PEER REVIEW REPORT ON **FLUOPICOLIDE** 26 05 2009

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1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

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	Section 1 Data requirements: ***5*** Open points: ***17***			Section 1 Data requirements: ***1*** Open points: ***1***
1.1	Data requirement Once full scale manufacturing is in progress, the specification of the technical fluopicolide produced at the manufacturing plant must be compared with that from the pilot plant. If the specifications are comparable then no further work is required. If differences emerge then at least 5 different production batches from the manufacturing plant will have to be analysed with a view to revising the specification. See reporting table 1(1).	BCS agrees that once full scale manufacturing is in progress a new five batch analysis is required	RMS: When full scale manufacturing is in progress and data submitted it will be evaluated and included it in an addendum Addressed RMS (Dec 2008): See 1.6 below.	PRAPeR 36 (27. – 30.11.2007): Data requirement redundant. New data requirement: Once full scale manufacturing is in progress then new 5 batch data must be provided. PRAPeR 61 (13 – 16 January 2009): Data requirement redundant, see new data requirement 1.6.

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1.6	New data requirement identified at PRAPeR 36: Once full scale manufacturing is in progress then new 5 batch data must be provided.	**Comment BCS May 2008:** Full scale manufacturing will in future be done in a new production facility. A five batch analysis (Bowen, T; 2008, report M-295708-01-1) from this facility was submitted to the RMS and all relevant MSs to register the new source and to incorporate the results into an addendum to the DAR. The report can be made available upon request.	RMS (Dec 2008): 5 batch data from full scale manufacturing plant and QC data has been submitted. This has been evaluated and incorporated into the Volume 4, Addendum 2 (December 2008). To be discussed at an Expert Meeting.	PRAPeR 36 (27. – 30.11.2007): Data requirement open. PRAPeR 61 (13 – 16 January 2009): Data requirement fulfilled. 5 batch data from full scale manufacturing plant and QC data has been submitted and evaluated in Addendum 2 to Volume 4 (December 2008).
	Open point 1.1 In the PRAPeR toxicology expert meeting 09 it was concluded for the active substance flonicamid that toluene is relevant it is therefore unclear why in this case it would not be relevant. See reporting table 1(5).	BCS refer again to our comment made in the reporting tables. With respect to a possible increase of toluene during storage of formulated products, BCS would like to point out that in the case of fluopicolide, toluene is a residual solvent coming from the production process. There is no possibility for an increase of toluene during storage since chemically, it is not possible to form toluene as a result of the degradation of either fluopicolide or its impurities.	RMS: The RMS considers that toluene as an impurity in the technical material fluopicolide is not a relevant impurity based on the assessment of fluopicolide **with** toluene present as an impurity in the technical material. The properties or classification of toluene as a separate chemical entity at high concentration do not apply to that of fluopicolide **with** toluene as impurity at concentrations of ≤ 5% because the technical material was in fact not irritating to skin, harmful for reproduction or harmful by inhalation after prolonged exposure at tested concentrations. Fluopicolide does not have any constituents that would give rise to toluene on storage. Please refer to further discussion in Volume 4, Addendum 1 (Nov 2007).	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.

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			Open Point: to be discussed at Expert Meeting.	
	Open Point 1.2 Rapporteur to clarify the chromatographic separation of impurities AE C636523 from toluene. From column 3 of the reporting table it is noted that some additional data have been supplied by the applicant. If this data are useful then it should be evaluated in an addendum. See reporting table 1(7).	The additional data (Bowen, T; report AF05/100; M-261425-01-1) can be made available upon request.	RMS: The retention times of toluene and AE C636523 are very close at 11.8 and 11.4 minutes, when determining AE C636523 in technical material, however there are two distinct peaks in the chromatogram. In addition, the content of toluene and AE C636523 in technical material are determined by two separate methods, one of the batches contained 3.9 g/kg toluene and 0.1 g/kg AE C636523, therefore if toluene had co-eluted the result for AE C636523 would have been much higher. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.3 For the impurity method Bowen, 2004 there are no calibration ranges given and this should be clarified. It is noted that in column 3 of the reporting table it is mentioned that additional data have been submitted. If the new data are relevant then they should be evaluated and presented in an addendum. See reporting table 1(8).	The additional data (Bowen, T; report AF05/100; M-261425-01-1) can be made available upon request.	RMS: The calibration ranged in the methods of analysis used to analyse the technical material for the impurities (see table C.3 in volume 4) covers the levels of impurities determined in the batches of technical material. The calibration standard run, during the determination of the levels of impurities in the batches was set at a level of 10 g/kg for all the impurities, although slightly higher than the impurities in the batches (0.1-2.8 g/kg). Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.

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	Open point 1.4 The corrected formulation details should be given. See reporting table 1(10).		RMS: The '@ 14.9' in the contents column should read 'up to 14.9' or 'maximum 14.9' in order to give a closure of 1000 g/kg. See Confidential Volume 4, Addendum 1. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.5 It should be discussed by a meeting of experts if recovery and accuracy determinations at 10 times the specification levels for impurities can be accepted. See reporting table 1(11).	Regarding the acceptability of recovery and accuracy determinations at 10 times the specification levels of impurities, BCS has prepared an additional position paper in the context of the national evaluation of fluopicolide in Germany. This paper (Bowen, T; report AF07/023, M-284628-01-1) can be made available upon request.	RMS: As stated the accuracy data were generated at 10 times the specification levels. Although not ideal, when taking into account that the concentration of the impurities in the batches lie with in the linear calibration range and the high recoveries obtained (97-101%), it is hard to justify the need for further data. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.6 A justification with respect to chemical structure and chromatographic behaviour concerning the use of a different reference material for the validation of one impurity is required. In addition to this it was requested in the comments on column 4 of the reporting table that the retention times for all impurities and the active	BCS has prepared a position paper to justify the use of a different reference material for the validation of impurities. This report (Bowen, T; report AF07/045, M-287053-01-1) can be made available upon request.	RMS: As stated in the footnote at the bottom of table C.4, a 'reference standard was not available and thus quantification was based on fluopicolide standard. The fluopicolide response factor used to determine the levels of AE1050605 was refined by the isolation of AE1050605 by prep HPLC and running a standard of the isolated AE1050605 against an equivalent fluopicolide standard'. To further clarify this, on running the AE1050605 standard the response factor was determined and the results amended	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.

