the predicted 80th percentile annual concentration at 1m depth was exceeded by flupicolide (one of nine scenarios), M-03 (two of nine scenarios), M-01 (nine of nine scenarios; trigger of 0.75 μg / L exceeded in eight scenarios; 0.727 – 3.25 μg / L), M-05 (seven of nine scenarios), M-10 (six of nine scenarios), M-11 (five of nine scenarios), M-12 (two of nine scenarios), M-13 (one of nine scenarios). Additionally, calculations for application every year and every three years are available in addendum 2 and may be considered by MSs for situations were such application regimes may occur. For applications every year concentrations of M01 are above 0.75 μg / L in all nine scenarios. For application in vines the FOCUS PEARL modelling exercise show that the 0.1 μg / L trigger for the predicted 80th percentile annual concentration at 1m depth was exceeded by fluopicolide (six of seven scenarios), M-03 (one of seven scenarios), M-01 (seven of seven scenarios; trigger of 0.75 μg / L exceeded in the seven scenarios; 1.62 – 6.07 μg / L), M-05 (six of seven

[42] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models. The EFSA Journal (2004) 93, 1-20.

scenarios), M-10 (six of seven scenarios), M-11 (seven of seven scenarios), M-12 (four of seven scenarios) and M-13 (one of seven scenarios).

In the lysimeter study, where potatoes were planted, annual average concentration of metabolites M-05, M-10, M-11, M-12, M-13 and M-15 at 1 m depth reach or exceed the 0.1 μg / L trigger, in the case of M-05 and M-10 also the trigger of 0.75 μg / L was exceeded in at least one of the lysimeters one of the three years that lasted the experiment; as noted in previous sections, the lysimeter study used fluopicolide radio-labelled in the pyridine ring and thus no information on leaching of metabolite M-01 was available from this study. In the field leaching study metabolite M-01 reached an annual average concentration of 2.9 μg / L in the leachate at 120 cm depth the third year after the product was applied.

4.3. Fate and behaviour in air

Half life in the atmosphere was estimated to be 3.4 d assuming 24 d OH radical concentration of 0.5 x 10 ^{6} radicals/cm^{3}. However, the vapour pressure of fluopicolide is 3 x 10^{-7} Pa at 20 ºC and Henry's Law Constant is 4.15 x 10^{-5} m^{3} / mol at 20 ºC. Therefore, it is unlikely that the fluopicolide enters in the atmosphere through volatilization. However, since half life in the atmosphere is longer than 2 d and fluopicolide is sprayed, formation of aerosols and long range transport through the atmosphere cannot be excluded.

5. Ecotoxicology

Fluopicolide was discussed at two PRAPeR expert meetings for ecotoxicology (PRAPeR 38 and 63) in December 2007 and on January 2009 on basis of the draft assessment report (November, 2005) , the Addendum 1 Vol 3 B.9 (November, 2007) and Addendum 2 Vol 3 B.9 (December, 2008). The Addendum 3 (February, 2009) was submitted after the meetings.

The representative uses evaluated were the uses as fungicide in vine and potato at the application rate of 0.4 kg a.s./ha. The formulated products were "EXP 11074B" (WG) containing 44.4 g of fluopicolide/kg + 6667 g fosetyl–Al and "EXP 11120A" (SC) containing 62.5 g fluopicolide /L + 625 g propamocarb Hydrochloride/L.

An impurity was detected in the technical material, toluene. Toluene was present at (1.0-4.06 g /kg which is (0.1 - 0.406% w/w) in the fluopicolide batches used in the ecotoxicological studies. The RMS included the assessment of the ecotoxicological relevance of toluene in Addendum 3 (February, 2009). The toluene derived from the fluopicolide technical is not relevant from an ecotoxicological point of view

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000 September 2002; Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC.

5.1. Risk to terrestrial vertebrates

Fluopicolide was of low toxicity to birds and mammals based on the available information. The acute and short-term endpoints for birds were obtained from studies on *Colinus virginianus* exposed to fluopicolide. The lowest acute and short-term endpoints LC_{50}/LD_{50} for birds were 2250 mg a.s./kg bw and > 1744 mg a.s./kg bw/day, respectively. The lowest

end-point observed in a reproduction study with the *C. virginianus* , NOEC = 88.9 mg .a.s./kg bw/day.

The lowest acute and long-term endpoints in mammals were observed in rat LD_{50} > 5000 mg a.s./kg bw and NOAEL = 20 mg a.s./kg bw/day.

The RMS proposed in the DAR to assess the risk for an insectivorous bird and herbivorous mammal in potatoes and vines. The risk was also calculated for a medium herbivorous bird and mammal in potatoes although potato foliage is considered unpalatable to birds and mammals. Although not specifically foreseen by SANCO/4145/2000 for leafy crops, such as potatoes, the risk to an insectivorous mammal was also assessed for this use.

EFSA considers that the risk for the herbivorous birds and mammals for this unpalatable crop should not be considered as relevant.

The acute, short and long-term risk to birds was considered to be low as the TER values exceed the Annex VI trigger value for both intended uses in potatoes and vines. The acute and long-term risk for herbivorous and insectivorous mammals was assessed as low for the use in potatoes. Also a low acute risk to herbivorous mammals was identified for the use in vine. However, a potential high long-term risk to mammals was observed for the use in vine. The RMS included in the Addendum 1 a refinement of the long-term risk based on the higher canopy interception (70% of spray interception). However, taking into account that fluopicolide is applied to vine at growth stage of BBCH 53-81, the experts at the PRAPeR 38 meeting agreed that the actual risk assessment for mammals cover only one out of three applications in vineyards during the early growth stages (up to BBCH 57). The other two applications should be at later growth (up to BBCH 81) where the interception higher than the 60%. Therefore, the experts agreed to included a footnote in the list of endpoints for the long-term risk assessment for herbivorous mammals that current risk assessment covers only one out of three applications in vineyards during the early growth stages (up to BBCH 57). The RMS included the following explanation in the updated list of endpoints in February 2009 and in the new Addendum 3 (February, 2009) by the RMS. "The long term risk to herbivorous mammals consuming contaminated sub-canopy ground vegetation in vineyards was refined by correcting for canopy interception. A canopy interception ≥70% (assumption used in all environmental exposure modelling) gave a TER of 4.98, close to the Annex VI trigger (5), and indicative of acceptable risk. However, a canopy interception of 60% was considered more appropriate for treatment at earlier growth stages (BBCH 53-57) where the canopy may be less fully developed. Assuming ≥60% interception a TER of 3.73 was derived indicating possible risk which could be mitigated by reducing the number of applications. Hence, for earlier treatments (BBCH 53-57), if the canopy is not fully developed then a reduction in the number of applications should be considered".

The risk from secondary poisoning to birds and mammals was assessed although the Log_{Pow} for fluopicolide equals 2.9. The resulting TER values all exceed the Annex VI trigger value indicating a low risk to fish- and earthworm eating birds and mammals.

Furthermore the acute risk to birds and mammals from consumption of contaminated drinking water was assessed. A low acute risk to birds and mammals from this exposure route was identified for the two representative uses.

The risk to birds and mammals from plant metabolites was considered to be low.

Overall it was concluded that the risk to birds and mammals was low, except for the long-term risk for mammals for the use in vines. Risk mitigation measures should be required at

Member Stated level. The risk form secondary poisoning and from consumption of contaminated drinking water was assessed as low for birds and mammals.

5.2. Risk to aquatic organisms

Based on the available data the fluopicolide was considered to be very toxic to aquatic organisms. *Navicula pelliculosa* was the most sensitive organisms tested to fluopicolide and the lead formulations EXP 11074B and EXP 11120A. The 72 h E_bC_{50} for *N. pelliculosa* was 0.29 mg a.s./L, this endpoint was driving the risk assessment. The risk from fluopicolide was calculated using PECsw-values derived from FOCUS.

At the end of the peer-review process one Member State pointed out , that the Hoberg, 2003 study with *N. pelliculosa* , which drives the aquatic risk assessment is not considered valid any longer. A the recent re-evaluation of algae studies within their national registration procedure, revealed that studies for fluopicolide on the two diatom and one cyanobacteria species which were also used in the DAR are not valid since they do not meet the validity criteria. In the Hoberg, 2003b study with *N. pelliculosa*_the variation coefficient of the sectional growth rate in the solvent control is 96%. In the Young & Abedi, 2003 study with Anabaena flos-aquae the cell growth between control and solvent was significantly different. The variation coefficient of the sectional growth rate in the solvent control is 62%.

However, EFSA considered, that as far as both studies were performed in 2003, they meet the validity criteria of the test guidance available at this dates, OECD 201 1984.

However, EFSA proposed that Member States should considered this .

Vine

The TERs values estimated based on the PEC_{sw} FOCUS step 1 for the *Lemna gibba* and sediment dwellers were all above the Annex VI trigger value. The acute and chronic TERs based on the PECsw FOCUS step 2 for the aquatic invertebrates were all above the trigger values. A low acute and chronic risk to aquatic invertebrates and aquatic plants was identified from the representative use in vine. Acute and chronic TERs values estimated for fish and algae, were all above the Annex VI trigger values, based on Focus step 3 PEC_{sw} values for all scenarios apart from the R4 (stream) scenario (late application) for the use in vine. The applicant proposed different options to refine the potential high risk. A refinement of the risk assessment based on the $FOCUS_{sw}$ step 4 was not presented in the DAR.

Potato

The TERs estimated for the *Lemna gibba* and sediment dwellers based on the PEC_{sw} FOCUS step 1 were all above the Annex VI trigger value. The chronic TER based on the PEC_{sw} FOCUS step 2 for the aquatic invertebrates was above the trigger values. TERs estimated for fish and algae based on Focus step 3 PEC_{sw} values, were all above the Annex VI trigger values, for all scenarios apart from the acute risk to fish and the chronic risk to algae in D6 (ditch, 2nd crop), R1 (stream) and R3 (stream) scenarios (early application). Risk mitigation measures should be also considered at Member State level to refine the potential risk. A refinement of the risk assessment based on the $FOCUS_{sw}$ step 4 was not presented in the DAR.

A refined of the risk assessment based on the $FOCUS_{sw}$ step 4 was not presented in the DAR. Therefore, EFSA identified after the PRAPeR meeting a data requirement for the submission of a refined risk assessment for aquatic organisms for both intended uses.

Fluopicolide was found in concentrations above 10% of the applied amount in a water/sediment study. Therefore the risk to sediment dwelling organisms from exposure to the active substance needs to be addressed. A spiked sediment study is available. Based on the PEC_{sed} values, the risk to sediment dwelling organisms from the representative uses in vines and potatoes can be regarded as low.

Acute toxicity studies on fish (*Oncorhynchus mykiss*) with the metabolites M-01, M-02 and M-05 were available. Algae toxicity tests were also available with *N. pelliculosa* for the metabolites M-01 and M-05. Furthermore, metabolite M-01 was tested on *Daphnia magna* and *Lemna gibba*. The risk from these metabolites for the representative uses in vine and potatoes was assessed as low. The RMS included the assessment of the ecotoxicological relevance of the ground water metabolites M-01, M-03, M-05, M-10, M-11, M-12, M-13 in Addendum 3 and in the updated list of endpoints (Feb. 2009). The risk of ground water metabolites for aquatic organisms was assessed by deriving TERs for the most sensitive aquatic species *N. pellicullosa* and with the worst case FOCUS PEC_{gw} x 0.1 (PEC_{gw} to PEC_{sw} dilution correction) from use in vine and potatoes. The TERs estimated were above the Annex VI trigger values; therefore, low risk to aquatic organism was expected from metabolites formed in groundwater following proposed uses in vine and potatoes.

A study on bioaccumulation in fish was available although the log_{Pow} is 2.9 for fluopicolide. The resulting BCF was 121. Elimination of the radioactive residues was nearly complete within 18 days. Therefore the risk for bioaccumulation in fish from fluopicolide was considered to be low. In addition the risk to fish eating birds and mammals was considered to be low (see section 5.1 above) for the representative uses of fluopicolide in vine and potatoes.

Overall a potential chronic aquatic risk to algae from fluopicolide use on vine was identified in one $FOCUS_{sw}$ step 3 scenario and a potential acute risk to fish and chronic risk to algae from fluopicolide used on potatoes was identified in three $FOCUS_{sw}$ step 3 scenarios, for which risk mitigation measures will be required. However, the risk of the relevant metabolites to aquatic organism was assessed as low. The risk for bioaccumulation in fish from fluopicolide is considered to be low.

5.3. Risk to bees

Acute contact and oral toxicity studies with fluopicolide and the lead formulations EXP 11074B and EXP 11120A were available. The resulting HQ values do not breach the Annex VI trigger value indicating a low risk to bees for the representative uses of fluopicolide in vine and potatoes.

5.4. Risk to other arthropod species

Standard laboratory studies with *Aphidius rhopalosiphi* and *Typhlodromus pyri* with the lead formulations EXP 11074B and EXP 11120A were available. In addition to this a laboratory study on *Chrysoperla carnea* and extended laboratory studies with *T. pyri* and *A. rhopalosiphi* with the lead formulation EXP 11120A were available.

The resulting in-field and off-field HQ values are below 2 for both the representative uses indicating a low risk to non-target arthropods. This was confirmed by the laboratory study on

C. carnea and the extended laboratory studies with *T. pyri* and *A. rhopalosiphi* during which effects were below 50% at dose rates exceeding the in-field application rate in potatoes.

5.5. Risk to earthworms

A study on the acute and long term toxicity of fluopicolide to earthworms was available as well as long term toxicity studies with the lead formulations EXP 11074B and EXP 11120A. The resulting acute and long term TER values were above the appropriate Annex VI trigger values indicating a low risk to earthworms from the representative uses of fluopicolide evaluated.

M01 and M03 were identified as major metabolites in soil by the section on fate and behaviour. Acute toxicity studies with the metabolites M-01, M-02 and M-03 are available and a long term toxicity study with the metabolite M-01. No long term study on earthworms with the metabolite M-03 was considered necessary as this metabolite was not considered to be persistent. The resulting acute and long term TER values were above the appropriate Annex VI trigger values indicating a low risk to earthworms from the major metabolites M-01 and M-03 and from the metabolite M-02.

5.6. Risk to other soil non-target macro-organisms

Fluopicolide and the major metabolite M-01 are persistent in soil as the soil DT_{90} for both substances exceeds 1 year. Therefore studies on the effects on *Folsomia candida* and soil litter degradation were made available. No studies on soil non-target macro-organisms with the major soil metabolite M-03 were considered necessary as this metabolite was not considered to be persistent.

Based on the resulting TER values the risk to *F. candida* from fluopicolide and M-01 were regarded as low for the representative uses in vine and potatoes.

Straw decomposition in the litter bags in the soil treated with the fluopicolide and metabolite M-01 was not significantly affected over a period of 184 days of incubation. Therefore, overall the weight of evidence indicate that the risk to organic matter decomposition in soil contaminated by fluopicolide and M-01 residues from the proposed uses in vine and potatoes was assessed as low.

5.7. Risk to soil non-target micro-organisms

The effects of fluopicolide were tested on soil microbial respiration and nitrogen transformation. Effects were less than 25 % at day 28 at 1.84 mg a.s./kg d.w. soil (1380 g a.s/ha). This tested concentration exceeds the predicted environmental concentrations in soil and therefore the risk to soil non-target micro-organisms from fluopicolide was considered to be low for the representative uses evaluated. This was confirmed by studies with the lead formulations EXP 11074B and EXP 11120A. In these studies effects were less than 25% at day 28 at dose rates exceeding the application rates.

Also the effects of metabolite M-01 on soil microbial respiration and nitrogen transformation were tested. Effects were less than 25 % at day 28 at 0.92 mg/kg d.w. soil. This tested concentration exceeds the predicted environmental concentrations in soil and therefore the risk to soil non-target micro-organisms from M01 is considered to be low.

5.8. Risk to other non-target-organisms (flora and fauna)

To address the risk of fluopicolide to non-target plants, a glasshouse screening trial with 5 crop species, 11 broad-leaved weed species, 9 grass weed species and 2 sedges, exposed to EXP 11074B was submitted. . Effects were less 50% at 1280 g fluopicolide/ha.

This is confirmed by 5 further studies on seedling emergence and vegetative vigour with AE C638206 SC480 (a solo formulation containing 480 g fluopicolide/L) and the lead formulations EXP 11074B and EXP 11120A. An ER_{50} of > 3.0 kg/ha was established for both seedling emergence and vegetative vigour tests for EXP 11074B. An ER_{50} of > 2.13 L/ha was established for both seedling emergence and vegetative vigour tests for EXP 11074A. The TERs values estimated were all above the Annex VI trigger values, indicating a low risk to non-target plants from this substance in vines and potatoes..

To address the risk of the metabolite M-01 to non-target plant, a study on seedling emergence with 9 plant species from 6 plant families was conducted (corn, cucumber, oat, oilseed rape, pea, soybean, sugar beet, radish). The pre-emergent M-01 study revealed that no effects > 50 % on seedling germination and growth at rates < 0.0121 mg/kg soil and an ER_{50} of > 0.0121 mg /kg was established. The TERs of >6 and >31 could be established for M01 off-field pre-emergent effects on non-target plants indicating a low risk.

5.9. Risk to biological methods of sewage treatment

The respiration rate EC_{50} for fluopicolide exceeds 25.4 mg a.s./L. This probably reflects fluopicolide concentration in suspension rather than in solution as fluopicolide solubility is 2.86 mg/L. The risk to biological methods of sewage treatment is considered to be low for the representative uses of fluopicolide evaluated.

6. Residue definitions

6.1. Soil

Definition for risk assessment:	fluopicolide, M-03, M-01, M02.
Definition for monitoring:	fluopicolide

6.2. Water

6.2.1. Ground water

Definition for exposure assessment:	fluopicolide, M-03, M-01, M-05, M-10, M-11, M-12, M-13, M-15.
Definition for monitoring:	fluopicolide, M15 (pending of the finalization of the ground water assessment for this metabolite)

6.2.2. Surface water

Definition for risk assessment in surface water:	fluopicolide, M-03, M-01, M-02 (from soil)

in sediment:	fluopicolide, M-03, M-01, M-02 (from soil)
Definition for monitoring:	fluopicolide

6.3. Air

Definition for risk assessment:	fluopicolide
Definition for monitoring:	fluopicolide

6.4. Food of plant origin

Definition for risk assessment:	fluopicolide and metabolite M-01 separately
Definition for monitoring:	fluopicolide

6.5. Food of animal origin

Definition for risk assessment:	fluopicolide and metabolite M-01 separately
Definition for monitoring:	fluopicolide

6.6. Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
fluopicolide	High to very high persistent ($DT_{50\ lab\ 20\ °C}$ = 196 d – 413 d)	The risk to earthworms and for soil micro-organism was assesses as low.
M-01	Very high persistent in soil ($DT_{50\ lab\ 20\ °C}$ = 401 – 893 d)	The risk to earthworms and for soil micro-organism was assesses as low.
M-03	Low persistent (pH 4-5.4: $DT_{50\ lab\ 20\ °C}$ = 2.2 – 5.0 d) or very low persistent (pH 7.1-7.2: $DT_{50\ lab\ 20\ °C}$ < 5h)	The risk to earthworms was assessed as low.
M-02	Low persistent ($DT_{50\ lab\ 20\ °C}$ = 3.2 – 4.6 d)	The risk to earthworms was assessed as low

6.6.2. Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Fluopicolide	medium mobile (K_{oc} = 172-580 mL / g)	FOCUS GW: Yes, 0.1 µg / L trigger exceeded for vines and potatoes. Lysimeter: No	Yes	Yes	Fluopicolide was considered to be very toxic to aquatic organisms. The risk to aquatic organisms

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
					was assessed as high.
M-03	high mobile (K_{oc} = 82-133 mL / g)	FOCUS GW: Yes, 0.1 µg / L trigger exceeded for vines and potatoes. Lysimeter: No	No	No As a transient intermediate forming M01 and M02, genotoxic properties of M03 are considered to be covered by the non genotoxic potential of the parent, M01 and M02	Low risk was identified for the aquatic organisms.
M-01	very high mobile (K_{oc} = 31-51 mL/g)	FOCUS GW: Yes, 0.1 µg/L trigger exceeded for vines and potatoes; trigger of 0.75µg/L exceeded for vines and potatoes. Field leaching study: trigger of 0.75 µg/L exceeded.	No	No Rat oral LD_{50} = 500 mg/kg bw (Xn, R22, harmful if swallowed) No potential for genotoxicity, carcinogenicity or toxicity for reproduction ADI $_{(M01)}$ = 0.05 mg/kg bw/day ARfD $_{(M01)}$ = 0.3 mg/kg bw/day 10 % ADI was not exceeded by the consumers risk	M-01 was considered to be low toxic. Low risk was identified for the aquatic organisms.