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	substance should be reported. These issues should be discussed in a meeting of experts. See reporting table 1(16).		accordingly. Therefore, although not initially, the results in the end were generated using the correct response factor determined using an AE1050605 standard. Retention times of active substance and impurities **Method (a)** Fluopicolide – 13.0 min AEC636523 – 11.1 min AC0553913 – 13.0 min AEC639035 – 19.7 min AEC648994 – 25.2 min AE1050605 – 39.5 min **Method (b)** Fluopicolide - 21.3 min M-01 - 4.6 min AEC648995 – 6.5 min AEF125577 – 18.4 min Open Point: to be discussed at Expert Meeting.	

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	Open point 1.7 LOEP relative density the purity should be given.. See reporting table 1(24).		RMS: Purity = 99.3%. However, relative density is no longer included in the current end points template. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.8 It should state for the Log Pow that it is independent of pH. See reporting table 1(27).		RMS: Agreed. Log Pow is independent of pH. The end points have been updated. Addressed.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.9 It should be noted in the endpoints that the method is not required as no MRLs will be set. This does not impact on the reliance on this method for the pre-registration data. See reporting table 1(29).		RMS: End points have been updated indicating that the method of analysis for animal products is not required, as no MRLs have been set for these commodities. Addressed.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.10 The endpoints should use the current agreed template. See reporting table 1(33).		RMS: The LOEP have been updated to the current template.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.

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	Open point 1.11 For melting point which sub method of A1 was used. See reporting table 1(40).		RMS: Sub method 1.4.4.2 Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.12 For the UV/VIS More detailed information about the measurement should be given, e.g. solvent, maximum absorbance. See reporting table 1(44).		RMS: The maximum absorbance is stated in B.2.1.10 as UV absorb 203 nm (ε = 44159 l mol^{-1} cm^{-1}), solvent was methanol Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
1.2	Data requirement Explosive properties mechanical sensitivity data should be provided. [This should be considered as a technical data requirement as the study has already been submitted] See reporting table 1(48).	BCS will include the report (Smeykal, H. M-269406-01-1) in the updated dossier.	RMS: Mechanical sensitivity data generated using EEC method A14 was submitted in BCS report 20060164.01. The data indicated that fluopicolide did not explode as a result of either friction or shock. Addressed	PRAPeR 36 (27. – 30.11.2007): Data requirement fulfilled.

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1.3	Data requirement A 2 year storage stability study in the commercial packaging. [This should be regarded as a technical data requirement as it is noted that a study has already been provided (SC).] See reporting table 1(59).	Study was already submitted with the updated dossier in 2005 to all MSs	RMS: Study has been evaluated and reported in B.2.2.15, the packaging used in the study was the proposed commercial pack (HDPE), which on examination showed no negative interactions with the SC formulation after 2 years storage. Addressed	PRAPeR 36 (27. – 30.11.2007): Data requirement fulfilled.
1.4	Data requirement A 2 year storage stability study in the commercial packaging. [This should be regarded as a technical data requirement as it is noted that a study has already been provided (WG).] See reporting table 1(60).	Study was already submitted with the updated dossier in 2005 to all MSs	RMS: Study has been evaluated and reported in B.2.2.15, Addendum 1, the packaging used in the study was the proposed commercial pack (Aluminium/PE kraft bag in a cardboard box), which on examination showed no negative interactions with the WG formulation after 2 years storage. See also Open Point 1.13 below Addressed	PRAPeR 36 (27. – 30.11.2007): Data requirement fulfilled.
	Open point 1.13 The reference Güldner, 2005, Lab. ID. 02-99 should be added to the list of references relied on. The storage stability correction should be considered in a revised DAR		RMS: See corrected text and reference in Section 2, Addendum 1. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.

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	or corrigendum (WG). See reporting table 1(62).			
	Open point 1.14 The studies Zietz, 2004b and Billian and Schöning, 2004 should be deleted from the list of references relied on because they belong to Annex II, 6.0. See reporting table 1(64).		RMS: References have been deleted from Section 2, Addendum 1. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
1.5	Data requirement The relevant impurity must be analysed for before and after two years storage and a validated method of analysis is required SC and WG formulation. It should be noted that the applicant has stated in there comments that they disagree with this compound being considered as relevant. See reporting table 1(66).	BCS refer again to our comment made in the reporting tables. **Comment BCS May 2008:** Full scale production will be done in future in a new BCS production site in [redacted] (see also comment on point 1.6, page 1). A new five batch analysis showed that the content of the impurity 2,6-dichlorobenzamide (BAM) will in future be clearly below 1 g/kg in the technical active ingredient. Relevance in general is dependent upon the relative hazards of the active ingredient and impurity. As BAM is (eco)toxicologically neither qualitatively different nor quanitatively more adverse than the active substance fluopicolide, it cannot be considered a	RMS: Agree with Notifier, no further storage stability data are required, as the active substance content only fell by 0.8% after 2 years storage of the SC and by 2.8% after 2 years storage of the WG. If considered necessary, to be discussed at the expert meeting Addressed RMS (December 2008): The applicants comments of May 2008 cover the initial concern with the levels of BAM before storage of the product i.e. BAM being removed from the technical material. However, they do not address the possibility of the formation of BAM as a result of the breakdown of fluopicolide, during 2 years storage (0.8% after 2	PRAPeR 36 (27. – 30.11.2007): Data requirement reworded: The new data requirement would read as follows The analysis of the relevant impurity in the SC and WG formulation before and after storage, methods of analysis for this impurity in the formulation and spectral data have to be submitted. Data requirement open. PRAPeR 61 (13 – 16 January 2009): Data requirement open and pending on the discussions during the meeting on