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
				assessment performed by EFSA	
M-02	K_{oc} = 1.1 – 10.5 mL / g	FOCUS GW: No Lysimeter: No	no data, no assessment required	No Rat oral LD_{50} > 2000 mg/kg bw; no genotoxic potential; NOAEL (28-day, dietary rat) = 1574 mg/kg bw/day, the highest dose tested (less toxic than parent)	M-02 was considered to be harmful. Low risk was identified for the aquatic organisms.
M-05	very high mobile (K_{oc} = 11-49 mL/g)	FOCUS GW: Yes, 0.1 µg/L trigger exceeded for vines and potatoes) Lysimeter: trigger of 0.75 µg/L exceeded.	No	No Rat oral LD_{50} > 2000 mg/kg bw; no genotoxic potential; NOAEL (28-day, dietary rat) = 152 mg/kg bw/day (less toxic than parent)	M-05 was considered to be low toxic. Low risk was identified for the aquatic organisms.
M-10	very high mobile (K_{oc} = 0-2.5 mL/g)	FOCUS GW: Yes, 0.1 µg/L trigger exceeded for vines and potatoes. Lysimeter: trigger of 0.75 µg/L exceeded.	No	No Rat oral LD_{50} > 2000 mg/kg bw; no genotoxic potential; NOAEL (28-day, dietary rat) = 163.2 mg/kg bw/day (less toxic than parent)	Low risk was assessed for the aquatic organisms.
M-11	very high	FOCUS GW: Yes, 0.1 µg/L	No	No	Low risk was assessed for

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
	mobile (K_{oc} = 0 mL/g)	trigger exceeded for vines and potatoes. Lysimeter: trigger of 0.1 µg/L exceeded.		Structure similar to M10 (considered less toxic than parent)	the aquatic organisms.
M-12	very high mobile (K_{oc} = 0 mL/g)	FOCUS GW: Yes, 0.1 µg/L trigger exceeded for vines and potatoes. Lysimeter: trigger of 0.1 µg/L exceeded.	No	No Structure similar to M10	Low risk was assessed for the aquatic organisms.
M-13	very high mobile (K_{oc} = 0 mL/g)	FOCUS GW: Yes, 0.1 µg/L trigger exceeded for vines and potatoes. Lysimeter: trigger of 0.1 µg/L exceeded.	No	No Structure similar to M10	Low risk was assessed for the aquatic organisms.
M-14	very high mobile (K_{oc} = 19.2 mL/g)	FOCUS GW: No Lysimeter: No	No	No No genotoxic potential	Low risk was assessed for the aquatic organisms.
M-15	very high mobile (K_{oc} = 0 mL/g)	FOCUS GW: No Lysimeter: trigger of 0.1 µg/L reached (0.095 µg/L).	No	No data, data required	Low risk was assessed for the aquatic organisms.

6.6.3. Surface water and sediment+

Compound (name and/or code)	Ecotoxicology
Fluopicolide (water and sediment)	Fluopicolide was considered to be very toxic to aquatic organisms. The risk for aquatic organisms was assessed as high.
M-01 (water and sediment)	Low toxicity and low risk for the aquatic organisms.
M-03 (water and sediment)	Low risk for the aquatic organisms.
M-02 (soil metabolite, potentially may reach water and sediment)	M-02 was considered to be harmful for aquatic organisms. Low risk was identified for the aquatic organisms.

6.6.4. Air

Compound (name and/or code)	Toxicology
fluopicolide	Rat LC_{50} inhalation > 5.16 mg/L air/4 h, nose-only, as a dust aerosol, no classification proposed

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Toxicological information on the metabolite M15 to assess its relevance as groundwater metabolite (relevant for all representative uses evaluated; submission date proposed by the notifier: none; refer to point 2.8 and 4.2.2)
- Operator, worker and bystander exposure risk assessment to both combi-formulations have to be considered at Member State level, as there is no agreed procedure for performing combined risk assessment for more than one active substance and this assessment has only considered the fluopicolide component of the representative formulations (relevant for all representative uses evaluated; see section 2.12)
- A data requirement for a full transparent assessment of the photolysis in soil study contract laboratory's comparison of the light energy used in the experiment and how it related to natural conditions and an updated of the GLP report with the new calculations was identified. In absence of the report amendment applicant should update their estimate of photolytic half life at 40 – 45 ºN (relevant for all representative uses evaluated; no submission date proposed by the notifier; see section 4.1)
- EFSA identified after the PRAPeR meeting a data requirement for the submission of a refined risk assessment for aquatic organisms (relevant for all representative uses evaluated; submission date proposed by the notifier: Unknown; see section 5.2).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the applicant against downy mildew (*Plasmopara viticola)* in vine grapes, from growth stage of BBCH 53 up to growth stage of BBCH 77-81, in all EU countries, up to a maximum of three applications at a maximum individual application rate per spray of 133 g a.s./ha, with an interval of 10 to 14 days between applications, and against late blight (*Phytophtora infestans*) in potatoes, from growth stage of BBCH 20 up to growth stage of BBCH 89-91, in all EU countries, up to a maximum of four applications at a maximum individual application rate per spray of 100 g a.s./ha, with an interval of 5 days between applications.

The representative formulated products for the evaluation were 'AE F053616 06 WG71 A1' or 'EXP 11074B', a water dispersible granule (WG), containing 44.4 g/kg fluopicolide and 666.7 g/kg fosetyl-aluminium and 'AE B066752 04 SC61 A1' or 'EXP 11120A', a suspension concentrate (SC), containing 62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible. Fluopicolide residues in food/feed of plant origin can be monitored with the modified version of the German modular multi-residues method DFG S19. Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of animal origin and environmental matrices. Since

fluopicolide is not classified as acute toxic or very toxic, analytical methods for the determination of residues of fluopicolide in body fluids and/or tissues are not required.

In the mammalian metabolism studies, fluopicolide was moderately rapidly but incompletely absorbed orally (approximately 62 %) and widely distributed. There was no evidence of bioaccumulation, fluopicolide was extensively metabolised and rapidly excreted mainly via faeces.

The acute toxicity of fluopicolide in rats was low, either by the oral, dermal or inhalation route, no skin irritation and only slight irritation to the eyes were observed. Fluopicolide did not exhibit skin sensitisation potential.

The liver was the main target organ of fluopicolide in short-term tests in rats, mice and dogs. A sub-acute NOAEL of 17.7 mg/kg bw/day was based on the 28-day rat study. The relevant short term NOAEL was 7.4 mg/kg bw/day from the 90-day dietary study in rat, based on haematological changes, clinical signs, liver and kidney toxicity at the next higher dose level of 109 mg/kg bw/day. As indicated in a mechanistic study, fluopicolide appears to be a phenobarbital-like inducer of liver enzymes.

It is unlikely that fluopicolide presents a genotoxic hazard to humans. In a chronic rat study, effects on liver and kidneys were observed, but no tumour induction was found. Similarly, in a chronic study with mice liver toxicity was observed. The increased incidence of hepatocellular adenomas seen at the high dose level was considered not relevant for human risk assessment, based on mechanistic considerations. Accordingly, no classification for carcinogenicity was proposed. The relevant long term NOAEL was based on the mice study with a NOAEL of 7.9 mg/kg bw/day, which was supported by the rat NOAEL of 8.4 mg/kg bw/day.

In a two-generation study no effect on reproduction or fertility was seen. Premature delivery, effects on body weight (dams and pups) and reduced crown-rump lengths at maternally toxic doses were observed in developmental studies in rats and rabbits; the relevant developmental NOAEL was the dose level of 20 mg/kg bw/day from the rabbit study.

A series of fluopicolide metabolites was assessed for their toxicological relevance with the aid of toxicological studies conducted with M01, M02, M04, M05, M10 and M14. Plant metabolites M04, M05, M08 and M09 were considered less toxic than the parent. The M01 metabolite may be considered of comparable toxicity as the parent, although slightly more acutely toxic. In principle, the ADI of the parent could have been applied, however, as an acceptable set of studies were conducted with M01 and considering that M01 is also a metabolite of another active substance, an acceptable daily intake (ADI) of 0.05 mg/kg bw/day was set for this metabolite as well as an acute reference dose (ARfD) of 0.3 mg/kg bw. The metabolites M01, M03, M05, M10, M11, M12, M13 and M14 were not considered relevant according to the guidance document on groundwater metabolites even if they appear at levels above 0.1 µg/L in groundwater, however information is lacking on the metabolite M15, which was not peer-reviewed.

The acceptable daily intake (ADI) of fluopicolide was set at 0.08 mg/kg bw/day derived from the 78-week dietary study in mice and supported by the 2-year study in rats; a safety factor of 100 was applied. The acceptable operator exposure level (AOEL) was set at 0.05 mg/kg bw/day, derived from the 90-day rat study, corrected for limited oral absorption of 62 % and applying a safety factor of 100. The acute reference dose (ARfD) was set at 0.18 mg/kg bw, derived from the 28-day dietary rat study and the rabbit developmental study, applying a safety factor of 100.

For both representative preparations, the dermal absorption values were agreed at 0.24 % for the concentrate and 2.75 % for the in-use spray dilution. Considering only the fluopicolide component of these formulations, the level of operator exposure estimated at a maximum dose rate of 0.133 kg fluopicolide/ha in grapevines and 0.1 kg fluopicolide/ha in potatoes was below the AOEL for all scenarios proposed when gloves were used during mixing/loading and application and even when no personal protective equipment (PPE) was considered according to the German model and EUROPOEM. Estimated exposures for unprotected re-entry workers and bystanders were below the AOEL for both fluopicolide representative formulations.

Metabolism of fluopicolide was investigated in grapes, potatoes and lettuce. Metabolism was found to be moderate. Besides fluopicolide, its metabolites M-01, M-02 and M-06 were identified. With the exception of M-01 for which an ADI and an ARfD was set by the toxicology section, the metabolites were regarded as less toxic than the parent and/or were also found in the rat metabolism studies. It was decided to include M-01 in the residue definition for risk assessment for plant matrices. As the metabolite M-01 is not unique to fluopicolide it was not included in the residue definition for monitoring. A sufficient number of residue trials on grapes and potatoes supporting the notified GAPs have been submitted to propose MRLs for these crops.

Metabolism in rotational crops was found to be similar, but more extensive as in primary crops. Additionally identified metabolites were M-04, M-05, M-08 and M-09. On the basis of the results of field studies on rotational crops, no quantifiable levels of fluopicolide are expected in consumable crop parts.

Metabolism studies on lactating diary and laying hens showed a low transfer into tissues, milk and eggs. Metabolism was extensive, mainly by hydroxylation followed by conjugation. The only hydrolysis product identified was metabolite M-01, which was included in the residue definition for risk assessment because of its toxicological potential. Dietary burden calculations showed only significant intake of fluopicolide residues for cattle. On the basis of available feeding studies on lactating cows, no quantifiable residues are expected in animal products.

Chronic and acute dietary intake calculations showed that an exceedance of ADI or ARfD are not expected for intake of crops after treatment with fluopicolide according to the notified GAPs. The level of 0.75 µg/L is expected to be exceeded in groundwater by metabolites M-01, M-05, M-10 and M-11. A consumer risk assessment for the consumption of drinking water for these metabolites showed that an exceedance of the relevant reference values is not expected after chronic or acute intake of fluopicolide through drinking water.

Fluopicolide is of high to very high persistence in soil under aerobic conditions at 20 ºC. In soil, fluopicolide forms M-03. This compound breaks down to M-01 and M-02. M-03 is of low persistence in soils at acidic pH and of very low persistence in soils at neutral or slightly alkaline pH and may be considered and intermediate in the formation of M-01 and M-02. M-01 is of very high persistence in soil and M-02 is of low persistence. No other metabolites were detected in significant amounts in the laboratory soil studies. Extent of degradation in sterilized and non sterilized samples was in the same range, indicating little contribution of microbiological degradation. Degradation of M-02 produced an extensive number of pyridine derivatives. Some of them were identified and characterized: M-10, M-05, M-14, M-11/12 and M-13. M-05 and M-10 are moderate to high persistent, M-14 is low persistent in soil. RMS considered that values obtained for half lives metabolites M-11/12, M-13, and M-10

were not robust due to low and variable levels of these metabolites but acceptable to be used in groundwater modelling.

Fluopicolide was very stable under dark anaerobic conditions and only metabolites M-01 and M-02 were identified at minor amounts.

Photolysis degradation occurs to some extend but no new metabolites are identified in the available studies. On the absence of further data, the meeting considered that photolysis may contribute to some extend to the degradation of fluopicolide under natural conditions in EU and that the applicant should update their estimate of photolytic half life at latitudes of 40 – 45 ºN.

Dissipation of fluopicolide under field conditions has been investigated in a number of field dissipation studies in Germany, Spain, Southern France and Northern France. One of the studies performed in Germany and the studies performed in France were prolonged over some seasons to investigate the potential for accumulation of fluopicolide residues. The meeting of experts agreed with the RMS and confirmed the initial evaluation that indicates that the plateau has not been reached in some of the studies.

For PEC soil calculations, the meeting of experts (PRAPeR 37) agreed in using a SFO DT_{50} = 290 d for fluopicolide and a SFO DT_{50} = 315 d for M01 since they result in DT_{90} corresponding approximately to the worst case observed in the field studies. Potential for accumulation of fluopicolide and metabolite M-01 was confirmed by PEC soil calculation (plateau are reached for the parent after 7 yr in potatoes and after 9 years in vines and for the metabolite M-01 after 5 yr in potatoes and 6 yr in vines).

Fluopicolide exhibits medium mobility in soil. M-01 and M-02 are very high mobile in soil. Metabolite M-03 is high mobile in acidic soil. Finally metabolites M-05 and M-10 are very high mobile in soil.

A three year lysimeter study was performed in Germany. A number of metabolites not previously identified in the laboratory degradation in soil studies were identified in the leachate of these lysimeters: M-05 (max. annual average concentration = 0.9 μg / L), M-10 (max. annual average concentration = 0.83 μg / L), M-11/12 (max. annual average concentration = 0.55 / 0.36 μg / L), M-13 (max. annual average concentration = 0.14 μg / L), M-14 (max. annual average concentration = 0.19 μg / L), M-15 (max. annual average concentration = 0.1 μg / L), M-16 (max. annual average concentration = 0.08 μg / L), M54 (max. annual average concentration = 0.03 μg / L), P6A (max. annual average concentration = 0.03 μg / L), P6 (max. annual average concentration = 0.07 μg / L), M3 (max. annual average concentration = 0.04 μg / L) and M29 (max. annual average concentration = 0.09 μg / L)[43]. In the field leaching study metabolite M-01 reached an annual average concentration of 2.9 μg / L in the leachate at 120 cm depth the third year after the product was applied.

Mobility of lysimeter metabolites M-14, M-11/12 and M-13 was assessed by the HPLC method. All these metabolites are very high mobile. Due to the high polarity of M-11/12 and M13 the results obtained were considered meaningless and a K_{oc} = 0 was assumed for the risk assessment. For M-14 was possible to estimate acceptable soil sorption parameters (K_{oc} = 19.2 mL / g).

[43] Metabolites M54, P6A, P6, M3 and M29 were not characterized and their chemical identity remains unknown.

Fluopicolide and its metabolite M-01 may be considered stable to hydrolysis under most relevant environmental conditions. Hydrolysis M-03 was pH dependent with half lives between 45.5 h (pH 5.1) to 9 min (pH 8.1).

Aqueous photolysis is unlikely to be a significant route of degradation of fluopicolide in the natural aqueous environment.

Fluopicolide and M-01 compounds should be considered not readily biodegradable.

Degradation of fluopicolide in the water sediment systems was very limited. RMS calculated whole systems half lives for fluopicolide in both systems ($DT_{50\ whole\ system}$ = 873 – 1428 d). During the experiment, fluopicolide was partitioned to the sediment. At the equilibrium about 10 to 40 % AR remained as parent fluopicolide in the water phase. Only M-01 and M-02 were identified as degradation metabolites at low levels.

$PEC_{SW\ /\ SED}$ were calculated by means of FOCUS SW. FOCUS Step 1-2 were calculated for fluopicolide and metabolites M-01, M-02 and M-03. FOCUS SW Step 3 values were also calculated for fluopicolide.

Potential of ground water contamination by fluopicolide and metabolites M-03, M-01, M-02, M-05, M-10, M-11, M-12, M-14 and M-13 was assessed in the original dossier for the use in vines and potatoes with FOCUS PELMO 3.3.2. Further modelling with FOCUS PEARL has become available during the peer review. Fluopicolide and its metabolites M-03, M-01, M-05, M-10, M-11, M-12 and M-13 may exceed the limit of 0.1 μg / L annual average concentration at 1 m depth for at least one of the scenarios simulated. Metabolite M-01 also exceeded the limit of 0.75 μg / L in a number of scenarios. For the use in vines fluopicolide exceeds 0.1 μg / L annual average concentration at 1 m depth for more than half of the scenarios simulated.

In the lysimeter study, where potatoes were planted, annual average concentration of metabolites M-05, M-10, M-11, M-12, M-13 and M-15 at 1 m depth reach or exceed the 0.1 μg / L trigger, in the case of M-05 and M-10 also the trigger of 0.75 μg / L was exceeded in at least one of the lysimeters one of the three years that lasted the experiment. In the field leaching study metabolite M-01 reached an annual average concentration of 2.9 μg / L in the leachate at 120 cm depth the third year after the product was applied.

Since half life in the atmosphere is longer than 2 d and fluopicolide is sprayed, formation of aerosols and long range transport trough the atmosphere cannot be excluded.

It was concluded that the risk to birds and mammals was assessed as low for both evaluated uses, except for the long-term risk for mammals for the use in vines. Risk mitigation measures should be required at Member Stated level. The risk form secondary poisoning and from consumption of contaminated drinking water was assessed to be low for birds and mammals.

A potential high risk was identified for aquatic organism for both evaluated uses; therefore risk mitigation measures should be required. The risk for bioaccumulation in fish from fluopicolide is considered to be low. The risk for the relevant metabolites to aquatic organism was assessed as low.

The risk for bees, non-target arthropods, earthworms, other non-target macro-organisms, soil non-target micro-organism, non-target plants and biological methods for swage treatments, was assessed to be low.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

Potential risk of ground water contamination above the regulatory limit of 0.1 μg / L when fluopicolide is used under vulnerable situations on potatoes every two years following the GAP proposed for the representative uses. Need for risk management measures should be considered by MSs under the evaluation of their authorizations.

CRITICAL AREAS OF CONCERN

- Potential risk of ground water contamination above the regulatory limit of 0.1 μg / L. Ground water assessment of lysimeter metabolite M15 needs to be finalized (found at annual average concentrations of up to 0.095 μg / L).
- Fluopicolide has potential for long range transport through the atmosphere when applied by spraying as for the representative uses evaluated.
- Long-term risk for mammals for the use in vine was identified. Risk mitigation measures should be considered at Member State level.
- A potential high risk was identified for the aquatic organism. Risk mitigation measures should be required. Acute and chronic TERs values estimated for fish and algae, were all above the Annex VI trigger values, based on Focus step 3 PEC_{sw} values, for all scenarios except from the R4 (stream) scenario (late application) for the use in vines. TERs estimated for fish and algae based on Focus step 3 PEC_{sw} values, were all above the Annex VI trigger values, for all scenarios except from the D6 (ditch, 2nd crop), R1 (stream) and R3 (stream) scenarios in the use in potato.