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		(eco)toxicologically relevant impurity in the technical material. In the context of the impurity BAM, Bayer CropScience wishes to point out that because the content of BAM in the technical material manufactured in the full-scale production by BCS at [redacted] is clearly below 1 g/kg and thus does not need to be specified, the need for analysis of this impurity in formulated products doesn`t arise any longer.	years storage of the SC and 2.8% after 2 years storage of the WG). Therefore data requirement remains open. However, the RMS considers that this can be addressed at member state level. RMS (February 2009): The RMS considers that this data requirement can be closed as the PRAPeR mamtox and ecotox meetings agreed that M-01 (BAM) is not a relevant impurity.	mammalian toxicology and ecotoxicology. Written procedure: Data requirement obsolete PRAPeR mamtox and ecotox meetings agreed that M-01 (BAM) is not a relevant impurity
	Open point 1.15 The LOQs should be given for each analyte in the list of end points. See reporting table 1(72).		RMS: LOQs are as follows: Grape = 0.1 mg/kg Wheat grain = 0.02 mg/kg Potato = 0.02 mg/kg Endpoints table have been updated. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled. New open point, see open point 1.18
	New open point 1.18: The wording in the end points should be clarified. The ranges given in the list of end points should be changed to specific LOQs for each matrix.		RMS (December 2008): The Endpoints have been updated.	PRAPeR 36 (27. – 30.11.2007): Open point open. PRAPeR 61 (13 – 16 January 2009): Open point fulfilled.

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	Open point 1.16 At least the linearity range should be given for all the residue methods. See reporting table 1(78).		RMS: Linearity ranges are as follows; Plant (Parent) = 0.01–1 µg/ml Soil (Parent/M03) = 0.4–75 µg/l Soil (M01/M02) = 0.4–100 µg/l Water (Parent/M01/M02) = 0.2–25 µg/l Air (Parent) = 0.01–1 µg/ml Animal(Parent/M01/M02) = 0.1-10µg/ml Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.17 For the residue methods the mean recovery at each fortification level should be given. The % RSD should be calculated and given for each level and the number of samples should also be given. See reporting table 1(81).		RMS: Disagree, as all the recoveries were greater than 70%, if that had not been the case would have presented individual recovery data for each fortification levels were recoveries of less than 70% resulted. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	New open point 1.19: RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting.		RMS (December 2008): The Endpoints have been updated.	PRAPeR 36 (27. – 30.11.2007): Open point open. PRAPeR 61 (13 – 16 January 2009): Open point fulfilled.

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	New open Point 1.20: RMS to amend the list of end points according to the discussions during the PRAPeR 61 meeting.			PRAPeR 61 (13 – 16 January 2009): Open point open. Written procedure: Open point fulfilled

2. Mammalian toxicology

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	Section 2 Data requirements: ***2*** Open points: ***11***			Section 2 Data requirements: ***0*** Open points:***0***
	Open point 2.1 The relevance of the liver weight increase in the 90 day study in dog to be agreed on in an experts' meeting See reporting table 2(3).	BCS refers to the corresponding comment made on the reporting tables	RMS: The RMS notes revision to Table 6.57 in Vol 3 and can be found in **Addendum 1 (Nov 2007)**. It provides further information on elevated statistically non-statistically significant levels of cholesterol and alkaline phosphatase (however, statistically significant increase in alkaline phosphatase in females at 13 weeks is noted) and suggests that 1000 mg/kg bw/day is a LOAEL for the 90-day study. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled. The NOAEL of 70 mg/kg bw/d in the 90-day dog study was confirmed.
	Open point 2.2 The carcinogenic potential of fluopicolide to be discussed in an experts' meeting, in particular with regard to the possible mode of action involved and the need for classification See reporting table 2(6).	BCS refers to the corresponding comments made on the reporting tables. For BCS, an R40 is unwarranted for both fluopicolide and M-01. BCS has prepared detailed position papers regarding fluopicolide (Payraudeau, V. Report M-275342-01-1) and M-01 (Payraudeau, V. Report M-274220-02-1; Pallen, C. Report M-273467-01-1) which can be submitted upon request. An additional expert opinion has recently been provided by Dr. C. Gopinath who was responsible for the	RMS: A summary and assessment of the additional information by the RMS and position of the Notifier is provided in Addendum 1 (Nov 2007). To be discussed at the expert meeting. Carcinogenic Potential of Fluopicolide: The RMS notes that in the chronic toxicity and carcinogenicity study in mice, Fluopicolide caused an increase in hepatocellular adenomas in male and female mice at a dose level of 3200	PRAPeR 39 (10– 13 12.2007): Open point fulfilled. Neither for fluopicolide nor for metabolite M01 was a classification for carcinogenicity proposed.

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	Continued: Open point 2.2 The carcinogenic potential of fluopicolide to be discussed in an experts' meeting, in particular with regard to the possible mode of action involved and the need for classification See reporting table 2(6).	reassessment report (M-234672-01-1) stating that M01 is non-carcinogenic. BCS considers this paper essential to be considered at any expert meeting. The document can be submitted upon request.	ppm a dose level at which the MTD had been attained by a mechanism considered to be not relevant to humans. In a mechanistic study, dietary administration of fluopicolide at 3200ppm in the diet induced liver changes such as higher liver weights, hepatocellular hypertrophy as well as a transient and marked hepatocellular proliferation in C57BL/6mice after 7days of treatment, which returned to control levels after 28 days of treatment. Fluopicolide was shown to be an inducer of cytochrome P-450 and BROD and PROD enzyme activities comparable with the liver enzyme induction profile of phenobarbital. Bromodeoxyuridine-labelling in the 28-day mechanistic study showed a transient marked increase in labelling index which is known to be sufficient to induce hepatocellular tumours in mice (Grasso P et al., 1991, Hildebrand B. et al, 1991) and is considered be of no relevance to humans. Further investigation with Proliferating Cell Nuclear Antigen staining at 90 days did not reveal any PCNA-positive hepatocytes at 90 days and is consistent with the findings with BrDU at 28 days. The Notifier provided a position paper	

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	Continued: Open point 2.2 The carcinogenic potential of fluopicolide to be discussed in an experts' meeting, in particular with regard to the possible mode of action involved and the need for classification See reporting table 2(6).		(Virginie Payraudeau 2/11/2006 – See Appendix 6, Addendum 1). The RMS agrees with the conclusion that the hepatocellular adenomas in mice are caused by a mechanism not relevant to humans. <u>Carcinogenic Potential of M-01 (BAM)</u> The key elements of the RMS assessment the following: i. The incidence of benign hepatocellular adenomas in female rats at the top dose level was stated to be marginally statistically significant (P=0.049) according to the report of the reviewing pathologist. However the investigating laboratory have subsequently stated that the statistical methods used in this report were not appropriate, and that the tumour incidence in this group is not in fact significant. A statistical re-evaluation by the Notifier identified a P-value of 0.14. However, it should be noted that the statistical evaluation comparing control and top-dose animals is complicated by the small population size for this kind of study and the absence of adenomas in all dose groups except for top dose females.	

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	Continued: Open point 2.2 The carcinogenic potential of fluopicolide to be discussed in an experts' meeting, in particular with regard to the possible mode of action involved and the need for classification See reporting table 2(6).		ii. There was no indication of progression from adenomas to carcinomas. iii. Non-neoplastic indications of hepatotoxicity (e.g. eosinophilic foci) were similar in both sexes indicating that if M-01 were carcinogenic, a similar tumour response might be expected in both sexes. A combined assessment of liver tumours for both sexes does not suggest a treatment-relationship for the increased number of adenomas in top dose females. Comparatively in males, hepatocellular carcinomas were observed at dose levels of ≤ 180 ppm but no carcinomas were observed at the 500 ppm in males, the dose responsible for the slight increase in adenomas in females, and only a single incidence of adenoma was observed in top dose males. iv. Changes routinely seen with compounds producing liver tumours were not reported in the study with BAM. Clinical chemistry parameters did not show any changes suggestive of liver toxicity. Organ weights of the liver also did not reveal any changes normally associated with a liver	

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	Continued: Open point 2.2 The carcinogenic potential of fluopicolide to be discussed in an experts' meeting, in particular with regard to the possible mode of action involved and the need for classification See reporting table 2(6).		carcinogen. To conclude, the RMS concludes that there was no evidence of substance related carcinogenicity and the weight of evidence as discussed above suggests that BAM is unlikely to pose a carcinogenic risk to humans and does not meet the EC criteria for classification for carcinogenicity. Open Point: to be discussed at Expert Meeting.	
	Open point 2.3 The amount of bioavailable fluopicolide after oral administration to be agreed on in an experts' meeting See reporting table 2(8).	BCS supports the value of 74% as given in the dossier. A detailed position paper (Fluopicolide: Evaluation of the oral bioavailability of fluopicolide in the rat, Fisher, P; 10-04-2007) is available and can be submitted upon request	The appropriate extent of oral absorption is to be agreed at an expert meeting. Detailed considerations submitted by the Notifier and explanations of the proposal by the RMS are provided in Addendum 1 (Nov 2007) and in the reporting table. The main route of elimination of radiolabel is in faeces. The critical point is the difference in biliary excretion levels between pyridyl and phenyl radiolabel and the biological reasons for such a difference. For the biliary studies, recovery of radiolabel was excellent, approximately 100% so justification for attempting to use another study in which biliary study is unknown is not necessary. "A	PRAPeR 39 (10– 13 12.2007): Open point fulfilled. Value of 62% for oral absorption was confirmed.

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			correction factor of 0.62 was allowed to account for the extent of oral absorption which is based on that determined for the pyridyl radiolabel in the biliary excretion study. The basis for using the lower oral absorption estimate (pyridyl radiolabel - 62% rather than phenyl radiolabel - 80% or an average of the two is because the mechanism or biological reasons for the difference is unclear and hence the more conservative estimate has been relied upon for the derivation of the AOEL." Open Point: to be discussed at Expert Meeting.	
	Open point 2.4 The need for setting an ARfD, and the most relevant study to be considered, to be discussed in an experts' meeting See reporting table 2(12).	BCS considers that the setting of an ARfD is not appropriate for fluopicolide. A position paper addressing this is available (Payraudeau, V. Report M-269338-01-1) and can be submitted upon request.	RMS: The RMS has proposed an ARfD of **0.18 mg/kg bw/day (**100-fold safety margin) based on the 28-day dietary study in rats 200 ppm (17.7 mg/kg bw/day) for systemic toxicity based on impaired growth and histopathological changes in the liver and kidney at 1400 ppm (106 mg/kg bw/day). See Addendum 1 (Nov 2007) for further details. Expert meeting to consider the non-relevance of an ARfD as suggested by the Notifier (see Appendix 5, Addendum 1 (Nov 2007)). Opinions are also provided by MS in the Reporting Table.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled. ARfD: 0.18 mg/kg bw