APPENDICES

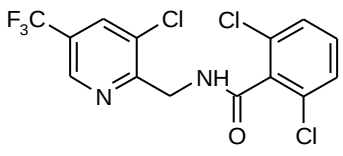
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Fluopicolide
Function (*e.g.* fungicide)	Fungicide

Rapporteur Member State	UK
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2,6-dichloro-*N*-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl]benzamide
Chemical name (CA) ‡	benzamide, 2,6-dichloro-*N*-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]
CIPAC No ‡	787
CAS No ‡	239110-15-7
EC No (EINECS or ELINCS) ‡	not yet allocated
FAO Specification (including year of publication) ‡	None
Minimum purity of the active substance as manufactured ‡	970 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene: max 0.3%
Molecular formula ‡	$C_{14}H_8Cl_3F_3N_2O$
Molecular mass ‡	383.59 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	150°C (99.3%))
Boiling point (state purity) ‡	Not measureable, decomposes above 320°C
Temperature of decomposition (state purity)	>320°C (99.3%)
Appearance (state purity) ‡	Beige solid (pure 99.3% and technical 96.1%)
Vapour pressure (state temperature, state purity) ‡	3.03 x 10^{-7} Pa at 20°C (99.6%)
Henry's law constant ‡	4.15 x 10^{-5} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	0.0028g/l at pH7 and 20°C (solubility is independent of pH) (99.3%)
Solubility in organic solvents ‡ (state temperature, state purity)	n-hexane 0.2g/l at 20°C (99.3%) dichloromethane 126g/l at 20°C (99.3%) ethanol 19.2g/l at 20°C (99.3%) toluene 20.5g/l at 20°C (99.3%) acetone 74.7g/l at 20°C (99.3%) ethyl acetate 37.7g/l at 20°C (99.3%) dimethylsulfoxide 183g/l at 20° (99.3%)
Surface tension ‡ (state concentration and temperature, state purity)	71.3 mN/m at 20°C (concentration = 2.52 mg/l) (96.1%)
Partition co-efficient ‡ (state temperature, pH and purity)	Log P_{OW} = 2.9 at 20°C (pH7) (Log P_{OW} is independent of pH) (99.3%)
Dissociation constant (state purity) ‡	No dissociation (96.1%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Purity (99.3%) neutral, methanol solution: λ_{max} (nm); ε ($L.mol^{-1}.cm^{-1}$) 203; 44519 271; 3601 No absorbance above 290nm.
Flammability ‡ (state purity)	Not highly flammable (96.1%)
Explosive properties ‡ (state purity)	Non-explosive (96.1%)
Oxidising properties ‡ (state purity)	Non-oxidising (96.1%)

Summary of representative uses evaluated (*Fluopicolide*)*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (i)	Method kind (f-h)	Growth stage & season (j)	Number min max (k)	Min interval between applications (day)	g as/hL min max	water L/ha min max	g as/ha min max		
Vine	France Italy Portugal Spain Slovenia Greece Romania Czech Repub	AE F053616 06 WG71 A1[44]	F	Downy mildew *Plasmopara viticola*	WG	44.4 g/kg fluopicolide + 666.7 g/kg fosetyl-Al	Foliar spray	BBCH 53 – 77 BBCH 53 - 81	1 - 3	10-14	10 fluopicolide + 150 fosetyl-Al to 133 fluopicolide + 2000 fosetyl-Al	100 - 1500	100 fluopicolide + 1500 fosetyl-Al to 133 fluopicolide + 2000 fosetyl-Al	28 21	**[1]**

[44] Named also as: 'EXP 11074B'

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (i)	Method kind (f-h)	Growth stage & season (j)	Number min max (k)	Min interval between applications (day)	g as/hL min max	water L/ha min max	g as/ha min max		
potato	Czech Repub. Germany Greece Poland Spain Belgium France Ireland Netherlands UK	AE B066752 04 SC61 A1[45]	F	Late blight *Phytophthora infestans*	SC	62.5 g/L fluopicolide + 625 g/L propamocarb	Foliar spray	BBCH 20 – 89 BBCH 20-91	1 - 4	5	7.5 fluopicolide + 75 propamocarb to 50 fluopicolide + 500 propamocarb	200 - 1000	75 fluopicolide + 750 propamocarb to 100 fluopicolide + 1000 propamocarb	7	**[2]** # Application at symptoms appearance during these growth stages

[1] Potential ground water contamination by fluopicolide above the 0.1 µg / L over a wide range of geoclimatic conditions and groundwater non relevance assessment for metabolite M15 not finalised (data gap).

[2] Groundwater non relevance assessment for metabolite M15 not finalised (data gap).

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).	(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).**
(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)	(j) Growth stage at 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
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)	(k) Indicate the minimum and maximum number of application possible under practical conditions of

[45]Named also as: 'EXP 11120A'

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (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	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

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	Fluopicolide in technical material was determined by HPLC-UV
Impurities in technical as (analytical technique)	Organic impurities in technical material were determined by HPLC-UV Water content was determined by Karl Fischer titration
Plant protection product (analytical technique)	Fluopicolide in plant protection products was determined by HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Fluopicolide
Food of animal origin		Fluopicolide
Soil		Fluopicolide
Water	surface	Fluopicolide
	drinking/ground	Fluopicolide
Air		Fluopicolide

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Fluopicolide was determined by a modified version of the German multi residues method S19, with an LOQ of 0.1 mg/kg, 0.02 mg/kg and 0.02 mg/kg for (grape, wheat grain and potato respectively).
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Fluopicolide and its metabolites M-01 and M-02 in animal product were determined by HPLC/MS/MS, with an LOQ of 0.01 – 0.05 mg/kg. However, a method is not required as currently no MRLs are set for animal products.
Soil (analytical technique and LOQ)	Fluopicolide and its metabolites M-01, M-03 and M-02 in soil were determined by HPLC/MS/MS, with an LOQ of 0.005 mg/kg.
Water (analytical technique and LOQ)	Fluopicolide and its metabolites M-01 and M-02 in water (tap and surface) were determined by HPLC/MS/MS, with an LOQ of 0.1 μg/l.
Air (analytical technique and LOQ)	Fluopicolide was determined by GC/ECD and GC/MS with an LOQ of 3 $\mu g/m^3$

Body fluids and tissues (analytical technique and LOQ)	Not required as fluopicolide is not classified as toxic

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Moderately rapid absorption. Cmax in blood at 6 – 8 h. Approximately 62 % for the pyridyl radiolabel
Distribution ‡	Well distributed into organs and tissues. Highest concentrations in liver, kidneys, spleen and blood
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Rapid and extensive (approximately 95 %) within 48 h mainly via faeces. Biliary fraction was approximately 52 % for the pyridyl radiolabel
Metabolism in animals ‡	Extensively metabolised. Biotransformations observed included aromatic ring hydroxylation, hydrolysis, dealkylation, acetylation, oxidative N-dealkylation and conjugation with glucuronic acid, sulphate and glutathione. Further metabolism of glutathione conjugates to cysteine conjugates.
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and M 01
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.16 mg/l (the mean achieved concentration, 4 h nose only)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Not sensitising (Buehler and Magnusson and Kligman methods)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver, kidney, spleen and red blood cell parameters	
Relevant oral NOAEL ‡	17.7 mg/kg bw/day; 28-day dietary study in rats 7.4 mg/kg bw/day; 90-day dietary study in rats 70 mg/kg bw/day; 90-day dog 300 mg/kg bw/day; 1-year dog	

Relevant dermal NOAEL ‡	1000 mg/kg bw/day; 28-day dermal toxicity study in rats	
Relevant inhalation NOAEL ‡	No data. Not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Liver: non-neoplastic lesions including centrilobular hepatocyte hypertrophy in the liver of rats and mice; and neoplastic lesions, hepatocellular adenomas in mice	
Relevant NOAEL ‡	8.4. mg/kg bw/day in rats 7.9 mg/kg bw/day in mice	
Carcinogenicity ‡	Hepatocellular adenomas in mice. Carcinogenic in mice by a mechanism considered to be not relevant in humans.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No specific evidence of reproductive toxicity. Birth weights were normal, however a reduction (ca. 8 – 14 %) in bodyweight gain in offspring in F_1 and F_2 generations at maternally toxic dose level of 103.4 mg/kg bw/day	
Relevant parental NOAEL ‡	25.5 mg/kg bw/day	
Relevant reproductive NOAEL ‡	103.4 mg/kg bw/day for F_0 males and 127.3 mg/kg bw/day for F_0 females for the period before pairing absence of reproductive toxicity at the highest test dose	
Relevant offspring NOAEL ‡	25.5 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Reduction in mean foetal body weights and crown-rump lengths in foetuses in rats and rabbits at maternally toxic dose levels (60 mg/kg bw/day in rabbits and 700 mg/kg bw/day in rats). Maternal toxicity: reduced body weight in rats and rabbits; apparent exceptional toxicity was noted in rabbits including mortality, increased incidence of premature delivery and reduced food consumption	
Relevant maternal NOAEL ‡	20 mg/kg bw/day in rabbits 60 mg/kg bw/day in rats	
Relevant developmental NOAEL ‡	20 mg/kg bw/day in rabbits 60 mg/kg bw/day in rats	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Range-finding acute oral toxicity study: Peak effects in FOB tests were observed at approximately 6 hours. Acute neurotoxicity study: The NOAEL in the acute neurotoxicity study was 100 mg/kg bw based on reduction in body temperature and excessive grooming in females only at 2000 mg/kg bw in neurobehavioural screening.	
Repeated neurotoxicity ‡	The NOAEL for neurotoxicity in the 90-day neurotoxicity study was 781 mg/kg bw/day-based on the absence of abnormal responses in repeated neurobehavioural screening tests; The systemic NOAEL was 15 mg/kg bw/day based on liver and kidney findings.	
Delayed neurotoxicity ‡	No data; not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Mechanistic study to investigate liver toxicity in mice at a dose level of 3200 ppm for 28 days: - Increased Bromodeoxyuridine labelling index (ca.6.5 x at interim sacrifice on day 7 but not on day 28. - Evidence of increased Cytochrome P450 content and induction of the liver enzymes Benzoxyresofurin O-debenzylation, Ethoxyresofurin O-deethylation, pentoxyresofurin O-dependentylation suggested indicating a phenobarbitone-type liver-enzyme induction and effects.	
Studies performed on metabolites or impurities ‡	Extensive metabolism and toxicity studies including genotoxicity studies on metabolites: AE C653711 (M-01) AE C657188 (M-02) AE C657378 (M-04) AE 1344122 (M-05) AE 1344123 (M-10) AE 1388273 (M-14)	
M01 or BAM		
Toxicokinetic (M01)	Oral absorption: ca 82 % of the dose based on urine, cage wash and tissues six days after dosing. Distribution: highest concentration found in kidneys and liver. No potential for bioaccumulation. Excretion mainly via urine. Metabolism by hydrolysis of the amide group, hydroxylation and subsequent conjugation with glucuronic acid or sulphate, loss of chlorine atom following glutathione conjugation and further metabolism of the glutathione group to the mercapturic acid or S-methyl metabolites.	
Acute toxicity (M01)	Rat LD_{50} oral = 500 mg/kg bw (females); 2000 mg/kg bw (males) – acute toxic class method	**Xn; R22**

Short term toxicity (M01)	Target / critical effect: Decreased body weight gain, food intake and clinical signs Relevant oral NOAELs: 14 mg/kg bw/day (90-day rat) 22.5 mg/kg bw/day (90-day dog)
Genotoxicity (M01)	No genotoxic potential
Long term toxicity and carcinogenicity (M01)	Target / critical effect: Decreased body weight gain, liver toxicity (rat only) Relevant oral NOAELs: 5.7 mg/kg bw/day (2-year rat) 4.5 mg/kg bw/day (2-year dog) Carcinogenicity: No potential for carcinogenicity
Reproductive toxicity (M01)	Reproduction target / critical effect: No effect on reproduction. Parental and offspring's reduced body weight. Organ weight changes in adults. Relevant parental, NOAEL: 7.5 mg/kg bw/day Relevant reproductive NOAEL: 13.5 mg/kg bw/day Relevant offspring NOAEL: 7.5 mg/kg bw/day
	Developmental target / critical effect: Maternal clinical signs; decreased body weight gain and food consumption. (rabbit) Relevant maternal NOAEL: 30 mg/kg bw/day Relevant developmental NOAEL: 30 mg/kg bw/day
ADI (M01)	0.05 mg/kg bw/day (2-year rat and dog studies; SF 100)
ARfD (M01)	0.3 mg/kg bw (developmental study in rabbit; SF 100)
M02	
Toxicokinetic (M02)	Oral absorption: ca 87 % of the dose based on urine, cage wash and tissues six days after dosing. No potential for bioaccumulation. Excretion mainly unchanged via urine.
Acute toxicity (M02)	Rat LD_{50} oral > 2000 mg/kg bw

	Short term toxicity (M02)	Target / critical effect: None Relevant oral NOAELs: 1574 mg/kg bw/day (28-day rat)
	Genotoxicity (M02)	No genotoxic potential
M04		
	Acute toxicity (M04)	Rat LD_{50} oral > 2000 mg/kg bw
	Short term toxicity (M04)	Target / critical effect: Liver and kidneys effects at 1775 mg/kg bw/day Relevant oral NOAELs: 159.2 mg/kg bw/day (28-day rat)
	Genotoxicity (M04)	No genotoxic potential
M05		
	Acute toxicity (M05)	Rat LD_{50} oral > 2000 mg/kg bw
	Short term toxicity (M05)	Target / critical effect: Reduced body weight and kidney degeneration at 1495 mg/kg bw/day Relevant oral NOAELs: 152 mg/kg bw/day (28-day rat)
	Genotoxicity (M05)	No genotoxic potential
M10		
	Acute toxicity (M10)	Rat LD_{50} oral > 2000 mg/kg bw
	Short term toxicity (M10)	Target / critical effect: Clinical signs and diarrhoea at 1748.2 mg/kg bw/day Relevant oral NOAELs: 163.8 mg/kg bw/day (28-day rat)
	Genotoxicity (M10)	No genotoxic potential

M14

Genotoxicity (M14)	No genotoxic potential
	The metabolites were shown to be most likely non-genotoxic and were of lesser or comparable toxicity with the parent, fluopicolide. M-01, one of the principal metabolites was more acutely toxic than fluopicolide by the oral route tested (LD_{50} of 500 mg/kg bw compared with 5000 mg/kg bw for the parent) but the NOAEL for chronic toxicity was comparable and or a similar order or magnitude to that of fluopicolide. Differences in findings and dose levels at LOAELs were noted. For the rotational crop metabolites not found in rat metabolism studies (M-04, M-05, M-08 and M-09) relevant data was provided for M-04 and M-05 as assessed above for groundwater metabolites, whilst M-08 and M-09 were shown to have substantial structural similarities with M-02 and predicted to share intermediate metabolic pathways and have similar toxicity profiles.

Medical data ‡ (Annex IIA, point 5.9)

Limited; a new active ingredient

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.08 mg/kg bw/day	78-week dietary study in mice, supported by the 2-year rat study	100
AOEL ‡	0.05 mg/kg bw/day	90 day dietary study in rats	161.3 (100 + 62 %*)
ARfD ‡	0.18 mg/kg bw/day	28-day dietary study in rats and the rabbit developmental study	100

* Correction for low oral absorption (62 %).

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (EXP11120A: SC containing 62.5 g fluopicolide/L and 625 g propamocarb hydrochloride/L)	Concentrate: 0.24 % Spray dilutions: 2.75 % Based on rat *in vivo* and comparative *in vitro* (human/rat skin)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Grapevines** 'EXP 11074B' maximum application rate of 0.133 kg fluopicolide/ha German Model (% of AOEL) *Tractor-mounted/trailed broadcast air-assisted sprayers* No PPE 11 % Gloves handling conc. 10 % Gloves handling conc. & during appl. 10 % Gloves hand. conc. & sturdy footw. coverall gloves during appl. 2 % *Hand-held equipment* No PPE 6 % Gloves handling conc. 5 % Gloves handling conc. & during appl. 4 % Gloves hand. conc. & sturdy footw. coverall gloves during appl. 2 % UK POEM (% of AOEL) *Broadcast air-assisted sprayer's* medium vol./high vol.

No PPE	113 %/49 %
Gloves handling conc.	112 %/48 %
Gloves handling conc. & during appl.	79 %/40 %
Hand-held equipment (based on low crop data)	
No PPE	132 %
Gloves handling conc.	130 %
Gloves handling conc. & during appl.	66 %
Gloves hand. conc. &. coverall gloves during appl.	29 %
<u>EUROPOEM (%AOEL)</u>	
Spraying using tractor-mounted/trailed equipment	
No PPE	28 %
Gloves handling conc.	27 %
Gloves handling conc. & during appl.	26 %
Gloves hand. conc. &. coverall gloves during appl	19 %
Potatoes 'EXP 11120A' maximum application rate of 0.1 kg fluopicolide/ha	
<u>German Model</u>	
Tractor-mounted/trailed field crop sprayers	
No PPE	4 %

	Gloves handling conc. 3 % Gloves handling conc. & during appl. 3 % Gloves hand. conc. & sturdy footw. coverall gloves during appl. 0.3 % <u>UK POEM</u> *Tractor-mounted/trailed field crop sprayers* No PPE 21 % Gloves handling conc. 20 % Gloves handling conc. & during appl. 4 %
Workers	**Grapevines** 'EXP 11074B' (% of AOEL) According to Hoernicke et al. 1998 40 % **Potatoes** 'EXP 11120A' (% of AOEL) According to Hoernicke et al. 1998 11 %
Bystanders	**Grapevines** 'EXP 11074B' (% of AOEL) According to Lloyd *et al* 1987 5 % **Potatoes** 'EXP 11120A' (% of AOEL) According to Lloyd and Bell 1983 0.1 %

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (fluopicolide)	None proposed

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Leafy crops (lettuce), root vegetables (potatoes) and fruit crops (grapes)
Rotational crops	Lettuce, Wheat and Radish
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Hydrolysis studies simulating pasteurisation, boiling and sterilisation: Fluopicolide was shown to be stable under these conditions.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Fluopicolide
Plant residue definition for risk assessment	Fluopicolide and metabolite M-01 separately
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Dairy cattle and hens
Time needed to reach a plateau concentration in milk and eggs	Milk = 4 days Egg = 8 days
Animal residue definition for monitoring	Fluopicolide
Animal residue definition for risk assessment	Fluopicolide and metabolite M-01 separately
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

The rotational crop metabolism study indicated that 'cold' rotational crop studies would be required. Therefore, rotational crop studies were carried out in the UK, Germany and France. The studies showed that residues of parent fluopicolide in rotational crops at harvest were below the limit of determination (0.01 mg/kg), with the exception of wheat straw which contained residues of up to 0.12 mg/kg. Therefore, as long as the residue definition for monitoring remains as parent, EU MRLs will not need to be set for rotational crops (EU MRLs are not currently set on straw).

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Freezer storage stability study indicated that residues of fluopicolide, M-01 and M-02 are stable for up to 30 months in grape, potato and wheat grain. Fluopicolide, M-01, M-04 and M-05 are stable in wheat straw for at least 18 months.

For animal products, residues of fluopicolide, 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.

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):			
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Fluopicolide:

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Grape (table and wine)	N	0.18, 0.2, 0.21, 0.27, 0.32, 0.32, 0.32, 0.33, 0.37, 0.38, 0.44, 0.48, 0.5, 0.52, 0.56, 0.66, 0.83, 0.96	EU MRL = 2 mg/kg	2		0.38
Grape (table and wine	S	0.11, 0.11, 0.15, 0.16, 0.2, 0.21, 0.21, 0.21, 0.28, 0.32, 0.36, 0.39, 0.4, 0.46, 0.54, 0.65, 0.69, 0.69, 0.97, 1.1, 1.2		2		0.36
Potato (early and ware)	N	13 x <0.01	EU MRL = 0.02 mg/kg	0.01		0.01
Potato (early and ware)	S	11 x <0.01 and 2 x 0.01		0.02		0.01

M-01:

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Grape (table and wine)	N	17 x < 0.01, 2 x 0.01			0.01	0.01
Grape (table and wine	S	9 x < 0.01, 0.01, 6 0.02; 2 x 0.03, 0.04, 0.05			0.05	0.02
Potato (early and ware)	N	13 x <0.01			<0.01	0.01
Potato (early and ware)	S	13 x <0.01			<0.01	0.01

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.08 mg/kg bw/day (fluopicolide) 0.05 mg/kg bw/day (M-01)
TMDI (% ADI) according to WHO European diet	0.00087 mg/kg bw/day (<2%) – fluopicolide + M-01(not including intake from water) (a)
TMDI (% ADI) – EFSA Model	Less than 11% (FR all population) – fluopicolide + M-01 (not including intake from water) Less than 2% (DK child) – M-01 (including intake from water)
NEDI (specify diet) (% ADI)	The total NEDIs (UK) for adults, children, toddlers, infants, vegetarians and the elderly are all less than 3% – fluopicolide + M-01(not including intake from water) The total NEDIs (UK) for adults, children, toddlers, infants, vegetarians and the elderly are all less than 4% – M-01 (including intake from water)
Factors included in IEDI and NEDI	Transfer factor of 0.4 was used in calculating the NEDIs and NESTIs for wine.
ARfD	0.18 mg/kg bw/day (fluopicolide) 0.3 mg/kg bw/day (M-01)
IESTI (% ARfD) – EFSA Model	Less than 73% (DE) – fluopicolide + M-01(not including intake from water) Less than 2% (DE child) – M-01 (including intake from water) (b)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	The NESTIs (UK) for adults, children, toddlers, infants, vegetarians and the elderly are all less than 50% – fluopicolide + M-01 (not including intake from water) The NESTIs (UK) for adults, children, toddlers, infants, vegetarians and the elderly are all less than 2% – M-01 (including intake from water)
Factors included in IESTI and NESTI	Transfer factor of 0.4 was used in calculating the NEDIs and NESTIs for wine

(a) EFSA made a chronic risk assessment for the consumption of drinking water following the WHO guideline for drinking water quality (not peer-reviewed) for M-01 (max. 2% of ADI set for M-01) and the sum of metabolites M-05, M-10 and M-11 respectively (max. 0.5% of ADI set for fluopicolide).

(b) No acute risk for the consumer is expected for intake of drinking water (for details see EFSA conclusion)

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Wine	6	0.4		
Must	6	0.5		
Raisin	2	4		

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Grape	2 mg/kg
.....	
Potato	0.02* mg/kg
.....	
.....	
.....	
.....	