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			Open Point: to be discussed at Expert Meeting.	
2.1	Data requirement Applicant to provide a GLP revision of the acute dermal study (Krotlinger 2003) The applicant announced in the written procedure that the report M-220872-02-1 (Krotlinger 2003) is available and can be submitted immediately. See reporting table 2(16).	The amended report will be submitted with the updated dossier.	RMS: The GLP compliant revision of the acute dermal study report (Krotlinger 2003) has been provided and is acceptable. The dose applied to animals was 2000 mg/kg/bw. Addressed.	PRAPeR 39 (10– 13 12.2007): Data requirement fulfilled.
	Open point 2.5 RMS to provide further details on the results of the *in vivo* dermal absorption study (see comment by NL) in an addendum See reporting table 2(18).		RMS: Further details are presented in Addendum 1 (Nov 2007). See Section B.6.12. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled.
	Open point 2.6 Dermal absorption to be discussed in a meeting of experts See reporting table 2(19).		See Open Point 2.2 above. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled.

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	Open point 2.7 The experts to consider whether the default given by the UK POEM model for high-volume broadcast air-assisted sprayers (500 l/ha) is representative for the real scenarios. See reporting table 2(21).		RMS: It is the RMSs view that although the maximum proposed application volume for the use of EXP 11074B (the lowest spray concentration) is 1500 l/ha, the worst case for operator exposure when using the UK POEM for high-volume broadcast air-assisted sprayers is 500 l/ha (i.e. the highest spray concentration representing high-volume use). Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled.
	Open point 2.8 The experts to agree on the operator exposure assessment for fluopicolide. It is noted that the EUROPOEM is not yet validated for use in the regulatory risk assessment; the EUROPOEM group highlighted in the final report some drawbacks still to be clarified. See reporting table 2(22).		RMS: The approach taken in the DAR is to select appropriate data on grapevine spraying from the EUROPOEM database and to calculate 75th percentile surrogate exposure values based on these relevant data points. Because the model, as such, has not been used, some of the problems associated with it have been avoided. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled.

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2.2	New data requirement Applicant to provide information on the composition of the batch mixture tested in acute toxicity, genotoxicity and reproductive toxicity, and its comparability to the proposed specification See reporting table 2(24).	Information on the composition of the batch mixture tested in the tox studies was submitted with the updated dossier in 2005. The corresponding report (Cousin, J. Report M-232334-01-1) will be submitted again with the requested dossier update.	RMS: The information provided has been presented in Volume 4, Addendum 1 (Nov 2007) and is considered acceptable. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Data requirement fulfilled.
	New open point 2.9 Based on information provided in Annex C to the DAR, it seems that some of the impurities present in the tested tox batches will be increased in the proposed specification (pending also on data requirement 2.2). Experts to discuss in a meeting. See reporting table 2(24).	see BCS comment under data requirement 2.2	RMS: See also Data Requirement 2.2 above. The RMS considers there are adequate toxicology data on fluopicolide batches to support the proposed technical specification. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): see data requirement 2.2

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	Open point 2.10 RMS to present the complete assessment for the relevance of ground water metabolites in an addendum. Special attention should be paid to the fact that at this stage for metabolites M01, M05 and M10 the trigger of 0.75 µg/L is also exceeded either in the lysimeter or the FOCUS modelling. See reporting table 2(25).		RMS: Following the submission of new FOCUS groundwater modelling a completely revised Relevance of Metabolites in Groundwater assessment (following EU Guidance Document - Sanco/221/200-rev 10, 25 February 2003) has been presented for all those metabolites that exceed 0.1 µg/l (in either the original DAR or the addendum). See Section B.6.1.4.1, Addendum 1 (Nov 2007). This includes a refined risk assessment for those metabolites found to be above 0.75 µg/l (M-01, M-05, M-10 and M-11) in either consideration. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled. New data requirmentr identified, see 2.3
2.3	Data requirement identified at PRAPeR 39: Notifier to provide further information on M01 if deemed necessary.	**Comment BCS May 2008:** A new position paper (Leake et al, 2008, report no. M-300114-01-1), title "The non-relevance of the fluopicolide metabolite M01 (AE C653711): 2,6-dichlorobenzamide (also known as BAM)" was submitted to the RMS and several MSs. This position paper takes into account a) data already submitted with the fluopicolide dossier b) tox data on BAM submitted in the US for dichlobenil which were not	RMS (December 2008): The Notifier has provided the critical additional studies reported in the US EPA assessment of BAM for dichlobenil but were not available at PRAPeR 39 (10–13 12.2007). The Rapporteur has evaluated the studies and the reports are presented in the Addendum 2 (dated December 2008). These data include further information on longer term toxicity in dogs, reproductive toxicity in rats, and	PRAPeR 39 (10– 13 12.2007): Data requirement open. PRAPeR 64 (19 -23 01.2009): Data requirement obsolete. M-01 is not relevant according to the guidance document on groundwater metabolites, however a consumer risk assessment is needed as its concentration in groundwater can exceed 0.75 µg/L and an ADI of 0.05 mg/kg bw/day is set for this

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	Continued: Data requirment identified at PRAPeR 39: Notifier to provide further information on M01 if deemed necessary.	submitted in Europe for neither fluopicolide nor dichlobenil but were included into the negative reference list of the dichlobenil dossier. The position paper can be made available upon request The following conclusions can be drawn from the available data: **Pesticidal /biological assessment** – M01 has been shown to have no fungicidal or herbicidal activity. **Toxicological assessment** - M01 has been shown: - not to be genotoxic in an Ames, HPRT and UDS tests *in-vitro*, and in micronucleus test *in-vivo*. - that the majority is excreted via urine, both unchanged and following biotransformation, small quantities were excreted via the faeces and very low quantities were retained, showing that it is not subject to bioaccumulation. - to have a LD_{50} is in the range between 500 and 2330 mg/kg and therefore not toxic (T) or very toxic (T+).	developmental toxicity in rabbits. No significant toxicity was identified in these studies which now widen the capacity for the risk assessment of BAM. The Rapporteur considers these data are adequate for the risk assessment of BAM. The Notifier has provided a case for the non-relevance of BAM as a metabolite of Fluopicolide. In accordance with the guidance document for the assessment of groundwater metabolites (EU Guidance Document - SANCO/221/200-rev 10, 25 February 2003), the Rapporteur agrees with the conclusion that BAM is not a relevant metabolite. The detailed assessment of the relevance/non-relevance is provided in the Addendum 2 (dated December 2008). Addressed. RMS (February 2009): The RMS has presented a consumer risk assessment in Addendum 3 (dated February 2009). The risk assessment indicates exposures of less than 4% chronic exposure and less than 2% acute exposure for M-01 (BAM). For, M-05, M-10 and M-11 the chronic and acute exposures are less than 1%.	metabolite.

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	Continued: Data requirement identified at PRAPeR 39: Notifier to provide further information on M01 if deemed necessary.	- not to be carcinogenic - not to be a reproductive toxicant therefore to be non-toxicologically relevant **Total Dietary Risk Assessment** considering all sources of the diet: It has been shown that when all sources of the diet are included; primary crops, rotational crops and water, M01 will contribute, **as a worst-case,** no more than 6% of the acceptable daily intake in total. The worst case contribution from water is only 5% of the ADI. **Ecotoxicological assessment** – M01 (AE C653711) has been shown not to be toxic to any of the tested aquatic organisms. Therefore it can be considered as not ecotoxicologically relevant in aquatic systems. **M01 (AE C653711) has been shown clearly and comprehensively to be non-relevant.**		

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	Open point 2.11 Some metabolites are found in rotational crops. Their toxicity should be discussed compared to the toxicological properties of the parent. See reporting table 2(26).	BCS refers to the corresponding comment made on the reporting tables ((3(10) and 3(33))	RMS: Further information on the toxicity is presented in Addendum 1 (Nov 2007). See Section B.8.6.1. In conclusion the RMS is of the opinion that all metabolites not of toxicological relevance. Open Point: to be discussed at Expert Meeting.	PRAPeR 39 (10– 13 12.2007): Open point fulfilled.
	Message from section 1 to section 2: Please confirm the relevance of 2,6-dichlorobenzamide (BAM or M01) and confirm the maximum level			Answer from section 2 to section 1: BAM is not relevant as impurity in the technical specification of fluopicolide.
	Message from section 5 to section 2: Please confirm the new ADI for M-01 (0.045 mg/kg bw/day?) Can we still use the ARfD set for fluopicolide also for M-01?			Answer from section 2 to section 5: The ADI for BAM (M-01) is 0.05 mg/kg bw/day and the ARfD for BAM is 0.3 mg/kg bw.
	Data requirement: Toxicological information on the metabolite M15 to assess its relevance as groundwater metabolite			Data requirement identified by EFSA during the drafting of the conclusion: Data requirement identified

3. Residues

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	Section 3 Data requirements: **-** Open points: ***6***			Section 3 Data requirements: **-** Open points: ***3***
	Open point 3.1 Residue definition for risk assessment in rotational crops to be discussed in an expert meeting See reporting table 3(10).	see comment on open point 2(11)	RMS: As previously stated, in section B.7.3 (definition of Residue), M-01 has been included in the residues definition for risk assessment, due to it having similar mammalian toxicity to parent fluopicolide. However, the residue definition for monitoring is *parent fluopicolide only* because M-01 is not unique to fluopicolide. In addition, as stated the M01 is present at significant levels in lettuce and radish in the rotational crop metabolism studies, accounting for more than 40% of the TRR. However, in the cold study Section B.7.10, M01 only gives positive residues in a few cases at maturity, with the highest being 0.04 mg/kg in cabbage. Therefore for the above reasons, M01 should not be included in the residues definition for monitoring. Addressed	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled. The residue definition for enforcement is set as the parent compound only. For risk assessment the residue definition is set as the sum of the parent compound and its metabolite M01. For the supported uses no conversion factors are set.

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	Open point 3.2 MS to consider whether rotational crop studies are sufficient for drawing final conclusions and whether restrictions are needed in an expert meeting. See reporting table 3(23).	BCS refers to the corresponding comment made on the reporting tables ((3.(23))	RMS: Rotational crop studies carried out in the UK, Germany and France, indicated 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 remains as parent, EU MRLs will not need to be set for rotational crops (EU MRLs are not currently set on straw). For risk assessment purposes, residues in crops of parent fluopicolide plus its metabolite M-01 were below the limit of determination (0.01 mg/kg), with the exception of cabbage (0.04 mg/kg) and wheat straw (0.15 mg/kg). The crops looked at in the above study gave a fair representation of the crops that would normally be rotated with potatoes, with studies being carried out on cereals (wheat spring and winter), pulse crop (field beans) and a leafy crop (cabbage). To conclude, a sufficient variety of crops have been looked at with sufficient residues data (8 trials on each rotational crop) to conclude that	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled.