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	0 - 0.2% AR at 94-98 days in 3 soils (pyridinyl label) 0 - 2.0% AR at 94-98 days in 5 soils (benzoyl label) sterile conditions: not detected
Non-extractable residues after 100 days ‡	9.2 - 16.2% AR at 94-116 days in 3 soils (pyridinyl label) 4.0 - 12.0% AR at 94-120 days in 5 soils (benzoyl label) sterile conditions: 3.1 – 8.0% AR at 120 days
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	M-01: range of max. formed 4.8-25.0% AR at 94-120 days in 5 soils (benzoyl label), *detected to a maximum of 40.2% at day 369 in one study but this is over the 120 day acceptable limit for laboratory studies.* M-02: range of max. formed 1.5-7.3% AR at 42-116 days in 3 soils (pyridinyl label). M-03: range of max. formed 1.4-10.6% AR at 77-120 days in 5 soils (benzoyl label). Range of max. formed 1.5-7.8% AR at 77-120 days in 3 soils (pyridinyl label). Highest levels found in acid soils.

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days	Not detected after 120 d (pyridinyl label) (n= 1) 0.1% AR after 120 d, (benzoyl label) (n= 1)
Non-extractable residues after 100 days	4.4% AR after 120 d (pyridinyl label) (n= 1) 4.5% AR after 120 d, (benzoyl label) (n= 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	M-01 (max 2.1% AR at 120 days) (n = 1) M-02 (max 8.9% AR at 120 days) (n = 1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Continuous irradiation, equivalent to 4x the average daily irradiation at 55˚N, 15 days duration. M-01 max 8.6%AR at 15 days (n=1) M-02 max 2.6%AR at 10 days (n=1)

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Fluopicolide	Aerobic conditions						
Soil type	X[46]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.5	20/pF2-2.5	282/936	277/920	0.997/ 0.998	SFO, mean of 2 labels
Clay loam		5.9	25/75% of ⅓ bar	276/917	276/917	0.983/ 0.988	SFO, mean of 2 labels
Loamy sand		5.7	25/75% of ⅓ bar	329/1093	300/997	0.988/ 0.991	SFO, mean of 2 labels
Silty clay loam		7.4	20/pF2	194/644	194/644	-	SFO, single label position
Loamy sand		4.9	20/pF2	266/884	266/884	-	SFO, single label position
Clay loam		5.6	20/pF2.5	411/1365	333/1106	0.991/ 0.997	SFO, mean of 2 labels
Sandy loam		7.2	10/40%	667/2216		0.998	SFO, pyridinyl label only
Geometric mean (excludes 10˚C study)					271/900		

Note: field derived DT50 values used in FOCUS modelling

M-01 (BAM)	Aerobic conditions, metabolite applied as starting substance							
Soil type	X[1]	pH (H_2O)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		4.8	25/75% of ⅓ bar	1831/6083	-	1848/6139	0.775	SFO
Sandy loam		7.7	25/75% of ⅓ bar	557/1850	-	808/2684	0.874	SFO
Geometric mean/median				N/A	-	N/A		

N/A = not appropriate, i.e. due to small database; note: field derived DT50 values used in FOCUS modelling

[46] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

M-02	Aerobic conditions, metabolite applied as starting substance							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-50%	4.5/15	-	3	0.99	SFO
Loamy sand		5.4	20/40-50%	3.2/10.6	-	2.5	0.98	SFO
Silty clay loam		7.5	20/40-50%	4.5/15	-	3	0.99	SFO
Geometric mean				4.0/13.3	-	2.8*		

* used in FOCUSgw modelling

M-03	Aerobic conditions, metabolite applied as starting substance							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		5.4	20/40%	2.2/7.3	-	1.7	0.99	SFO
Loamy sand		4.9	20/40%	5.0/16.6	-	4.7	0.96	SFO
Sandy loam		7.2	20/40%	0.1/0.3	-	0.1	1.0	SFO
Silt loam		7.1	20/40%	0.1/0.3	-	0.09*	1.0	SFO
Geometric mean				0.6/2		0.5		

*FOCUSgw modelling DT50 of 0.09 days for scenarios with pH>6 and 55.5 days for scenarios with pH<6 (from field studies)

M-05	Aerobic conditions, metabolite applied as starting substance							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-45%	60/199	-	41	0.99	SFO
Loamy sand		5.4	20/40-45%	130/432	-	100	0.96	SFO
Silty clay loam		7.5	20/40-45%	34/113	-	22	0.98	SFO
Geometric mean				64/213	-	45		
	Aerobic conditions, metabolite M-02 applied as starting substance							
Sandy loam		7.2	20/40-50%	31	0.256	20.7		SFO
Loamy sand		5.4	20/40-50%	118	0.184	90.7		SFO
Silty clay loam		7.5	20/40-50%	53	0.17	35.2		SFO
Geometric mean				58	0.203*	40.4		
Geometric mean of all M-05 normalised DT50 values for modelling						42.6		

* arithmetic mean used as some formation fractions were 0 in modelling of M-02 study; geometric mean cannot be calculated where 0 is present in the range of values

M-10	Aerobic conditions, metabolite applied as starting substance							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-45%	253/840	-	194	0.89	SFO
Loamy sand		5.4	20/40-45%	36/120	-	24	0.95	SFO
Silty clay loam		7.5	20/40-45%	24/80	-	16	0.96	SFO
Geometric mean				60/199		42		
	Aerobic conditions, metabolite M-02 applied as starting substance							
Sandy loam		7.2	20/40-50%	4.5/	0.175	3.0		SFO
Loamy sand		5.4	20/40-50%	307/	0.036	236		SFO
Silty clay loam		7.5	20/40-50%	9.7/	0.074	6.4		SFO
Geometric mean/median				24/79	0.095*	16.5		
Geometric mean of all M-10 normalised DT50 values for modelling						26.4		

* arithmetic mean used as some formation fractions were 0 in modelling of M-02 study; geometric mean cannot be calculated where 0 is present in the range of values

M-14	Aerobic conditions, metabolite applied as starting substance							
Soil type	X^1	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-45%	8/27	-	6.3	1.0	SFO
Loamy sand		5.4	20/40-45%	5/17	-	3.3	1.0	SFO
Silty clay loam		7.5	20/40-45%	6/20	-	3.8	1.0	SFO
Geometric mean					-	4.3		
	Aerobic conditions, metabolite M-02 applied as starting substance							
Sandy loam		7.2	20/40-50%	7.9/26	0.384	5.3		SFO
Loamy sand		5.4	20/40-50%	-	0	-		SFO
Silty clay loam		7.5	20/40-50%	13.7/46	0.371	9.1		SFO
Geometric mean				10.4/35	0.384*	6.9		
Geometric mean of all M-10 normalised DT50 values for modelling						5.2		

* not applicable as some formation fractions were 0 in modelling of M-02 study. Worst case 0.384 was agreed by PRAPeR 37 as end point for the metabolite M14.

M-11/12	Aerobic conditions, metabolite M-02 applied as starting substance							
Soil type	X^1	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-50%	41/136	0.013	27.3		SFO
Loamy sand		5.4	20/40-50%	86.1/286	0.127	66.2		SFO
Silty clay loam		7.5	20/40-50%	38.5/128	0.019	25.8		SFO
Geometric mean				51.4/171	0.053*	36		

* arithmetic mean used

M-13	Aerobic conditions, metabolite M-02 applied as starting substance							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.2	20/40-50%	10.9/36	0.085	7.3		SFO
Loamy sand		5.4	20/40-50%	43/143	0.03	33.1		SFO
Silty clay loam		7.5	20/40-50%	10.3/34	0.07	6.9		SFO
Geometric mean				16.9/56	0.062*	11.8		

* arithmetic mean used

Field studies ‡

Fluopicolide	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2, chi^2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand, bare	Germany (Philippsburg)		6.4	50	99	1184	0.879, 15.9	177.7	Actual: HS, k1=0.0206 d^{-1}, k2 0.00148 d^{-1}, bp 28.6 d Norm: SFO
Clay, bare	Germany (Rodelsee)		7.3	50	132	863	0.940, 12.2	123.3	Actual: HS, k1=0.0309 d^{-1}, k2 0.0022 d^{-1}, bp 14.0 d Norm: SFO
Loamy sand, bare	Germany (Huntlosen)		4.9	50	172	1000	0.789, 14.0	117.5	Actual: HS, k1=0.0440 d^{-1}, k2 0.0019 d^{-1}, bp 8.5 d Norm: SFO
Sandy silt loam, bare	N France (Appilly)		7.1	50	104	1134	0.891, 14.9	161.2	Actual: HS, k1=0.0067 d^{-1}, k2 0.0014 d^{-1}, bp 136.0 d Norm: SFO

Field studies ‡

Fluopicolide	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2, chi^2)	DT_{50} (d) Norm.	Method of calculation
Sandy loam, bare	Spain (Valencia)		7.3	50	50	973	0.953, 11.8	223.6	Actual: HS, k1=0.0138 d^{-1}, k2 0.00163 d^{-1}, bp 60.4 d Norm: SFO
Sandy silt loam, bare	S France (Senas Yr 1)		7.6	50	115	619	0.832, 8.7	77.0	Actual: HS, k1=0.0608 d^{-1}, k2 0.0032 d^{-1}, bp 5.6 d Norm: SFO
Sandy silt loam, bare	S France (Senas Yr 2)		7.3	50	58	679	0.928, 12.7	77.0	Actual: HS, k1=0.0119 d^{-1}, k2 0.00242 d^{-1}, bp 69.8 d Norm: SFO
Geometric mean/median								138.8	

HS = Hockey stick; BP = break point in days

Note RMS calculated SFO dissipation rates resulting in inferior fits compared to Applicant 'best fit' approach listed above. However, for simplistic PECsoil approaches, a worst-case SFO DT50 of 290 days (r^2 = 0.818) is proposed on the basis of the following RMS calculated SFO values:

Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	DT_{50} (d) actual	St. (r^2)
Loamy sand, bare	Germany (Philippsburg)	248	0.727
Clay, bare	Germany (Rodelsee)	253	0.818
Loamy sand, bare	Germany (Huntlosen)	290	0.818
Sandy silt loam, bare	N France (Appilly)	187	0.884
Sandy loam, bare	Spain (Valencia)	174	0.817
Sandy silt loam, bare	S France (Senas Yr 1)	174	0.931
Sandy silt loam, bare	S France (Senas Yr 2)	133	0.826

M-01	Aerobic conditions								
Soil type	Location		pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand, bare	Germany		6.4	50	120	399	0.881	144.4	Actual: SFO from peak Norm: SFO[1]
Clay, bare	Germany		7.3	50	315	1046	0.873	73.0	Actual: SFO from peak Norm: SFO[1]
Loamy sand, bare	Germany		4.9	50	257 (unreliable, 4 data points only)	854		141.5	Actual: SFO from peak Norm: SFO[1]
Sandy silt loam, bare	N France		7.1	50	186	618	0.930	173.3	Actual: SFO from peak Norm: SFO[1]
Sandy loam, bare	Spain		7.3	50	-	-		256.7	Actual: max too close to end of study Norm: SFO[1]
Sandy silt loam, bare	S France		7.6	50	267	887	0.800	136.6	Actual: SFO from peak Norm: SFO[1]
Sandy silt loam, bare	S France		7.3	50	120	399	0.881	81.5	Actual: SFO from peak Norm: SFO[1]
Geometric mean								137.7*	

* for calculation of geomean, the two S France results were meaned before calculating overall mean.. This value used in FOCUS exposure modelling

[1] represents degradation rate only for M-01, not dissipation rate

For simplistic PECsoil calculations for M-01, it proposed that the longest dissipation DT50 of 315 days is used with maximum observed formation of 14.6% wt/wt.

M-03: a SFO normalised field degradation DT50 was only calculable for this metabolite at one German loamy sand site with pH 4.9; this was 55.5 days from the Huntlosen, Germany site.

pH dependence ‡ (yes / no) (if yes type of dependence)	No pH dependence for fluopicolide or M-01. Possibility of pH dependence of degradation for M-03, slower degradation at acid pH.
Soil accumulation and plateau concentration ‡	Three sites Senas, S France, applications made 1999 – 2002; application at 500 g a.s./ha each year Appilly, N France, applications made 2000 – 2004; application at 400 g/ha each year Philippsburg, Germany, applications made 2000 – 2004; application at 400 g a.s./ha each year.

Location	**Plateau concentration**	**Fluopicolide (mg/kg)**		**M-01 (mg/kg)**	
		0-10 cm	**0-20 cm**	**0-10 cm**	**0-20 cm**
Senas	High[1]	0.354	0.192	0.047	0.030
	Low[2]	0.082	0.046	0.015	0.016
Appilly	High	0.387	0.197	0.036	0.026
	Low	0.144	0.080	0.034	0.025
Philippsburg	High	0.341	0.191	0.070	0.042
	Low	0.094	0.064	0.024	0.021

[1] maximum of the high values of the "saw teeth" curve
[2] maximum of the low values of the "saw teeth" curve

Laboratory studies ‡

Fluopicolide	Anaerobic conditions						
Soil type	X[47]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.5	20/flooded	424/1409	-	0.998	SFO, whole system, mean of 2 labels

Laboratory studies ‡

Fluopicolide	Soil photolysis						
Soil type	X[48]	pH ($CaCl_2$)	t. °C / % MWHC/illumination	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.3-7.4	20/air dry/15 days continuous, equiv. 30 days natural summer sunlight in N EU (55ºN)*	*40.4/~~134~~ 34 experimental days* *Dark control DT50 103 d/no degradation* *(Applicant's calculation)* 61 experimental days Dark control DT50 198d/ no degradation (RMS calculation)	-	0.998	SFO, mean of 2 labels

* Following expert meeting discussion, an assessment was made of the contribution of photolysis to degradation in soil at a range of European locations/latitudes from Athens, Greece (36.03ºN) to Dundee, UK (56.26ºN) based on example solar radiation in June for these locations; values for Tunisia have been ignored. Using the applicants calculated photolytic DT50 for the studies, environmental DT50 values were in the range 89 – 198 days.

[47] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[48] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Fluopicolide ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
							Top soils
Sand	**0.5**	**4.7**			**1.42**	**283**	**0.924**
Sandy loam	**2.21**	**7.5**			**7.53**	**341**	**0.929**
Silty clay loam	**0.9**	**7.4**			**3.20**	**356**	**0.905**
Loamy sand	**1.3**	**5.7**			**4.54**	**349**	**0.929**
Sandy loam	**0.6**	**6.3**			**1.49**	**248**	**0.841**
Loamy sand	**1.6**	**5.3**			**9.27**	**580**	**0.953**
Clay	**1.5**	**7.0**			**2.59**	**172**	**0.859**
Silty clay loam	**1.5**	**7.6**			**3.59**	**239**	**0.882**
Arithmetic mean of top soils					4.20	321.1	0.9028
							Sediment
Clay loam	**2.07**	**4.5**			**7.73**	**373**	**0.926**
							Sub soils
Sand	**0.2**	**6.2**			**0.21**	**106**	**0.931**
Loamy sand	**0.2**	**6.2**			**0.17**	**83**	**0.951**
pH dependence, Yes or No			No pH dependence				

M-01 ‡							
Soil Type	OC %	Soil pH (H_2O)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	0.9	4.8			0.3588	39.9	0.97
Sandy loam	5.7	7.7			1.761	31	0.8085
Sand	1.4	6.3			0.529	38	0.9163
Sand	4.2	4.9			1.89	45	0.9125
Clay loam	0.4	6.6			0.208	51	0.9718
Arithmetic mean/median					0.95	40.98	0.92
pH dependence (yes or no)			No pH dependence				

M-02 ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.6	7.2			0.029	1.1	0.725
Loamy sand	1.1	5.4			0.116	10.5	0.887
Silty clay loam	1.3	7.5			0.082	6.3	0.709
Arithmetic mean/median					0.076	6.0	0.774
pH dependence (yes or no)			No pH dependence				

M-03 ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	3.5	4.1			2.86	82	0.961
Loamy sand	1.7	4.5			2.26	133	1.012
Loamy sand	1.1	5.4			1.23	112	0.939
Arithmetic mean/median					2.12	109	0.971
pH dependence (yes or no)			No pH dependence at acid pH. M-03 not tested at more alkaline pH due to instability at such pH.				

M-05 ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.6	7.2			0.294	11	0.883
Loamy sand	1.1	5.4			0.544	49	0.954
Clay loam	1.3	7.5			0.218	17	0.918
Arithmetic mean/median					0.352	26	0.918
pH dependence (yes or no)			No pH dependence				

M-10 ‡							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.6	7.2	0.003	0.07			
Loamy sand	1.1	5.4	0.09	8.24			
Clay loam	1.3	7.5	0.14	10.66			
Arithmetic mean/median			0.08	6.3			
pH dependence (yes or no)			No pH dependence				

M-11, M-12, M-13: Koc value of 0 assumed as a worse-case; 1/n 0.9 assumed as default.

M-14: Koc 19.2 from HPLC determination; 1/n 0.9 assumed as default.

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	Not submitted, not required
Aged residues leaching ‡	Not submitted, not required

Lysimeter/ field leaching studies ‡	Location: Germany Study type (e.g. lysimeter, field): lysimeter Soil properties: loamy sand, pH = 5.2, OC= 1.1, MWHC = NA Dates of application : Lysimeter 32 – 27/5/99, 17/6/99, 20/7/99, 30/7/99; Lysimeter 33 – first year, 27/5/99, 17/6/99, 20/7/99, 30/7/99, second year 6/5/00, 19/5/00, 23/6/00, 10/7/00 Crop : /Interception estimated: Potato/applied post emergence, interception not quantified for whole lysimeter surface area but interception did occur. Number of applications: Lysimeter 32, 1 year, 4 applications per year; Lysimeter 33, 2 years, 4 applications per year. Duration. 3 years Application rate: Lysimeter 32, 422.2 g a.s./ha/year; Lysimeter 33, 429.5 g a.s./ha/year 1, 412.0 g a.s./ha/year 2. Pyridinyl labelling position used Average annual rainfall (mm): see below Average annual leachate volume (mm):see below % radioactivity in leachate (maximum/year): Lysimeter 32, 1.83 – 2.67 % AR; Lysimeter 33, 1.04 – 1.57 % AR Individual annual maximum concentrations (e.g. 1st, 2nd, 3rd yr): see below. Individual annual average concentrations (e.g. 1st, 2nd, 3rd yr): see below. Amount of radioactivity in the soils at the end of the study = Lysimeter 32, 43.12 % AR; 22.7% AR extractable in top 20cm, virtually all as parent; Lysimeter 33, 48.92 % AR; 28.9% AR extractable in top 20cm, virtually all as parent. M-01 not detected as benzoyl labelling position NOT used

Annual average concentration of metabolites in lysimeter leachate over 3 years.

	Year 1		Year 2		Year 3	
	L32	**L33**	**L32**	**L33**	**L32**	**L33**
Total rainfall (mm)	666.1		825.7		928.0	
Total rainfall + irrigation (mm)	850.1	830.1	875.7		1008.0	
Total leachate volume (mm)	335.6	360.3	374.2	333.5	469.2*	374.9
Fluopicolide (µg/l)	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
M-01 (µg/l)	-	-	-	-	-	-
M-05 (µg/l)	0.37	0.31	0.33	0.46	0.31	0.90
M-10 (µg/l)	0.83	0.68	0.07	0.23	0.10	0.29
M-11 (µg/l)[+]	0.55	0.47	0.45	0.47	0.30	0.34
M-12 (µg/l)[+]	0.36	0.31	0.30	0.31	0.20	0.23
M-13 (µg/l)	0.05	0.04	0.08	0.08	0.07	0.14
M-14 (µg/l)	0.04	0.05	0.08	0.06	0.08	0.19
M-15 (µg/l)	0.03	<LOD	0.04	0.09	<LOQ	0.10[1]
M-16 (µg/l)	0.03	<LOD	0.04	0.06	<LOD	0.08
M54	0.02	<LOD	0.02	0.03	<LOD	<LOQ
P6A	0.02	<LOD	0.02	0.03	<LOD	<LOQ
P6	<LOD	<LOD	0.04	0.03	0.06	0.07
M3	0.02	<LOD	0.03	0.02	0.02	0.04
M29	0.02	0.09	<LOD	<LOQ	<LOD	<LOQ
Unresolved	0.15	0.04	0.03	0.00	0.04	0.16

*52.1 litres collected in one day (10/07/01) – Applicant proposes that this is due to preferential flow during heavy thunderstorms.