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			residues in rotational crops will not be significant and restrictions are not needed. Open Point: to be discussed at Expert Meeting.	
	Open point 3.3 MRL proposal on grapes to be discussed in an expert meeting (validity of the trials with 4 applications, considering the persistency of the compound) RMS to provide the meeting with statistical analysis of the results. See reporting table 3(28).	A statistical evaluation of the residue data is available (Kaethner, M; Report no. M-234980-01-1) and can be submitted upon request	RMS: With regards to the validity of the five trials with 4 applications instead of 3, residues in these trials gave the highest and second and forth highest 0.96, 0.83 and 0.56 mg/kg, however the third, fifth, sixth, seventh highest were from trials with 3 applications 0.66, 0.52, 0.5 and 0.48 mg/kg. Therefore, although the trials with 4 applications give the highest residues, there is no significant difference in the residue levels and in any case the critical use on grapes was the southern member state use, with residues in grapes up to 1.2 mg/kg (3 applications applied in all cases). Based on the southern member state use an EU MRL of 2 mg/kg was proposed (R_{ber} = 1.34 and R_{max} = 1.22). Open Point: to be discussed at Expert Meeting.	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled.

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	Open point 3.4 MS to discuss the approach for risk assessment depending on final decision on residue definition for risk assessment in rotational crops See reporting table 3(33).	see comment on open point 2(11)	RMS: As previously stated, the risk assessment includes rotational crops, based on residues of parent fluopicolide plus M01 (similar toxicity to parent; M02 not considered relevant). Addressed	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled.
	Open point 3.5 RMS to check if balance data allow %ages of transference to be calculated See reporting table 3(39).	The % transference values should be 27% for wine, 45% for must and 100% for raisins.	RMS: Figures have been submitted by the notifier, reason for questioning them last time was due to the confusion over transfer factor and the calculation of % transference. Addressed	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled.
	Open point 3.6 RMS to present the complete assessment for the relevance of ground water metabolites in and addendum. Special attention should be paid to the fact that at this stage for metabolites M01, M05 and M10 the trigger of 0.75 μg/L is also exceeded either in the lysimeter or the FOCUS modelling. See reporting table 3(40).		RMS: A revised Relevance of Metabolites in Groundwater assessment (following EU Guidance Document - Sanco/221/200-rev 10, 25 February 2003) has been presented for all those metabolites that exceed 0.1 µg/l (in either the original DAR or the addendum). See Section B.6.1.4.1, Addendum 1 (Nov 2007). This includes a refined risk assessment for those metabolites found to be above 0.75 µg/l (M-01, M-05, M-10 and M-11) in either consideration. Open Point: to be discussed at Expert Meeting.	PRAPeR 40 (12 – 13 December 2007): Open point fulfilled.

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	New open point 3.7: RMS to amend the list of end points according to the discussions during the PRAPeR 40 meeting.		RMS (December 2008): Endpoint updated – Potato and other crops risk assessment change from 0.01 to 0.02 mg/kg and revised %ADI and ARfD updated in endpoints table No conversion factor required for MO1 for grapes and potatoes (insignificant levels present in the crops) may be required for other crops. Addressed. RMS (February 2009): The LOEPs have been amended as appropriate.	PRAPeR 40 (12 – 13 December 2007): Open point open. PRAPeR 65 (19 -23 01.2009): Open point closed.
	New Open point 3.8: RMS to amend the list of end points according to the discussions during the PRAPeR 65 meeting.		RMS (February 2009): The LOEPs have been amended as appropriate.	PRAPeR 65 (19 -23 01.2009): Open point open. Written procedures: In the meeting report the RMS was asked to amended following issues in the LoEPs according to the conclusions of the meeting: -DOR for RA in plant commodities, livestock dietary burden calculation, consumer risk assessment including drinking water risk assessment. The changes were only carried out partially. RMS to carry out changes

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				according to the comments made by EFSA in the darft conclusion and the revised LoEP. After written procedure: In their comments to the draft conclusion the RMS explained that the requested changes were regarded as not necessary. Open point closed.
	New Open point 3.9: for NL (RMS for Dichlobenil): NL to look to the general discussion within the EU review process just for clarification and to be consistent with the decisions drawn with dichlobenyl with regard to the toxicological reference values for M-01.		The following information was sent by NL to EFSA on 06/02/2009: *DAR dichlobenil* ADI Dichlobenil = 0.005 mg/kg bw/d ARfD: not necessary ADI BAM = 0.022 mg/kg bw/d ARfD BAM = 0.14 mg/kg bw *DAR fluopicolide* ADI fluopicolide = 0.08 mg/kg bw/d ARfD fluopicolide = 0.18 mg/kg bw At that time, For BAM it was concluded that it was covered by the same reference values. *Addendum fluopicolide and PRAPER meeting 64: separate reference values*	PRAPeR 65 (19 -23 01.2009): Open point open. Written procedure: Open point fulfilled. Requested information was sent by NL to EFSA on 06/02/2009.

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			for BAM ADI fluopicolide = 0.08 mg/kg bw/d (unchanged compared to DAR) ARfD fluopicolide = 0.18 mg/kg bw (unchanged compared to DAR) ADI BAM = 0.05 mg/kg bw/d ARfD BAM = 0.3 mg/kg bw/d It is emphasized that the *new dossier for BAM*, as summarised in the addendum for fluopicolide, is open/applicable to both dichlobenil (Chemtura) and fluopicolide (Bayer).	