[+]two isomers of the same metabolite

LOD = Limit of detection (0.004 to 0.014 µg/l)

LOQ = Limit of quantification (0.008 to 0.028 µg/l)

[1] = rounded to 0.10 µg/l from 0.095 µg/l

Individual annual max concentration in leachate samples (only results >0.1 µg/l given)

	Year 1		Year 2		Year 3	
	L32	**L33**	**L32**	**L33**	**L32**	**L33**
Total rainfall (mm)	666.1		825.7		928.0	
Total rainfall + irrigation (mm)	850.1	830.1	875.7		1008.0	
Total leachate volume (mm)	335.6	360.3	374.2	333.5	469.2*	374.9
Fluopicolide (µg/l)	<LOD	0.761	<LOD	<LOD	<LOD	<LOD
M-01 (µg/l)	-	-	-	-	-	-
M-05 (µg/l)			0.823	1.903	0.679	2.256
M-10 (µg/l)			0.187	0.629	0.224	0.609
M-11 (µg/l)[+]			0.916	1.082	0.699	0.721
M-12 (µg/l)[+]			0.611	0.721	0.466	0.480
M-13 (µg/l)			0.163	0.317	0.160	0.344
M-14 (µg/l)			0.156	0.197	0.217	0.418
M-15 (µg/l)				0.216		0.134
M-16 (µg/l)				0.118		0.127
P6A					0.102	
P6						0.202

Results for metabolites in year 1 not available

Non RL field leaching study (Germany), 400g/ha fluopicolide applied in year 1 to lettuce, leachate collected for 3 years using suction samplers installed at 5 different depths down to 150 cm. Range of maximum annual average concentration over the three years:

Fluopicolide: 30 cm 1.145-1.688 µg/l, 50 cm 0.078-0.173 µg/l, 85 cm <LOQ-0.081 µg/l, no residues found above LOQ (0.075µg/l) below this depth during remainder of study.

M-01: 30 cm 2.930-6.691 µg/l, 50 cm 3.257-5.764 µg/l, 85 cm 0.845-4.361 µg/l, 120 cm 0.282-2.928 µg/l, 150 cm 0.085-2.415 µg/l.

M-02: 30 cm 0.054-0.100 µg/l, 50 cm <LOQ-0.058 µg/l, no residues found above LOQ (0.075µg/l) below this depth during remainder of study.

M-03: No residues found above LOQ (0.075µg/l) throughout study.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent	
Method of calculation	Potato (based on applicant calculation): accumulation calculated using FOCUS-PELMO with Hamburg and Thiva scenarios. Soil bulk density 1.5 g/cm^3. GAP 4 x 100 g/ha, 2 applications with 50% interception, 2 applications with 80% interception, 5 day intervals, application once every two years. Fluopicolide DT_{50} = 200.7 days, M-01 DT50 215.0 days (both values 90th percentile worst case DT50 at 20˚C and pF2 calculated from field studies). Incorporation to 20 cm for potato, peak concentration adjusted for incorporation in 5/10 cm following final application. Vines (based on RMS calculation): accumulation calculated with simplistic spreadsheet method. Soil bulk density 1.5 g/cm^3. GAP 3 x 133 g/ha, 70% interception, 10 day intervals, application each year. DT50 290 days (longest 1st order un-normalised DT50 calculated by RMS from field dissipation studies). M-01 DT50 315 days, 11.9% w/w conversion from parent. Incorporation into 5cm depth of soil due to lack of cultivation.
Application data	See above

Crop	Fluopicolide		M-01	
	Peak (mg/kg)	Steady state (mg/kg)	Peak (mg/kg)	Steady state (mg/kg)
Potato (20cm)	0.2016[1]/0.1118[2]	0.0220	0.0087/0.0174[3]	0.0036
Vine (5cm)	0.268/0.134[3]	0.117	0.035/0.017[3]	0.015

[1] in top 5cm, based on (Peak in 20cm – steady state in 20cm) x 4) + steady state in 20cm
[2] in top 10cm, based on (Peak in 20cm – steady state in 20cm) x 2) + steady state in 20cm
[3] in top 10cm

Note for M-01 that only a simple correction is made to adjust concentration for depth, and does not require the more complicated correction needed for the applied active substance.

Metabolite Method of calculation	Based on accumulated parent concentration in vines and potato adjusted for maximum observed formation of metabolite. M-02 maximum observed formation 9.6% on mass basis from field studies (16.3% molar basis); M-03 maximum observed formation 6.4% on mass basis from field studies (6.1% molar basis).
Application data	See above

Metabolite	Crop	PECsoil (mg/kg)
M-02	Potato	0.019
	Vine	0.026
M-03	Potato	0.017
	Vine	0.013

Parent Method of calculation	Field accumulation/ dissipation trials were evaluated further. The accumulation potential of parent and M-01 at each trial site were evaluated using SFO kinetics. (M-02 and M-03 were not considered since M-02 was detected occasionally at low levels and M-03 was only detected in acidic soils). Concentrations were converted from mg/kg to g/ha for total soil depth assuming soil density of 1.5 g/cm^3. Plateau concentrations over each trial duration were reported. Potential accumulation in successive years was estimated by least squares optimisation of SFO degradation rate constants and initial soil residue in an Excel spreadsheet (using Solver tool). Predicted plateau concentrations were compared to the measured experimental data. RMS considers that: Overall data indicated that parent fluopicolide appeared to have reached a plateau concentration within the study duration at Phillipsburg and Senas sites. The data were considered inconclusive as to whether a plateau was reached during the trial at

	the Appilly site. Modelling did not predict significant increases of parent in soil in successive years after trial duration. (*Comments on the fit of this modelling reported in the Addendum*).
Metabolite M-01	As above, with parent compound assumed to be 100% transformed to M-01. RMS considers that: Based on the measured data there was insufficient evidence of a plateau concentration being reached at Philippsburg and Appilly sites, although it did appear to be reached at Senas site. Concentrations of M-01 were not predicted to increase significantly in soil in successive years after trial duration. However based on the modelling data, concentrations of M-01 compared to the measured data were underestimated at later time points for Philippsburg, overestimated at Senas and generally close to measured data at Appilly, with some initial under-estimation.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	**Fluopicolide** Stable (i.e. <10% degradation during study) at 50˚C (5 day duration) and 25 ˚C (30 day duration) at pH 4, 7 and 9
	M-01 Stable (i.e. <10% degradation during study) at 50˚C (5 day duration) and 25 ˚C (30 day duration) at pH 4, 7 and 9
	M-03 DT50 45.5 hours at pH5 and 20 ºC DT50 4.71 hours at pH6 and 20 ºC DT50 0.75 hours at pH7 and 20 ºC DT50 0.14 hours at pH8 and 20 ºC
Photolytic degradation of active substance and metabolites above 10 % ‡	Xenon lamp, wavelengths >290 nm only, 31 day duration in 12 hour light/dark cycles, equiv. midsummer sunlight at 37.45˚N. Benzoyl labelled study. DT_{50} 64 days under study conditions (initial concentration constrained to 100%); dark control no significant degradation over study period. Predicted DT_{50} values for the following latitudes during the summer season were calculated: 30°N 77 days, 40°N 81 days, 50°N 88 days, 35°N 231 days (spring season, Tokyo). M-01 detected up to 4.5% by study end. Pyridinyl labelled study only conducted over 10 days, no degradation seen. Sterile natural water study conducted over 16 days, no degradation seen. Aqueous photolysis is unlikely to be a significant route of degradation in natural surface waters. M-01 stable to aqueous photolysis.
Quantum yield of direct phototransformation in water at Σ > 290 nm	$z \cdot 3.50 \times 10^{-2}$ mol · Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	No (NOTE FOR LABELLING PURPOSES: substance failed the 10 day window criteria but mineralisation exceeded 70% within 28 days). M-01 ‘not readily biodegradable’.

Degradation in water / sediment

Fluopicolide	Distribution (Mill Stream system, max 76.2% AR in sediment at 85 DAT; Iron Hatch system, max 40.6 % AR in sediment at 182 DAT)									
Water / sediment system	pH water phase	pH sed ($CaCl_2$)	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	$DisT_{50}$-$DisT_{90}$ water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Mill Stream	8.4	6.5	20	1428/4570 days	0.996	8.9/29.5 days	0.944	Not calculated		SFO, mean of 2 labels
Iron Hatch	8.3	6.6	20	873/2881 days	0.998	263/873 days	0.958	Not calculated		SFO, mean of 2 labels
Geometric mean/median				1116.5						

Note: separate DegT50 for water and DegT50 for sediment not calculated. Inverse modelled DT50 in total system using TOXSWA gave geomean DT_{50} 809 days (710.1 – 921.42 days)

M-01	Distribution: Mill Stream system, 1.5% AR in water at 135 DAT (closest to 100 day SETAC duration; 5.1% AR at 365 DAT), 1.9% AR in sediment at 135 DAT (closest to 100 day SETAC duration; 3.9% AR at 365 DAT); Iron Hatch system ,3.9 % AR in water at 135 DAT (closest to 100 day SETAC duration; 18.2% AR at 365 DAT), 0.3% AR in sediment at 85 DAT (closest to 100 day SETAC duration; 2.1% AR at 365 DAT)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Mill Stream	8.4	6.5	20	Effectively no degradation		Not calc		Not calc		SFO degradation rate only
Iron Hatch	8.3	6.6	20	Effectively no degradation		Not calc		Not calc		SFO degradation rate only
Geometric mean/median										

M-02	Distribution: Mill Stream system, 0.8% AR in water at 135 DAT, 0.8% AR in sediment at 135 DAT; Iron Hatch system, 3.3 % AR in water at 135 DAT (closest to 100 day SETAC duration; 7.4% AR at 365 DAT), 0.1% AR in sediment at 28 DAT (within 100 day SETAC duration; 0.8% AR at 365 DAT)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Mill Stream	8.4	6.5	20	9.1 d		Not calc		Not calc		SFO degradation rate only with TopFit
Iron Hatch	8.3	6.6	20	1517 d		Not calc		Not calc		SFO degradation rate only with TopFit
Geometric mean/median										

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Mill Stream	8.4	6.5	1.2 – 1.3% at 365 d	7.9 – 10.3% at 182 d	6.1 – 9.7% at 365 d
Iron Hatch	8.3	6.6	1.9 – 2.8% at 365 d	6.6 – 7.7% at 182 d	4.9 – 5.8% at 365 d

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Fluopicolide

Parameters used in FOCUSsw step 1, 2 and 3

Parameter	Fluopicolide
Molecular weight	383.59
Vapour pressure (Pa)	3.03 x 10^{-7} at 20˚C
Solubility (mg/l)	3.02 at 20˚C
Plant uptake	0.5
Soil degradation	
DT50, 20˚C & pF2	138.8 days[2]
Water/Sediment (20˚C)	
Whole system DT50	809 days
WaterDegT50	809 days
Sediment DegT50	809 days
Adsorption	
Koc	321.1
1/n	0.9028

[2] = Derived from field dissipation studies

Application rate

Vines
3 x 133 g a.s./ha, GS 53 – 77 N & S Europe (up to GS81 in Czech Rep), 10 - 14 day interval.

Step 1-2: crop interception set to 'full canopy'. 'Late vines' chosen. Applicant used 'Southern Europe, Mar – May'; this provides the worst case PEC values for any combination of Northern Europe or Southern Europe with March – May and June – September timings.

Step 3: two application scenarios, 'early' and 'late', but crop option chosen in Step 3 is 'late vines'. It should be noted that this is a worst case in terms of spray drift, but it is not known what influence this has on crop interception. Minimum application window is 50 days, but in all cases has been set longer by the Applicant as detailed below.

Application window details for FOCUSsw Step 3 modelling of fluopicolide on vines:

Scenario	Beginning of early scenario; length of window	Beginning of late scenario; length of window
D6	8 March (day 67); 85 days	20 June (day 171); 56 days
R1	20 May (day 140); 73 days	20 June (day 171); 56 days
R2	19 April (day 109); 87 days	20 June (day 171); 56 days
R3	6 May (day 126); 124 days	20 June (day 171); 56 days
R4	14 April (day 104); 92 days	20 June (day 171); 56 days

Steps 1-2 PECsw and PECsed values for fluopicolide in late vines

application to:	vine, late				
crop interception:	full canopy, 70 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step 1}$	103.8			322.7	
$PEC_{init, step 2}$ (24)	17.48		0 (25)	53.81	
1	16.76	17.12	1	53.77	53.79
2	16.75	16.94	2	53.72	53.77
4	16.72	16.84	4	53.63	53.72
7	16.68	16.78	7	53.49	53.65
14	16.58	16.70	14	53.17	53.49
21	16.48	16.65	21	52.85	53.33
28	16.38	16.59	28	52.54	53.17
42	16.19	16.49	42	51.91	52.86
50	16.07	16.43	50	51.56	52.67
100	15.40	16.08	100	49.39	51.57

Step 3 PECsw and PECsed values for fluopicolide in vines

FOCUS Step 3 PEC_{SW} and PEC_{SED} for fluopicolide following multiple late application to 'late vines' (PEC_{SW} = R4 stream; PEC_{SED} = D6 ditch).

Days after global maximum	**Concentration in surface water (µg/l)**	**TWA PEC_{SW} (µg/l)**	**Concentration in sediment (µg/kg)**	**TWA PEC_{SED} (µg/kg)**
0	3.434	-	4.775	-
1	0.009	3.096	4.744	4.772
2	0.003	1.590	4.660	4.764
4	0.001	0.797	4.396	4.733
7	0.001	0.456	3.947	4.653
14	0.000	0.228	3.194	4.353
21	0.000	0.166	2.766	4.129
28	0.000	0.136	2.483	3.951
42	0.411	0.098	2.109	3.570
50	0.000	0.086	1.958	3.387
100	0.000	0.052	1.432	2.669
Scenario PEC_{SW} = R4 stream; PEC_{SED}= D6 ditch				

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'late vine', early timing, multiple application (FOCUS Step 3).

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D6 (ditch)	1.998	3.020
R1 (pond)	0.182	0.802
R1 (stream)	1.427	0.629
R2 (stream)	1.905	1.001
R3 (stream)	2.011	0.511
R4 (stream)	1.402	0.632

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'late vine', early timing, single application (FOCUS Step 3).

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D6 (ditch)	2.286	1.240
R1 (pond)	0.089	0.364
R1 (stream)	1.669	0.634
R2 (stream)	2.202	0.243
R3 (stream)	2.334	0.357
R4 (stream)	1.641	0.634

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'late vine', late timing, multiple application (FOCUS Step 3); highest global max in bold.

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D6 (ditch)	2.478	**4.775**
R1 (pond)	0.244	1.036
R1 (stream)	1.422	0.594
R2 (stream)	1.912	0.373
R3 (stream)	2.844	1.759
R4 (stream)	**3.434**	1.595

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'late vine', late timing, single application (FOCUS Step 3).

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D6 (ditch)	2.282	2.614
R1 (pond)	0.156	0.603
R1 (stream)	1.668	0.599
R2 (stream)	2.243	0.165
R3 (stream)	2.349	0.427
R4 (stream)	1.673	0.473

The highest 21 day TWA for use in ecotoxicological risk assessment is 1.476 µg/l from the D6 ditch scenario on late vines with multiple applications.

Potatoes

4 x 100 g/ha, GS – 20 – 89 (up to 91 in N. Europe), 7 – 10 day intervals, applicant has assumed 5 day min interval.

Step 1-2: crop interception set to 'intermediate'. Applicant used 'Southern Europe, Mar – May'; this provides the worst case PEC values for any combination of Northern Europe or Southern Europe with March – May and June – September timings.

Step 3: two application scenarios, 'early' and 'late'. Minimum application window is 45 days (for a 5 day interval), but in some cases has been set longer by the Applicant. This situation is the same as for vines, as explained above.

Application window details for FOCUSsw Step 3 modelling of fluopicolide on potato

Scenario	Beginning of early scenario; length of window	Beginning of late scenario; length of window
D3	31 May (day 151); 62 days	25 July (day 206); 45 days
D4	12 June (day 163); 50 days	2 Aug (day 214); 45 days
D6 (2 crops/year)	1 May/26 August (day 121/238); 92/52 days	24 May/4 October (day 144/277); 45 days
R1	26 May (day 146); 67 days	18 July (day 199); 45 days
R2	5 April (day 95); 118 days	24 April (day 114); 45 days
R3	1 May (day 121); 92 days	11 July (day 192); 45 days

Step2 1-2 PECsw and PECsed values for fluopicolide in potatoes

application to:	potatoes				
crop interception:	average, 50 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step 1}$	97.1			307.7	
$PEC_{init, step 2}$ (19)	19.55		0 (20)	62.09	
1	19.34	19.45	1	62.04	62.07
2	19.33	19.39	2	61.99	62.04
4	19.29	19.35	4	61.88	61.99
7	19.24	19.32	7	61.72	61.91
14	19.13	19.25	14	61.35	61.72
21	19.02	19.19	21	60.99	61.54
28	18.90	19.13	28	60.62	61.35
42	18.68	19.02	42	59.89	60.99
50	18.55	18.95	50	59.49	60.78
100	17.77	18.56	100	56.99	59.51

Step 3 PECsw and PECsed values for fluopicolide in potato

FOCUS Step 3 PEC_{SW} and PEC_{SED} for fluopicolide following multiple application to 'potato' (PEC_{SW} = D6 ditch, late application to second crop/year; PEC_{SED} = D4 pond, early application).

Days after global maximum	**Concentration in surface water (µg/l)**	**TWA PEC_{SW} (µg/l)**	**Concentration in sediment (µg/kg)**	**TWA PEC_{SED} (µg/kg)**
0	11.966	-	15.122	-
1	4.336	7.872	n/c	15.121
2	3.106	6.128	n/c	15.119
4	2.215	4.583	n/c	15.116
7	3.983	4.071	n/c	15.111
14	0.757	3.185	n/c	15.094
21	0.422	2.309	n/c	15.074
28	0.264	1.833	n/c	15.049
42	0.056	1.354	n/c	14.981
50	1.079	1.202	n/c	14.931
100	0.508	1.120	n/c	14.354
PEC_{SW} = D6 ditch, late application to second crop/year; PEC_{SED} = D4 pond, early application				

n/c = simulated period too short for calculation of PECsed

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'potato', early timing, multiple application (FOCUS Step 3); highest global max in bold.

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D3 (ditch)	0.354	0.233
D4 (pond)	2.794	**15.122**
D4 (stream)	2.746	5.437
D6 (ditch) 1st crop	1.332	2.617
D6 (ditch) 2nd crop	8.537	7.519
R1 (pond)	0.374	1.807
R1 (stream)	3.775	1.638
R2 (stream)	1.598	1.588
R3 (stream)	4.071	2.661

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'potato', early timing, single application (FOCUS Step 3).

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D3 (ditch)	0.522	0.197
D4 (pond)	0.599	3.461
D4 (stream)	0.594	1.249
D6 (ditch) 1st crop	0.550	0.603
D6 (ditch) 2nd crop	1.842	1.720
R1 (pond)	0.106	0.543
R1 (stream)	1.303	0.757
R2 (stream)	0.510	0.299
R3 (stream)	1.730	0.577

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'potato', late timing, multiple application (FOCUS Step 3); highest global max in bold.

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D3 (ditch)	0.356	0.313
D4 (pond)	2.432	12.899
D4 (stream)	2.647	4.633
D6 (ditch) 1st crop	1.863	3.395
D6 (ditch) 2nd crop	**11.966**	9.652
R1 (pond)	0.119	0.737
R1 (stream)	2.143	0.512
R2 (stream)	1.647	1.612
R3 (stream)	3.902	3.189

Summary of global maximum PEC_{SW} and PEC_{SED} of fluopicolide from all drainage (D) and runoff (R) scenarios following the use on 'potato', early timing, single application (FOCUS Step 3).

Scenario	**Global Max PEC_{SW} (µg/l)**	**Global Max PEC_{SED} (µg/kg)**
D3 (ditch)	0.523	0.212
D4 (pond)	0.400	2.436
D4 (stream)	0.450	0.858
D6 (ditch) 1st crop	0.549	0.664
D6 (ditch) 2nd crop	2.034	1.783
R1 (pond)	0.034	0.228
R1 (stream)	0.475	0.122
R2 (stream)	0.524	0.308
R3 (stream)	1.378	0.928

The highest 21 day TWA for use in ecotoxicological risk assessment is2.733 µg/l from the D4 pond scenario on potato, early timing with multiple applications.

Metabolites

Method of calculation	FOCUSsw Steps 1-2
Application rate	
Main routes of entry	

Parameter	**M-01**	**M-02**	**M-03**
Molecular weight	190.03	225.56	399.58
Vapour pressure (Pa)	2.0 x 10^{-5} at 25˚C	0.1016 at 25˚C[1]	**6.96 x 10^{-10} at 25 ˚C[1]**
Solubility (mg/l)	1830 at 20˚C	693.7 at 25˚C[1]	**7.20 at 25˚C**
Plant uptake			
Soil degradation			
DT50, 20˚C & pF2	137.7 days[2]	4.03 days[3]	**7.63 days[4]**
Observed formation in field (max, molar basis)	26%	11% (16.4%[4])	**10.57%**
Water/Sediment (20˚C)			
Whole system DT50	10,000 days	10,000 days	**1000 days[6]**
WaterDegT50	10,000 days	10,000 days	**1.9 days[7]**
Sediment DegT50	10,000 days	10,000 days	**1000 days[6]**
Observed formation whole system	20.3%	8.2%	**0.001%**
Adsorption			
Koc	40.9	6.0	**108.8**
1/n	0.9158	0.774	**0.9707**

[2] = Derived from field dissipation studies [3] = Derived from lab study, not corrected to pF2

[4] = Value is mean of two acidic laboratory soils and an acidic field soil, corrected to standard temperature and moisture

[5] = value in brackets considered by Rapporteur to be worst case.

[6] = Applicant considered value to be reasonable based on known behaviour of M-03
[7] = worst case aqueous hydrolysis DT50
All other input parameters are defaults. The selected substance specific input parameters are all considered by the Rapporteur to be justified.

Vines

PECsw and PECsed values for M-01 in late vines

application to:	vine, late				
crop interception:	full canopy, 70 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step\ 1}$	17.32			7.06	
$PEC_{init, step\ 2}$ (24)	**2.708**		0 (25)	1.101	
1	2.692	2.700	1	1.101	1.101
2	2.692	2.696	2	1.101	1.101
4	2.692	2.694	4	1.101	1.101
7	2.691	2.693	7	1.101	1.101
14	2.690	2.692	14	1.100	1.101
21	2.688	2.691	21	1.100	1.100
28	2.687	2.690	28	1.099	1.100
42	2.685	2.689	42	1.098	1.100
50	2.683	2.688	50	1.097	1.099
100	2.674	2.683	100	1.094	1.097

PECsw and PECsed values for M-02 in late vines

application to:	vine, late				
crop interception:	full canopy, 70 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step\ 1}$	9.05			0.54	
$PEC_{init, step\ 2}$ (24)	**0.647**		0 (25)	0.0388	
1	0.646	0.647	1	0.0388	0.0388
2	0.646	0.646	2	0.0388	0.0388
4	0.646	0.646	4	0.0388	0.0388
7	0.646	0.646	7	0.0388	0.0388
14	0.646	0.646	14	0.0387	0.0388
21	0.645	0.646	21	0.0387	0.0387
28	0.645	0.646	28	0.0387	0.0387
42	0.644	0.645	42	0.0387	0.0387
50	0.644	0.645	50	0.0386	0.0387
100	0.642	0.644	100	0.0385	0.0386

Using a maximum formation in the field of 16.4%, maximum Step 1 values are PECsw 13.24 µg/l and PECsed 0.76 µg/kg. Maximum Step 2 values are PECsw 0.7471 µg/l and PECsed 0.0448 µg/kg.

PECsw and PECsed values for M-03 in late vines

Application to:	Vine, late				
Crop interception:	Full canopy, 70%				
Region and season:	South Europe, Mar-May				
Days after max. conc. (1st applic.)	PEC_{sw} (µg/l)	$TWAC_{sw}$ (µg/l)	Days after max. conc. (1st applic.)	PEC_{sed} (µg/kg)	$TWAC_{sed}$ (µg/kg)
$PEC_{max, step 1}$	12.7890	-		13.9143	
$PEC_{init, step 2}$ (24)	0.5570	-	$PEC_{init, step 2}$ (24)	0.6060	-
1	0.3867	0.4719	1	0.6056	0.6058
2	0.2835	0.4035	2	0.4439	0.5653
4	0.1523	0.3081	4	0.2385	0.4493
7	0.0600	0.2189	7	0.0939	0.3237
14	0.0068	0.1218	14	0.0107	0.1812
21	0.0008	0.0821	21	0.0012	0.1222
28	0.0001	0.0617	28	0.0001	0.0918
42	0.0000	0.0411	42	0.0000	0.0612
50	0.0000	0.0345	50	0.0000	0.0514
100	0.0000	0.0173	100	0.0000	0.0257

Potato

PECsw and PECsed values for M-01 in potatoes

application to:	potatoes				
crop interception:	average, 50 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step\ 1}$	16.66			6.80	
$PEC_{init, step\ 2}$ (19)	**3.316**		0 (20)	1.3544	
1	3.312	3.314	1	1.3543	1.3544
2	3.311	3.313	2	1.3542	1.3543
4	3.311	3.312	4	1.3540	1.3542
7	3.310	3.311	7	1.3537	1.3541
14	3.309	3.310	14	1.3531	1.3537
21	3.307	3.309	21	1.3524	1.3534
28	3.305	3.309	28	1.3518	1.3531
42	3.302	3.307	42	1.3505	1.3524
50	3.300	3.306	50	1.3497	1.3521
100	3.289	3.300	100	1.3450	1.3497

PECsw and PECsed values for M-02 in potatoes

application to:	potatoes				
crop interception:	average, 50 %				
region and season:	South Europe, Mar. – May				
days after max. conc. (1st applic.)	PEC_{sw} (µg / L)	$TWAC_{sw}$ (µg / L)	days after max. conc. (1st applic.)	PEC_{sed} (µg / kg)	$TWAC_{sed}$ (µg / kg)
$PEC_{max, step\ 1}$	8.73			0.52	
$PEC_{init, step\ 2}$ (19)	**0.4797**		0 (20)	0.0288	
1	0.4794	0.4796	1	0.0288	0.0288
2	0.4794	0.4795	2	0.0288	0.0288
4	0.4793	0.4794	4	0.0288	0.0288
7	0.4792	0.4793	7	0.0287	0.0288
14	0.4790	0.4792	14	0.0287	0.0287
21	0.4787	0.4791	21	0.0287	0.0287
28	0.4785	0.4790	28	0.0287	0.0287
42	0.4780	0.4787	42	0.0287	0.0287
50	0.4778	0.4786	50	0.0287	0.0287
100	0.4761	0.4778	100	0.0286	0.0287

Using a maximum formation in the field of 16.4%, maximum Step 1 values are PECsw 12.94 µg/l and PECsed 0.77 µg/kg. Maximum Step 2 values are PECsw 0.6521 µg/l and PECsed 0.0391 µg/kg.

PECsw and PECsed values for M-03 in potatoes

Application to:	potatoes				
Crop interception:	average, 50 %				
Region and season:	South Europe, Mar. – May				
Days after max. conc. (1st applic.)	PEC_{sw} (µg/L)	$TWAC_{sw}$ (µg/L)	Days after max. conc. (1st applic.)	PEC_{sed} (µg/kg)	$TWAC_{sed}$ (µg/kg)
$PEC_{max, step 1}$	12.8213			13.9492	
$PEC_{init, step 2}$ (19)	1.0226	-	0 (19)	1.1126	-
1	0.7100	0.8663	1	1.1118	1.1122
2	0.5204	0.7408	2	0.8149	1.0378
4	0.2796	0.5657	4	0.4378	0.8248
7	0.1101	0.4018	7	0.1724	0.5943
14	0.0125	0.2235	14	0.0196	0.3326
21	0.0014	0.1507	21	0.0022	0.2244
28	0.0002	0.1132	28	0.0003	0.1685
42	0.0000	0.0755	42	0.0000	0.1124
50	0.0000	0.0634	50	0.0000	0.0944
100	0.0000	0.0317	100	0.0000	0.0472

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Model(s) used: (with version control no.(s)) PEARL3.3.3 see below for input parameters PELMO 3.3.2 see below for input parameters. Scenarios (list of names): Vines: Châteaudun, Hamburg, Kremsünster, Piacenza, Porto, Sevilla, Thiva. Potatoes: Châteaudun, Hamburg, Jokioinen, Kremsünster, Okehampton, Piacenza, Porto, Sevilla, Thiva. See degradation and sorption input parameters below. Degradation parameters were calculated from field dissipation data. Metabolites: M-01, M-02, M-03, M-05, M-10, M-11, M-12, M-13 and M-14. See input parameters below.
Application rate	Vine: 3 applications of 133 g/ha at 10 day intervals. Timing – first application set to 5 weeks after leaf emergence. Crop interception set to 60 +70+ 70%. Potato: 4 applications of 100 g/ha at 5 day intervals, applied (i) every year, (ii) every 2 years and (iii) every 3 years. Timing – first application set to 3 weeks after emergence.

Summary of degradation and sorption parameters used in FOCUS groundwater scenarios

Compound	FOCUS scenario	DT_{50} (days)	K_{oc} (L/kg)	K_{om} (L/kg)	Freundlich exponent (1/n)
Fluopicolide	All	138.8 [a]	321.1	186.2	0.9028
M-03	pH < 6	55.5 [c]	108.8	63.1	0.9707
	pH > 6	0.09 [d]			
M-01	All	137.7	40.9	24	0.9158
M-02	All	2.82	5.99	3.47	0.7737
M-05 (P1x)	All	42.6	25.9	15	0.9182
M-10 (P4)	All	26.4	6.3	3.7	0.9*
M-14 (P7)	All	5.2	19.2	11.14	0.9*
M-11 and M-12	All	35.95	0	0	0.9*
M-13	All	11.8	0	0	0.9*

[a] standard overall degradation half-life used in PELMO

[c] in acidic soils (Hamburg, Jokioinen, Okehampton, Porto)

[d] in alkaline soils (Châteaudun, Kremsmünster, Piacenza, Sevilla, Thiva)

* default 1/n

Formation fractions used for FOCUS PEARL and PELMO scenarios

Compound	FOCUS scenario	Formation fraction	k_{ij} (d^{-1})
f (fluopicolide → M-02/M-01)	pH < 6	0.712	0.00356
	pH > 6	0	0
f (fluopicolide → M-03)	pH < 6	0.288	0.00144
	pH > 6	1	0.00499
f (M-03 → M-02/M-01)	pH < 6	1	0.01249
	pH > 6	1	7.7016
f (M-02 → M-05)	all	0.203	0.05
f (M-02 → M-10)	all	0.095	0.0233
f (M-02 → M-13)	all	0.062	0.0152
f (M-02 → CO_2)*	all	0.587	0.1444
f (M-02 → M-14)	all	0.053	0.013
f (M-05 → M-14)	all	0.384#	0.006248#
f (M-05 → CO_2)	all	0.748	0.01002#
f (M-14 → CO_2)	all	1	0.1333
f (M-10→ CO_2)	all	1	0.02622
f (M-13 → CO_2)	all	1	0.05864

= worst case values used.

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

PEARL Model - Vines

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.231	0.001	5.172	0.017	0.580	0.027	0.216	0.144	0.089	0.307
Hamburg [a]	0.146	0.517	6.075	0.035	0.723	0.033	0.348	0.232	0.184	0.446
Krems-münster	0.123	< 0.001	4.599	0.008	0.463	0.022	0.215	0.143	0.083	0.267
Piacenza	**0.678**	< 0.001	4.549	0.041	0.604	0.027	0.166	0.110	0.086	0.283
Porto [a]	< 0.001	0.017	1.626	0.001	0.091	0.004	0.121	0.081	0.045	0.096
Sevilla	0.124	< 0.001	3.876	0.012	0.386	0.017	0.141	0.094	0.049	0.192
Thiva	0.220	< 0.001	4.056	0.034	0.395	0.018	0.132	0.088	0.040	0.180

[a] acidic soil, corresponding metabolism pathway used

PELMO Model - Vines

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.173	< 0.001	5.003	0.012	0.554	0.027	0.261	0.174	0.090	0.343
Hamburg [a]	0.067	0.525	6.265	0.036	0.715	0.033	0.516	0.344	0.216	0.586
Krems-münster	0.089	< 0.001	4.862	0.007	0.474	0.023	0.302	0.202	0.117	0.363
Piacenza	0.519	< 0.001	4.891	0.038	0.607	0.029	0.246	0.164	0.096	0.353
Porto [a]	< 0.001	0.018	1.981	0.001	0.126	0.006	0.208	0.138	0.069	0.140
Sevilla	0.001	< 0.001	4.118	0.001	0.236	0.011	0.296	0.197	0.037	0.203
Thiva	0.087	< 0.001	4.645	0.007	0.388	0.018	0.218	0.145	0.041	0.238

[a] acidic soil, corresponding metabolism pathway used

PEARL Model – Potatoes: Application every year

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.106	< 0.001	5.371	0.007	0.504	0.024	0.207	0.138	0.068	0.271
Hamburg [a]	0.119	0.477	6.743	0.033	0.749	0.035	0.408	0.272	0.202	0.492
Jokioinen [a]	0.003	0.183	5.684	0.011	0.518	0.023	0.502	0.335	0.272	0.486
Krems-münster	0.094	< 0.001	4.992	0.006	0.461	0.022	0.227	0.151	0.082	0.270
Okehamp-ton [a]	0.123	0.463	5.460	0.030	0.625	0.029	0.246	0.164	0.114	0.343
Piacenza	0.575	< 0.001	4.957	0.034	0.572	0.026	0.164	0.110	0.081	0.275
Porto [a]	< 0.001	0.014	1.641	< 0.001	0.092	0.004	0.120	0.080	0.047	0.096
Sevilla	0.003	< 0.001	3.611	< 0.001	0.186	0.008	0.090	0.060	0.025	0.099
Thiva	0.073	< 0.001	4.205	0.005	0.299	0.014	0.110	0.073	0.025	0.125

[a] acidic soil, corresponding metabolism pathway used

PEARL Model– Potatoes: Application every 2 years

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.038	< 0.001	2.557	0.003	0.228	0.011	0.103	0.069	0.032	0.126
Hamburg [a]	0.044	0.231	3.236	0.012	0.333	0.015	0.189	0.126	0.096	0.233
Jokioinen [a]	0.001	0.081	2.645	0.004	0.225	0.010	0.239	0.159	0.127	0.217
Krems-münster	0.034	< 0.001	2.394	0.002	0.212	0.010	0.114	0.076	0.040	0.125
Okehamp-ton [a]	0.046	0.219	2.598	0.013	0.289	0.013	0.117	0.078	0.058	0.168
Piacenza	**0.249**	< 0.001	2.321	0.014	0.293	0.013	0.078	0.052	0.040	0.134
Porto [a]	< 0.001	0.006	0.727	< 0.001	0.035	0.001	0.061	0.041	0.023	0.043
Sevilla	0.001	< 0.001	1.629	< 0.001	0.081	0.004	0.049	0.033	0.015	0.052
Thiva	0.025	< 0.001	2.047	0.002	0.132	0.006	0.056	0.037	0.011	0.059

a acidic soil, corresponding metabolism pathway used

PEARL Model – Potatoes: Application every 3 years

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.022	< 0.001	1.697	0.001	0.147	0.007	0.069	0.046	0.022	0.086
Hamburg [a]	0.024	0.143	2.133	0.007	0.224	0.010	0.118	0.079	0.064	0.151
Jokioinen [a]	0.001	0.049	1.634	0.002	0.132	0.006	0.145	0.097	0.084	0.134
Krems-münster	0.018	< 0.001	1.610	0.001	0.134	0.006	0.079	0.053	0.025	0.081
Okehamp-ton [a]	0.027	0.141	1.731	0.008	0.185	0.008	0.077	0.051	0.038	0.108
Piacenza	**0.151**	< 0.001	1.610	0.009	0.195	0.009	0.053	0.036	0.027	0.091
Porto [a]	< 0.001	0.003	0.454	< 0.001	0.020	0.001	0.039	0.026	0.015	0.025
Sevilla	< 0.001	< 0.001	0.699	< 0.001	0.051	0.002	0.035	0.023	0.009	0.033
Thiva	0.016	< 0.001	1.367	0.001	0.088	0.004	0.040	0.027	0.008	0.039

[a] acidic soil, corresponding metabolism pathway used

PELMO Model - Potatoes: Application every year

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	0.001	< 0.001	3.995	< 0.001	0.160	0.008	0.206	0.137	0.029	0.154
Hamburg [a]	0.010	0.275	6.733	0.016	0.592	0.027	0.496	0.334	0.199	0.525
Jokioinen [a]	< 0.001	0.028	4.536	0.002	0.240	0.011	0.813	0.542	0.369	0.534
Krems-münster	0.001	< 0.001	4.181	< 0.001	0.206	0.010	0.292	0.195	0.059	0.212
Okehamp-ton [a]	0.008	0.175	5.392	0.008	0.429	0.020	0.319	0.212	0.111	0.352
Piacenza	0.212	< 0.001	4.867	0.018	0.501	0.024	0.205	0.137	0.071	0.284
Porto [a]	< 0.001	0.001	1.079	< 0.001	0.021	0.001	0.165	0.11	0.055	0.093
Sevilla	< 0.001	< 0.001	0.114	< 0.001	0.001	< 0.001	0.041	0.027	0.005	0.009
Thiva	< 0.001	< 0.001	1.951	< 0.001	0.027	0.001	0.074	0.049	0.008	0.029

PELMO Model - Potatoes: Application every 2 years

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	< 0.001	< 0.001	1.913	< 0.001	0.072	0.003	0.097	0.064	0.014	0.068
Hamburg [a]	0.003	0.119	3.152	0.006	0.271	0.012	0.242	0.162	0.099	0.243
Jokioinen [a]	< 0.001	0.013	2.073	0.001	0.097	0.004	0.371	0.247	0.177	0.214
Krems-münster	< 0.001	< 0.001	1.986	< 0.001	0.089	0.004	0.136	0.090	0.029	0.100
Okehamp-ton [a]	0.003	0.079	2.542	0.004	0.183	0.008	0.157	0.104	0.051	0.157
Piacenza	0.076	< 0.001	2.357	0.005	0.247	0.012	0.098	0.065	0.036	0.139
Porto [a]	< 0.001	< 0.001	0.471	< 0.001	0.009	0.001	0.079	0.053	0.027	0.034
Sevilla	< 0.001	< 0.001	0.056	< 0.001	< 0.001	< 0.001	0.020	0.014	0.002	0.004
Thiva	< 0.001	< 0.001	0.830	< 0.001	0.010	< 0.001	0.029	0.019	0.003	0.013

[a] acidic soil, corresponding metabolism pathway used

PELMO Model - Potatoes: Application every 3 years

Scenario	Annual PEC_{gw} in µg/L									
	Fluo-picolide	M-03, AE 0608000	M-01, AE C653711	M-02, AE C657188	M-05, AE 1344122	M-14, AE 1388273	M-11, P2a	M-12, P2b	M-13, P3	M-10, AE 1344123
Châteaudun	< 0.001	< 0.001	1.223	< 0.001	0.043	0.002	0.065	0.044	0.009	0.043
Hamburg [a]	0.002	0.079	2.003	0.004	0.170	0.008	0.151	0.101	0.068	0.160
Jokioinen [a]	< 0.001	0.008	1.331	< 0.001	0.060	0.003	0.249	0.166	0.117	0.131
Krems-münster	< 0.001	< 0.001	1.224	< 0.001	0.051	0.003	0.091	0.060	0.019	0.061
Okehamp-ton [a]	0.001	0.049	1.627	0.002	0.113	0.005	0.104	0.069	0.034	0.099
Piacenza	**0.041**	< 0.001	1.526	0.003	0.166	0.008	0.065	0.043	0.024	0.093
Porto [a]	< 0.001	< 0.001	0.303	< 0.001	0.005	< 0.001	0.053	0.035	0.017	0.018
Sevilla	< 0.001	< 0.001	0.034	< 0.001	< 0.001	< 0.001	0.010	0.007	0.001	0.002
Thiva	< 0.001	< 0.001	0.559	< 0.001	0.006	< 0.001	0.019	0.013	0.002	0.008

[a] acidic soil, corresponding metabolism pathway used

PEC$_{(gw)}$ From lysimeter / field studies

Annual average concentration of metabolites in lysimeter leachate over 3 years.

	Year 1		Year 2		Year 3	
	L32	**L33**	**L32**	**L33**	**L32**	**L33**
Total rainfall (mm)	666.1		825.7		928.0	
Total rainfall + irrigation (mm)	850.1	830.1	875.7		1008.0	
Total leachate volume (mm)	335.6	360.3	374.2	333.5	469.2*	374.9
Fluopicolide (µg/l)	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
M-01 (µg/l)	-	-	-	-	-	-
M-05 (µg/l)	0.37	0.31	0.33	0.46	0.31	0.90
M-10 (µg/l)	0.83	0.68	0.07	0.23	0.10	0.29
M-11 (µg/l)$^{+}$	0.55	0.47	0.45	0.47	0.30	0.34
M-12 (µg/l)$^{+}$	0.36	0.31	0.30	0.31	0.20	0.23
M-13 (µg/l)	0.05	0.04	0.08	0.08	0.07	0.14
M-14 (µg/l)	0.04	0.05	0.08	0.06	0.08	0.19
M-15 (µg/l)	0.03	<LOD	0.04	0.09	<LOQ	0.10[1]
M-16 (µg/l)	0.03	<LOD	0.04	0.06	<LOD	0.08
M54	0.02	<LOD	0.02	0.03	<LOD	<LOQ
P6A	0.02	<LOD	0.02	0.03	<LOD	<LOQ
P6	<LOD	<LOD	0.04	0.03	0.06	0.07
M3	0.02	<LOD	0.03	0.02	0.02	0.04
M29	0.02	0.09	<LOD	<LOQ	<LOD	<LOQ
Unresolved	0.15	0.04	0.03	0.00	0.04	0.16

*52.1 litres collected in one day (10/07/01) – Applicant proposes that this is due to preferential flow during heavy thunderstorms.

$^{+}$two isomers of the same metabolite

LOD = Limit of detection (0.004 to 0.014 µg/l)

LOQ = Limit of quantification (0.008 to 0.028 µg/l) [1] = rounded to 0.10 µg/l from 0.095 µg/l

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	active substance: 3.50×10^{-2} mol · Einstein $^{-1}$
Photochemical oxidative degradation in air ‡	Atkinson calculation using AOPWIN v.1.90. Rate constant 4.757×10^{-12} cm^3/molecule/sec. Atmospheric half life 3.373 days assuming 24 hour OH radical concentration of 0.5×10^6 radicals/cm^3.
Volatilisation ‡	from plant surfaces (BBA guideline): no data submitted
	from soil surfaces (BBA guideline) no data submitted
Metabolites	None

PEC (air)

Method of calculation	Not calculated. Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggerred.	Soil: fluopicolide and metabolites M-01, M-02 and M-03 Surface Water: fluopicolide and soil metabolites M-01, M-02 and M-03 Sediment: fluopicolide and soil metabolites M-01, M-02 and M-03 Ground water: fluopicolide and metabolites M-01, M-02, M-03, M-05, M-10, M-11, M-12, M13 M-14 and M15 Air: fluopicolide

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	New active substance, none available
Surface water (indicate location and type of study)	New active substance, none available
Ground water (indicate location and type of study)	New active substance, none available
Air (indicate location and type of study)	New active substance, none available

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

R53 is proposed

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
C. virginianus	fluopicolide	Acute	>2250	-
C. virginianus	fluopicolide	Short-term	>1744	>5620
C. virginianus	Metabolite M01	Short-term	1171	3897
C. virginianus	fluopicolide	Long-term	88.9	1000
Mammals ‡				
Rat	fluopicolide	Acute	>5000	-
Rat	EXP 11074B	Acute	>2000(product)	-
Rat	EXP 11120A	Acute	>2000(product)	-
Rat	Metabolite M01	Acute	M2000/F500	-
Rat	Metabolite M02	Acute	>5000	-
Rat	Metabolite M05	Acute	>5000	-
Rat	Metabolite M10	Acute	>5000	-
Rabbit	fluopicolide	Long-term	20.0	
Additional higher tier studies ‡ - none				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81)

Indicator species/Category	Time scale	ETE	TER[1]	Annex VI Trigger
Tier 1 (Birds)				
Small insectivore	Acute	7.193	>312.82	10
	Acute[1]	71.82	>31.3	10
	Short-term	4.011	>434.80	10
	Long-term	4.011	22.16	5
Higher tier refinement (Birds) - not required				

[1] drinking water based on minimum spray volume 100L/ha

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81

Tier 1 (Mammals)				
Small herbivore	Acute	23.445	>213.26	10
	Acute[5]	38.0	>132	10
	Long-term	8.04	***2.49***	5
Higher tier refinement (Mammals): The long term risk to herbivorous mammals consuming contaminated sub-canopy ground vegetation in vineyards was refined by correcting for canopy interception. A canopy ≥70% interception (assumption used in all environmental exposure modelling) gave a TER of 4.98, close to the Annex VI trigger (5), and indicative of acceptable risk. However, a canopy interception of 60% was considered more appropriate for treatment at earlier growth stages (BBCH 53-57) where the canopy may be less fully developed. Assuming ≥60% interception a TER of 3.73 is derived indicating possible risk which is mitigated by reducing the no. of applications. Hence, for earlier treatments (BBCH 53-57), if the canopy is not fully developed then a reduction in the no. of applications should be considered.				
70% interception[1]	Long-term	4.02	***4.98***	5
60% interception[2]	Long-term	5.36	***3.73***	5
60% interception[3]	Long-term	4.47	***4.47***	5
60% interception[4]	Long-term	2.98	6.71	5

[1] BBCH 53-81
[2] BBCH 53-57 @ GAP
[3] BBCH 53-57 @ 2 applications (10 spray interval)
[4] BBCH 53-57 @ 1 application

[5] drinking water based on minimum spray volume 100L/ha

EXP 11120A potato (4 x 0.1 kg fluopicolide/ha; 7d spray interval; BBCH 20-91)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Small insectivore	Acute	5.408	>416.05	10
	Acute[2]	27.00	>83.3	10
	Short-term	3.016	>578.25	10
	Long-term	3.016	29.48	5
Medium herbivore	Acute	11.879	>189.41	10
	Acute[2]	8.80	>256	10
	Short-term	6.772	>257.52	10
	Long-term	3.567	24.92	5
Higher tier refinement (Birds) - not required				
Tier 1 (Mammals)				
Medium herbivore	Acute	4.377	>1142.46	10
	Acute[2]	8.90	>562	10
	Long-term	1.314	15.22	5
Small insectivore[1]	Acute	0.882	>5668.93	10
	Acute[2]	15.70	>318	10
	Long-term	0.321	62.25	
Higher tier refinement (Mammals) - not required				

[1] indicator insectivore species (large insects) included since potato foliage unattractive to herbivorous mammals

[2] drinking water based on minimum spray volume 200L/ha

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] mg/L
Laboratory tests ‡				
Fish				
O. mykiss	fluopicolide	96h(static)	Mortality, LC_{50}	0.36[mm]
P. pimales	fluopicolide	33d(flo thru)	Growth NOEC	0.155[mm]
O. mykiss	EXP 11074B	96h(static)	Mortality, LC_{50}	0.39(8.54[1])[nom]
O. mykiss	EXP 11120A	96h (static)	Mortality, LC_{50}	0.38(6.57[1])[nom]
O. mykiss	Metabolite M01	96h (static)	Mortality, LC_{50}	240[nom]
O. mykiss	Metabolite M02	96h (static)	Mortality, LC_{50}	>100[nom]
O. mykiss	Metabolite M05	96h (static)	Mortality, LC_{50}	>100[nom]
Aquatic invertebrate				
D. magna	fluopicolide	48h (static)	Mortality, LC_{50}	>1.8[mm]
D. magna	fluopicolide	21d (static ren)	Repro., NOEC	0.37[mm]
D. magna	EXP 11074B	48h (static)	Mortality, LC_{50}	>1.13(>25[1])[nom]
D. magna	EXP 11120A	48h (static)	Mortality, LC_{50}	>5.73(>100[1])[nom]
D. magna	Metabolite M01	48h (static)	Mortality, LC_{50}	180[nom]
Sediment dwelling organisms				
C. riparius	fluopicolide	28d (static[2])	Emergence,NOEC	49.0mg/kg[nom]
Algae				
Navicula pelliculosa	fluopicolide	72h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.029[mm] 0.069[mm]
Navicula pelliculosa	EXP 11074B	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.026(0.58[1])[nom] 0.041(0.91[1])[nom]
Navicula pelliculosa	EXP 11120A	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.023(0.40[1])[nom] 0.036(0.63[1])[nom]
Navicula pelliculosa	Metabolite M01	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>10.0[nom] >10.0[nom]
Navicula pelliculosa	Metabolite M05	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>10.0[nom] >10.0[nom]

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] mg/L
Higher plant				
L. gibba G3	fluopicolide	7d (static)	Biomass: E_bC_{50}	>3.2[mm]
L. gibba G3	Metabolite M01	7d (static)	Biomass: E_bC_{50}	>80.0[mm]
Microcosm or mesocosm tests - not required				

mm = mean measured; nom = nominal
[1] product; [2] spiked sediment

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

EXP 11074B - use on vine

FOCUS Step1

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81)

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}	TER	Annex VI Trigger
Fluopicolide	Fish	0.36	Acute	0.1038	-	***3.5***	100
Fluopicolide	Fish	0.155	Chronic	0.1038	-	***1.5***	10
Fluopicolide	Aq. invertebrates	>1.8	Acute	0.1038	-	***>17.3***	100
Fluopicolide	Aq. invertebrates	0.37	Chronic	0.1038	-	***3.6***	10
Fluopicolide	Algae	0.029	Chronic	0.1038	-	***0.3***	10
Fluopicolide	Higher plants	>3.2	Chronic	0.1038	-	>30.8	10
Fluopicolide	Sediment-dweller	49.0	Chronic	0.3227[1]	-	151.8	10
Metab. M01	Fish	240	Acute	0.01732	-	14118	100
Metab. M01	Algae	>10.0	Chronic	0.01732	-	>588	10
Metab. M02	Fish	>100	Acute	0.00905	-	>11050	100
EXP 11074B	Algae	0.58	Chronic	0.0802[2]	-	***7.2***	10
EXP 11074B	Algae	0.58	Chronic	0.0362[3]	-	24.0	10

[1] PECsed mg a.s./kg
PECsw from spray drift @[2]3m & [3]5m off-field

FOCUS Step 2

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81) S.EU

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}	TER	Annex VI Trigger
Fluopicolide	S	Fish	0.36	Acute	0.01748	-	***20.6***	100
Fluopicolide	S	Fish	0.155	Chronic	0.01748	-	***8.9***	10
Fluopicolide	S	Aq. inverts.	>1.8	Acute	0.01748	-	>103	100
Fluopicolide	S	Aq. inverts.	0.37	Chronic	0.01748	-	21.2	10
Fluopicolide	S	Algae	0.029	Chronic	0.01748	-	***1.7***	10

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81) S.MS

Test substance	Scen.	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC^i	TER	Annex VI trigger
Fluopicolide	D6	Ditch	Fish	Acute	0.36	0.002478	145	100
Fluopicolide	R1	Pond	Fish	Acute	0.36	0.000244	1475	100
Fluopicolide	R1	Stream	Fish	Acute	0.36	0.001422	253	100
Fluopicolide	R2	Stream	Fish	Acute	0.36	0.002243 [1]	160	100
Fluopicolide	R3	Stream	Fish	Acute	0.36	0.002844	127	100
Fluopicolide	R4	Stream	Fish	Acute	0.36	0.003434	105	100
Fluopicolide	D6	Ditch	Fish	Chronic	0.155	0.002478	62.6	10
Fluopicolide	R1	Pond	Fish	Chronic	0.155	0.000244	635	10
Fluopicolide	R1	Stream	Fish	Chronic	0.155	0.001422	109	10
Fluopicolide	R2	Stream	Fish	Chronic	0.155	0.002243 [1]	69.1	10
Fluopicolide	R3	Stream	Fish	Chronic	0.155	0.002844	54.5	10
Fluopicolide	R4	Stream	Fish	Chronic	0.155	0.003434	45.1	10
Fluopicolide	D6	Ditch	Algae	Chronic	0.029	0.002478	11.7	10

Test substance	Scen.	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC[i]	TER	Annex VI trigger
Fluopicolide	R1	Pond	Algae	Chronic	0.029	0.000244	119	10
Fluopicolide	R1	Stream	Algae	Chronic	0.029	0.001422	20.4	10
Fluopicolide	R2	Stream	Algae	Chronic	0.029	0.002243 [1]	11.9	10
Fluopicolide	R3	Stream	Algae	Chronic	0.029	0.002844	10.2	10
Fluopicolide	R4	Stream	Algae	Chronic	0.029	0.003434	***8.4***	10

[i] PEC initial for late vine use late vine multiple application; [1] late vine single applicatiom (worse case)

FOCUS Step 4 - Assessment not required (5x FOCUSsw Step3 scenarios TER>Annex VI)

EXP 11120A - use on potato

FOCUS Step1

EXP 11120A potato (4 x 0.1 kg fluopicolide/ha; 5d spray interval; BBCH 20-91)

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}	TER	Annex VI Trigger
Fluopicolide	Fish	0.36	Acute	0.0971	-	***3.7***	100
Fluopicolide	Fish	0.155	Chronic	0.0971	-	***1.6***	10
Fluopicolide	Aq. invertebrates	>1.8	Acute	0.0971	-	***>18.5***	100
Fluopicolide	Aq. invertebrates	0.37	Chronic	0.0971	-	***3.8***	10
Fluopicolide	Algae	0.029	Chronic	0.0971	-	***0.3***	10
Fluopicolide	Higher plants	>3.2	Chronic	0.0971	-	>33.0	10
Fluopicolide	Sediment-dweller	49.0	Chronic	0.3077[1]	-	159.2	10
Metab. M01	Fish	240	Acute	0.01666	-	14458	100
Metab. M01	Algae	>10.0	Chronic	0.01666	-	>588	10
Metab. M02	Fish	>100	Acute	0.00873	-	6024	100
EXP 11120A	Algae	0.40	Chronic	0.0167[2]	-	24.0	10

[1] PECsed mg a.s./kg
[2] PEC from spray drift @ 1m

FOCUS Step 2
EXP 11120A potato (4 x 0.1kg fluopicolide/ha; 5d spray interval; BBCH 20-91) S.EU

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}	TER	Annex VI Trigger
Fluopicolide	S	Fish	0.36	Acute	0.01955	-	***18.4***	100
Fluopicolide	S	Fish	0.155	Chronic	0.01955	-	***7.9***	10
Fluopicolide	S	Aq. inverts.	>1.8	Acute	0.01955	-	***>92.1***	100
Fluopicolide	S	Aq. inverts.	0.37	Chronic	0.01955	-	18.9	10
Fluopicolide	S	Algae	0.029	Chronic	0.01955	-	***1.5***	10

FOCUS Step 3

EXP 11120A potato (4 x 0.1kg fluopicolide/ha; 5d spray interval; BBCH 20-91)

Test substance	Scen.	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC^i	TER	Annex VI trigger
Fluopicolide	D3	Ditch	Fish	Acute	0.36	0.000523[3]	688	100
Fluopicolide	D4	Pond	Fish	Acute	0.36	0.002794[2]	129	100
Fluopicolide	D4	Stream	Fish	Acute	0.36	0.002746[2]	131	100
Fluopicolide	D6(1st)	Ditch	Fish	Acute	0.36	0.001863[1]	193	100
Fluopicolide	D6(2nd)	Ditch	Fish	Acute	0.36	0.011966[1]	***30.1***	100
Fluopicolide	R1	Pond	Fish	Acute	0.36	0.000374[2]	963	100
Fluopicolide	R1	Stream	Fish	Acute	0.36	0.003775[2]	***95.4***	100
Fluopicolide	R2	Stream	Fish	Acute	0.36	0.001647[1]	219	100
Fluopicolide	R3	Stream	Fish	Acute	0.36	0.004071[2]	***88.4***	100
Fluopicolide	D3	Ditch	Fish	Chronic	0.155	0.000523[3]	296	10
Fluopicolide	D4	Pond	Fish	Chronic	0.155	0.002794[2]	55.5	10
Fluopicolide	D4	Stream	Fish	Chronic	0.155	0.002746[2]	56.4	10

Test substance	Scen.	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC[i]	TER	Annex VI trigger
Fluopicolide	D6(1st)	Ditch	Fish	Chronic	0.155	0.001863[1]	83.2	10
Fluopicolide	D6(2nd)	Ditch	Fish	Chronic	0.155	0.011966[1]	13.0	10
Fluopicolide	R1	Pond	Fish	Chronic	0.155	0.000374[2]	414	10
Fluopicolide	R1	Stream	Fish	Chronic	0.155	0.003775[2]	41.1	10
Fluopicolide	R2	Stream	Fish	Chronic	0.155	0.001647[1]	94.1	10
Fluopicolide	R3	Stream	Fish	Chronic	0.155	0.004071[2]	38.1	10
Fluopicolide	D3	Ditch	Aq. inverts	Acute	>1.8	0.000523[3]	3442	100
Fluopicolide	D4	Pond	Aq. inverts	Acute	>1.8	0.002794[2]	644	100
Fluopicolide	D4	Stream	Aq. inverts	Acute	>1.8	0.002746[2]	655	100
Fluopicolide	D6(1st)	Ditch	Aq. inverts	Acute	>1.8	0.001863[1]	966	100
Fluopicolide	D6(2nd)	Ditch	Aq. inverts	Acute	>1.8	0.011966[1]	150	100
Fluopicolide	R1	Pond	Aq. inverts	Acute	>1.8	0.000374[2]	4813	100
Fluopicolide	R1	Stream	Aq. inverts	Acute	>1.8	0.003775[2]	477	100
Fluopicolide	R2	Stream	Aq. inverts	Acute	>1.8	0.001647[1]	1093	100
Fluopicolide	R3	Stream	Aq. inverts	Acute	>1.8	0.004071[2]	442	100
Fluopicolide	D3	Ditch	Algae	Chronic	0.029	0.000523[3]	55.4	10
Fluopicolide	D4	Pond	Algae	Chronic	0.029	0.002794[2]	10.4	10
Fluopicolide	D4	Stream	Algae	Chronic	0.029	0.002746[2]	10.6	10
Fluopicolide	D6(1st)	Ditch	Algae	Chronic	0.029	0.001863[1]	15.6	10
Fluopicolide	D6(2nd	Ditch	Algae	Chronic	0.029	0.011966[1]	***2.4***	10

Test substance	Scen.	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC[i]	TER	Annex VI trigger
	)							
Fluopicolide	R1	Pond	Algae	Chronic	0.029	0.000374[2]	77.5	10
Fluopicolide	R1	Stream	Algae	Chronic	0.029	0.003775[2]	***7.7***	10
Fluopicolide	R2	Stream	Algae	Chronic	0.029	0.001647[1]	17.6	10
Fluopicolide	R3	Stream	Algae	Chronic	0.029	0.004071[2]	***7.1***	10

[i] PEC initial for [1] multiple late ,[2] multiple early and [3] single early (worse case)

FOCUS Step 4 - Assessment not required (3x FOCUSsw Step3 scenarios TER>Annex VI)

FOCUSgw aquatic risk assessment

EXP 11074B: vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81) SEU

GW Metab.	Scenario	Test organism	Time scale	72h E_bC50 (mg/L)	PEC_{sw} [2] (mg/L)	TER	Annex VI trigger
Worse case PECgws from PEARL model							
M-01	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0006075	>16461	10
M-03	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000517	56	10
M-05	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.000723	>138313	10
M-10	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000446	65	10
M-11	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000348	83	10
M-12	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000232	125	10
M-13	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000184	158	10
Worse case PECgws from PELMO model							
M-01	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0006265	>15962	10
M-03	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000525	55	10
M-05	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0000715	>139860	10
M-10	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000586	49	10
M-11	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000516	56	10
M-12	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000344	84	10
M-13	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.000216	134	10

GW Metab.	Scenario	Test organism	Time scale	72h E_bC50 (mg/L)	PEC_{sw} [2] (mg/L)	TER	Annex VI trigger
[1] based on parent fluopicolide end point (0.029 mg/L) with 10x assessment factor [2] based on PECgw x 0.1 (PECgw to PECsw dilution correction – SANCO 3268/2001)							

FOCUSgw aquatic risk assessment

EXP 11120A: potato (4x 0.1 kg fluopicolide/ha; 5d spray interval; BBCH 20-91)

GW Metab.	Scenario	Test organism	Time scale	72h E_bC50 (mg/L)	PEC_{sw} [2,3] (mg/L)	TER	Annex VI trigger
Worse case PECgws from PEARL model							
M-01	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0006743	>14830	10
M-03	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000477	61	10
M-05	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0000749	>133511	10
M-10	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000492	59	10
M-11	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000502	58	10
M-12	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000335	87	10
M-13	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000272	107	10
Worse case PECgws from PELMO model							
M-01	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0006733	>14852	10
M-03	Hamburg	*N. pelliculosa*	Chronic	0.0029[1]	0.0000275	105	10
M-05	Hamburg	*N. pelliculosa*	Chronic	>10.0	0.0000592	>168919	10
M-10	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000534	54	10
M-11	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000813	36	10
M-12	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000542	54	10
M-13	Jokioinen	*N. pelliculosa*	Chronic	0.0029[1]	0.0000369	79	10

GW Metab.	Scenario	Test organism	Time scale	72h E_bC50 (mg/L)	PEC_{sw} [2,3] (mg/L)	TER	Annex VI trigger
[1] based on parent fluopicolide end point (0.029 mg/L) with 10x assessment factor [2] based on PECgw x 0.1 (PECgw to PECsw dilution correction – SANCO 3268/2001) [3] based on repeat annual applications (worse case)							

Fish bioconcentration

Bioconcentration	
	Fluopicolide
$logP_{O/W}$	2.9
Bioconcentration factor (BCF) ‡	121
Annex VI Trigger for the bioconcentration factor	100[1]
Clearance time (days) (CT_{50})	0.51
(CT_{90})	1.7
Level and nature of residues (%) in organisms after the 14d depuration phase	5%

[1] fish (ELS study) TER_{lt}>10

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	**Acute oral toxicity LD_{50} µg/bee**	**Acute contact toxicity LD_{50} µg/bee**
Fluopicolide ‡	>241	>100
EXP 11074B	>8.0[1] (>169[2])	>3.3[1] (>70[2])
EXP 11120A	>11.7[1] (>204[2])	>8.2[1] (>143[2])
Field or semi-field tests - not required		

[1] fluopicolide; [2] preparation

Hazard quotients for honey bees (Annex IIIA, point 10.4)

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81)

Test substance	**Route**	**Hazard quotient**	**Annex VI Trigger**
Fluopicolide	Contact	<1.33	50
	oral	<0.55	50
EXP 11074B	Contact	<40.39	50
	oral	<16.66	50

EXP 11120A potato (4 x 0.1kg fluopicolide/ha; 7d spray interval; BBCH 20-91)

Test substance	Route	Hazard quotient	Annex VI Trigger
Fluopicolide	Contact	<1.00	50
	oral	<0.41	50
EXP 11120A	Contact	<12.20	50
	oral	<8.55	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	LR50 preparation
Typhlodromus pyri ‡	EXP 11074B	Mortality	7.13 kg/ha
Aphidius rhopalosiphi ‡	EXP 11074B	Mortality	8.23 kg/ha
Typhlodromus pyri ‡	EXP 11120A	Mortality	>8.0 L/ha
Aphidius rhopalosiphi ‡	EXP 11120A	Mortality	2.48 L/ha

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81)

Test substance	Species	Effect (LR_{50} kg/ha)	HQ in-field	HQ off-field (@3m)	Trigger
EXP 11074B	*Typhlodromus pyri*	7.13	0.97	0.067	2
EXP 11074B	*Aphidius rhopalosiphi*	8.23	0.84	0.058	2

EXP 11120A potato (4 x 0.1 kg fluopicolide/ha; 7d spray interval; BBCH 20-91)

Test substance	Species	Effect (LR_{50} L/ha)	HQ in-field	HQ off-field (@1m)	Trigger
EXP 11120A	*Typhlodromus pyri*	>8.0	1.33	0.025	2
EXP 11120A	*Aphidius rhopalosiphi*	2.48	1.74	0.032	2

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (L/ha) [1]	End point	(L/ha) % repro effect vs control	Trigger value
Aphidius rhopalosiphi	Adult	EXP 11120A	1.0 2.0 4.0 8.0	Mortality LR50 Mean no. mummies/female	(>8.0) -7.6 -20.3 -50.0 -98.7	50 %
Typhlodromus pyri	Proto nymph	EXP 11120A	0.4 0.72 1.29 2.32 4.17	Mortality LR50 Mean no. eggs & larvae /female	(>4.17) -12.9 -17.9 -27.6 -29.8 -34.3	50 %
Chrysoperla carnea	Larvae	EXP 11120A	6.4	Mortality LR50 Mean no. eggs/ female/d	(>6.4) -2.7	50 %
Field or semi-field tests - not required						

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4, 8.5 and 8.7, Annex IIIA, points, 10.6 and 10.7)

Soil macroorganisms

Test organism	Test substance	Test	End point (mg/kg soil)
Earthworms			
	Fluopicolide ‡	Acute 14d LC50	>500[1]
	Fluopicolide ‡	Chronic 56d NOEC	62.5[1] (28d growth)
	EXP 11074B	Acute 14d LC50	>21.75[2,4]
	EXP 11074B	Chronic	2.435[2,4]
	EXP 11120A	Acute 14d LC50	>28.65[2,4]
	EXP 11120A	Chronic	2.587[2,4]
	Metabolite M01	Acute 14d LC50	750[3]
	Metabolite M01	Chronic 56d NOEC	250[3] (56d reproduction)
	Metabolite M02	Acute 14d LC50	>1000[3]
	Metabolite M03	Acute 14d LC50	>500[1]
Other soil macro-organisms			
Collembola			
	Fluopicolide	28d NOEC	31.25[1]
	Metabolite M01	28d NOEC	25.0[3]

[1] corrected endpoint (Log Pow>2; 10% w/w soil OM)

[2] correction not required (5% w/w/ soil OM)

[3] correction not required (Log Pow <2)

[4] expressed as fluopicolide (a.s.)

Toxicity/exposure ratios for soil organisms

EXP 11074B vine (3 x 0.133 kg fluopicolide/ha; 10d spray interval; BBCH 53-81)

Test organism	Test substance	Time scale	Max.Soil PEC[1] (mg/kg d.wt soil)	TER	Trigger
Earthworms					
	Fluopicolide ‡	Acute	0.268	>1866	10
	Fluopicolide ‡	Chronic	0.268	233	5
	EXP 11074B	Acute	0.268[3]	>81	10
	EXP 11074B	Chronic	0.268[3]	9.1	5
	Metabolite M01	Acute	0.035	21429	10
	Metabolite M01	Chronic	0.035	7143	5
	Metabolite M02	Acute	0.026	>38462	10
	Metabolite M03	Acute	0.013	>38462	10
Other soil macro-organisms					
Collembola	Fluopicolide	Chronic	0.268	117	5
	Metabolite M01	Chronic	0.035	714	5

EXP 11120A potato (4 x 0.1 kg fluopicolide/ha; 5d spray interval; BBCH 20-91)

Test organism	Test substance	Time scale	Max. Soil PEC[1] (mg/kg d.wt soil)	TER	Trigger
Earthworms					
	Fluopicolide ‡	Acute	0.202	>2475	10
	Fluopicolide ‡	Chronic	0.202	309	5
	EXP 11120A	Acute	0.202[3]	>142	10
	EXP 11120A	Chronic	0.202[3]	13	5
	Metabolite M01	Acute	0.0174[2]	43103	10
	Metabolite M01	Chronic	0.0174[2]	14368	5
	Metabolite M02	Acute	0.019	>52632	10
	Metabolite M03	Acute	0.017	>29412	10

Test organism	Test substance	Time scale	Max. Soil PEC[1] (mg/kg d.wt soil)	TER	Trigger
Other soil macro-organisms					
Collembola	Fluopicolide	Chronic	0.202	155	5
	Metabolite M01	Chronic	0.0174[2]	1437	5

[1] 5cm ([2]10cm) peak accumulated PECsoil
[3] expressed as fluopicolide (a.s.)

Soil organisms – field studies

Field studies - Litter bag studies (soil organic matter degradation)					
Test substance	**Total soil conc.[2] mg/ kg d.wt. soil**	**max PECsoil mg/kg d.wt. soil (% soil conc/PEC)**		**% straw deg. *vs*. control [DAT]**	**EPFES 2002 trigger**
		Potato	**Vine**		
Fluopicolide[1]	0.186	0.202[3]/0.112[4] (92) / (166)	0.268[3]/0.134[4] (69) / (139)	[29] +0.7 [92] -5.5 [184] -1.1	10%
M01	0.010	0.009[3]/0.017[4] (90) / (59)	0.035[3]/0.017[4] (29) / (59)	[29] +1.2 [92] -5.0 [184] -0.2	10%

[1] applied as SC480 formulation
[2] mean measured (10cm depth)
[3] 5cm depth (worse case –no soil tillage); [4] 10cm depth

Soil microorganisms

Soil microbial test	**Soil treatment**	**Test duration**	**Test rate (mg a.s./kg d.wt.soil)**	**Max. accum. PECsoil (mg a.s./kg d.wt.soil)[3]**	**% 28d deviation *vs* control (max % deviation)**	**Annex VI (%)**
N-metabolism						
	Fluopicolide ‡	28d	0.18[1]/1.84[2]	0.268	+5(±5)/+7(-9)	25
	EXP 11074B	28d	0.178[1]/1.775[2]	0.268	0(+4)/+11(-12)	25
	EXP 11120A	28d	0.18[1]/1.80[2]	0.202	+7(+9)/+11(-16)	25
	Metabolite M01	14d	0.19/3.80	0.035	(-6)/(+11)	25
	Metabolite M01	28d	0.09/0.92	0.035	-2(-9)/-4(-13)	25

C-metabolism						
	Fluopicolide ‡	28d	0.18[1]/1.84[2]	0.268	-8(-8)/-6(-6)	25
	EXP 11074B	28d	0.178[1]/1.775[2]	0.268	-7(-11)/-11(-15)	25
	EXP 11120A	28d	0.18[1]/1.80[2]	0.202	-11(-14)/0(-10)	25
	Metabolite M01	14d	0.19/3.80	0.035	(±3)/(+2)	25
	Metabolite M01	28d	0.09/0.92	0.035	-8(-10)/-7(-10)	25

equivalent to [1]1x and [2]10x fluopicolide field application rate

[3] 5cm soil depth

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)
Preliminary screening data

Fluopicolide (20% w/w WP) - herbicidal screen - 27 crop/weed spp.
Post em - max. conc 1.28 kg/ha - no herbicidal effect - ER50>1.28kg/ha
Pre em - max. 1.28 mg kg soil - no herbicidal effect - ER50>1.707 mg/kg soil

Laboratory dose response tests

Most sensitive species	**Test substance**	**ER_{50} veg. vigour**	**ER_{50} seedling emerg./growth**	**PER[6] PECsoil [depth cm]**	**TER**	**Trigger**
Vine (3 x 3.0kg EXP11074B [=3 x 0.133kg fluopicolide]/ha; 10d spray interval; BBCH 53-81)						
Lettuce/cucumber	EXP 11074B		>3.0 kg/ha	0.207 kg/ha[1]	>14.5	5
Oilseed rape	EXP 11074B	>3.0 kg/ha		0.207 kg/ha[1]	>14.5	5
Onion	M01		>0.0121 mg/kg d.wt soil	0.00366 [5][3] 0.00163[10][3] 0.00183[5][4] 0.00081[10][4]	>3.3 >7.4 >6.6 >14.9	5
Potato (4 x 1.6L EXP11120A [=4 x 0.1kg fluopicolide]/ha; 7d spray interval; BBCH 20-91)						
Onion	EXP 11120A		>2.13 L/ha	0.0296 L/ha[2]	>72.0	5
Oat	EXP 11120A	>2.13 L/ha		0.0296 L/ha[2]	>72.0	5
Onion	M01		>0.0121 mg/kg d.wt soil	0.00060[5][5]	>20.2	5
Additional studies (e.g. semi-field or field studies)						
None- not required. Both fluopicolide and metabolite M01 have no herbicidal activity.						

[1] PER = (6.9% drift @ 3m off-late vine crop) ; [2] PER = (1.85% drift @1m off-field crop)
M01 PECsoil based on late vine crop [3]6.9% drift @3m, [4]3.07%drift @5m
M01 PECsoil based on field crop [5]1.85% drift @1m
[6] spray drift BBA(2000)
(NB. M01 PECsoil assumes max. fluopicolide degradation to M01; 0% interception by off-crop vegetation)

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge (microbial respiration)	EC50 >25.4 mg fluopicolide/L

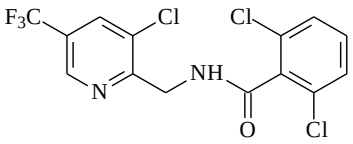
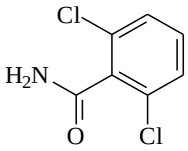
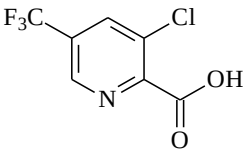
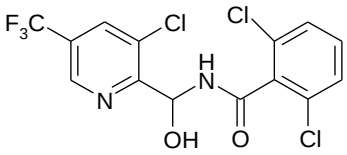
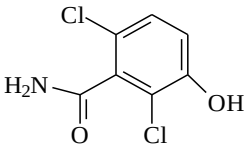
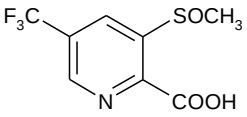
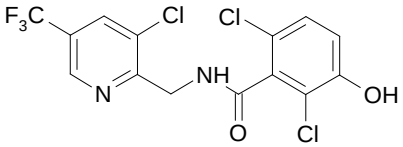
Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

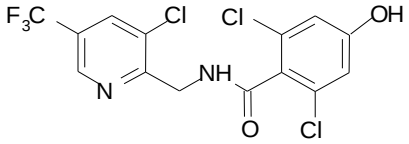
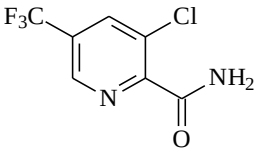
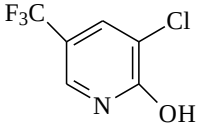
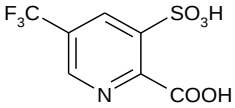
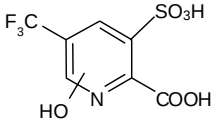
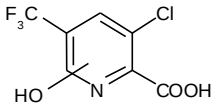
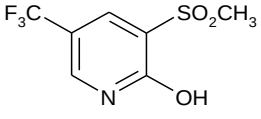
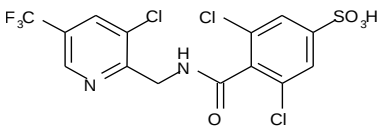
Env Compartment	Compound
soil	fluopicolide
surface water	fluopicolide
sediment	fluopicolide
groundwater	fluopicolide

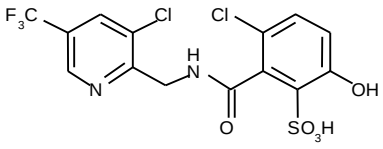
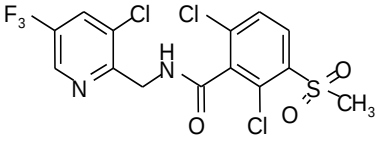
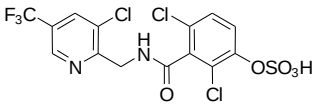
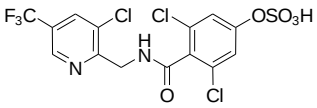
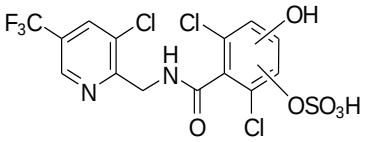
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	N, R50, R53, S60, S61

	RMS/peer review proposal
EXP 11074B	N, R50, R53, S35, S57
EXP 11120A	N, R50, R53, S35, S57

Code/Trivial name	Chemical name	Structural formula
fluopicolide (AE C638206)		2,6-dichloro-N-{[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl} benzamide
M-01 (AE C653711)		2,6-dichlorobenzamide
M-02 (AE C657188)		3-chloro-5-trifluoromethyl-pyridine-2-carboxylic acid
M-03 (AE 0608000)		4-N-[3-chloro-5-trifluoro-methylpyridin-2-yl) (hydroxyl)methyl]-2,6-dichlorobenzamide
M-04 (AE C657378)		2,6-dichloro-3-hydroxy-benzamide
M-05 (AE 1344122)		3-methylsulfinyl-5-trifluoro-methylpyridine-2-carboxylic acid
M-06 (AE C643890)		2,6-dichloro-N-[(3-chloro-5-trifluoromethylpyridin-2-yl) methyl]-3-hydroxybenzamide

Code/Trivial name	Chemical name	Structural formula
M-07 (AE 0712556)		2,6-dichloro-N-[(3-chloro-5-trifluoromethylpyridin-2-yl) methyl]-4-hydroxy benzamide
M-08 (AE C653598)		3-chloro-5-trifluoromethyl pyridine-2-carboxamide
M-09 (AE B102859)		3-chloro-2-hydroxy-5-trifluoromethylpyridine
M-10 (AE 1344123)		3-sulfo-5-trifluoromethyl pyridine-2-carboxylic acid
M-11 M-12		isomers x-hydroxy -y-sulfo-5-trifluoromethylpyridine-2-carboxylic acid
M-13 proposal not confirmed		
M-14 (AE 1388273)		3-mesyl-5-(trifluoromethyl) pyridin-2-ol
M-15 (AE 1413903)		3,5-dichloro-4-[3-chloro-5-trifluoromethylpyridine-2-yl-methyl) carbamoyl] benzene sulfonic acid

Code/Trivial name	Chemical name	Structural formula
M-16		3-chloro-2-[({3-chloro-5-trifluoromethylpyridine-2-ylmethyl}amino) carbonyl]-6-hydroxybenzene sulfonic acid
M-17		2,6-dichloro-N-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}-3-(methyl-sulfonyl)benzamide
M-18	 or 	2,4-dichloro-3-[({[3-chloro-5-(trifluoromethyl)-pyridin-2-yl]methyl} amino)carbonyl] phenyl hydrogen sulfate or 3,5-dichloro-4-[({[3-chloro-5-(trifluoromethyl) pyridin-2-yl]methyl}amino) carbonyl] phenyl hydrogen sulfate
M-19		3,5-dichloro-4-[({[3-chloro-5-(trifluoromethyl) pyridin-2-yl]methyl}amino) carbonyl] hydroxyphenyl hydrogen sulfate

APPENDIX B – LIST OF ABBREVIATIONS

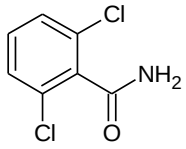
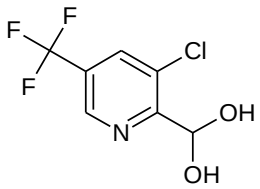
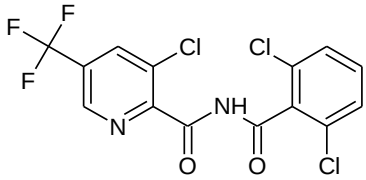
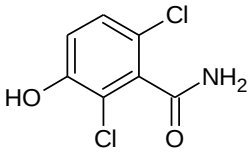
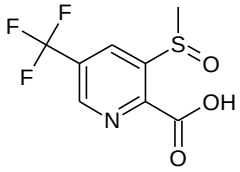
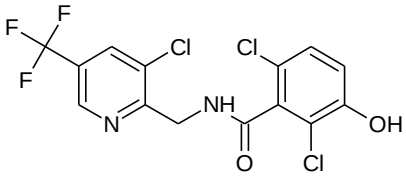
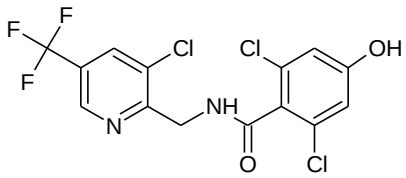
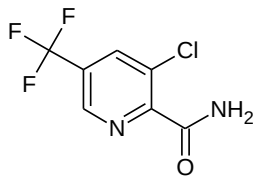
1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union

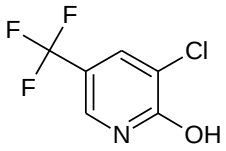
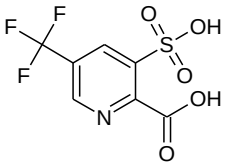
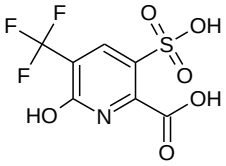
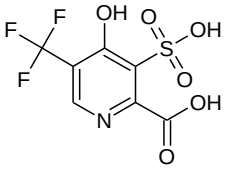
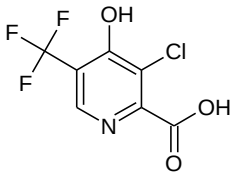
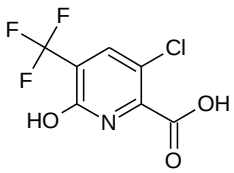
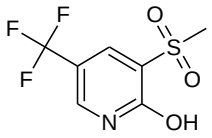
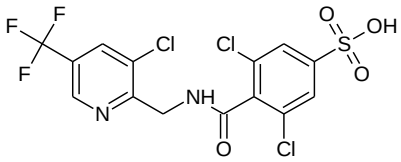
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor

MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
POEM	Predictive Operator Esposure Model
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)

TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
M-01 BAM	2,6-dichlorobenzamide	
M-02	3-chloro-5-(trifluoromethyl)pyridine-2-carboxylic acid	
M-03	2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl](hydroxy)methyl}benzamide	
M-04	2,6-dichloro-3-hydroxybenzamide	
M-05	3-(methylsulfinyl)-5-(trifluoromethyl)pyridine-2-carboxylic acid	
M-06	2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}-3-hydroxybenzamide	
M-07	2,6-dichloro-*N*-{[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}-4-hydroxybenzamide	
M-08	3-chloro-5-(trifluoromethyl)pyridine-2-carboxamide	

M-09	3-chloro-5-(trifluoromethyl)pyridin-2-ol	
M-10	3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid	
M-11	6-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid	
M-12	4-hydroxy-3-sulfo-5-(trifluoromethyl)pyridine-2-carboxylic acid	
M-13	3-chloro-4-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid 3-chloro-6-hydroxy-5-(trifluoromethyl)pyridine-2-carboxylic acid	 
M-14	3-(methylsulfonyl)-5-(trifluoromethyl)pyridin-2-ol	
M-15	3,5-dichloro-4-({[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}carbamoyl)benzenesulfonic acid	
M-16	3-chloro-2-({[3-chloro-5-(trifluoromethyl)pyridin-2-yl]methyl}carbamoyl)-6-hydroxybenzenesulfonic acid