4. Environmental fate and behaviour

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	Section 4 Data requirements: ***4*** Open points: ***20***			Section 4 Data requirements: ***1*** Open points: ***0***
	Open point 4.1 Half lives for metabolites derived in the studies where they are dosed as starting material are seen by the RMS as more reliable, specially with respect to M14 (see DAR p 661). Therefore, only these DT50 should be reported in the list of end points. RMS to amend the list of end points accordingly. MS experts to discuss if the half lives derived from the study dosed with M02 may however still be used for modelling. See reporting table 4(6).	As a general principle, BCS considers valid half lives can be derived for metabolites from studies dosed with parent or precursor metabolites.	RMS: Agree with Applicant. RMS understands that point regarding M02 study is in relation to the fact that end points are also available from studies where metabolites formed from M02 have been dosed as starting substances. Endpoints have been amended as appropriate to distinguish between half-lives from studies where metabolite was applied as starting substance and studies where M-02 was applied as starting substance. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.2 RMS to clarify normalized laboratory DT50's values for fluopicolide and metabolites. I.e for fluopicolide in LoEP the range is 194 – 333 d when for		RMS: Please see RMS Addendum 1 (Nov 2007), and updated LoEP. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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	example in Allan 2003 c study degradation in one soil results in a normalized DT_{50} = 373 d (or for another example 664 d for Lamberton soil in Allan 2003e). Please do it in an addendum or in an updated list of end points following the updated template where the origin of the different end points and normalization procedures may be easily tracked. See reporting table 4(10).			
	Open point 4.3 MSs to discuss the effect of the applied high concentration on the soil degradation study with metabolite M01 and the adequate DT50 for PECsoil and PECsw and PEC GW calculations. See reporting table 4(12).	The study with M01 was conducted at a nominal rate of 1.2 kg/ha which is equivalent to 1.6 kg/ha for Bethany Soil and 1 kg/ha for North Dakota soil. For fluopicolide the max. rate of M01 equivalent is ca 200 g/ha, thus the M01 study was dosed by a factor of 5-8 times higher. Modelling shows good fit to the data for SFO up to 120 days so provides for justification for degradation independent of concentration.	RMS: RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
4.1	Data requirement Notifier to provide an estimation of soil photolysis half lives at other latitudes (i.e 40 ºN and 45 ºN).	A report (Kley, C; Mackenzie, E; Report no. MEF-06/495; M-286182-01-1) is available which addresses the relevance of photolysis in soil degradation studies and contains in the	RMS: Soil photolysis has been calculated at a range of latitudes (36.80ºN - 56.26ºN) and is reported in RMS Addendum 1 (Nov 2007) and updated LoEP.	PRAPeR 37 (03. – 06.12.2007): Data requirement still open.

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	Applicant indicated to submit a position paper (Report MEF-06/495) by April 2007. See reporting table 4(14).	appendix a calculation of soil photolysis half lives at other latitudes. The report will be submitted with the updated dossier. **Comment BCS September 2008:** A paper has been prepared in which DT50 photolysis values for latitudes in Europe have been calculated (Hellpointner, E & Stupp, H-P; MEF-08/185, DART No. M-300764-02-1). This paper addresses the light intensity measured during studies on phototransformation of Fluopicolide on soil and the transfer of experimental to environmental phototransformation half-lives.	RMS concludes that soil photolysis at 40ºN and 45ºN is unlikely to significantly influence the degradation of fluopicolide in soil. Addressed. RMS December 2008: A new series of calculations have been submitted by the Applicant, and these are evaluated in Addendum 2 to the DAR (December 2008). RMS (February 2009): This issue has been drawn to the attention of the applicant and is still under discussion. However, reference to the record of the PRAPeR 37 meeting indicates that the meeting agreed that the soil photolysis issue would not affect the acceptance of the field dissipation studies for modelling endpoints (See OP4.9 of the discussion table where it is stated: "The experts are of the opinion that the results of the field studies can be used to derive DT50 for FOCUS exposure modelling"). Thus the issue of soil photolysis only relates simply to possible derivation of MS specific values for terrestrial risk assessment, and does not affect FOCUS groundwater or FOCUS surface water calculations. Therefore this issue could	Calculation of $DT50_{photolysis}$ for adequate latitudes in Europe. PRAPeR 62 (13 -17 10.2008): Data requirement amended. Applicant to clarify that the information the from CIE publication No. 20, 1972 is for ground level and how the angle of incidence of the radiation was accounted for (graphical spectrum used and its integration for the ranges proposed would help to visualize and complete this data). Applicant to provide a full transparent assessment of the contract laboratory's comparison of the light energy to Scotland conditions to include confirmation of the apparatus used in measurements and an update of the GLP report of the contract laboratory that clearly indicates any updating of the calculation approach justifying if changed why it is more appropriate than what was originally done. If no amendment to the original contract laboratory report is necessary applicant to update their estimate of photolytic half life at 40°N and 45°N consequently on basis of the results of the original GLP report. Written procedure:

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			potentially be addressed at MS level.	Data requirement maintained.
	Open point 4.4 MS experts to discuss the formation fractions derived from laboratory studies for modelling purposes. This discussion should also include the effect of temperature and moisture normalization procedures. See reporting table 4(17).		RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.5 MS experts to discuss potential influence of the different extraction method employed on the respective results of the laboratory and field studies. Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion. See reporting table 4(26).		RMS: As a reminder to MS experts, lab studies used 3-4 extractions at ambient temperature with acetonitrile/water followed by an acetonitrile Soxhlet extraction. Field studies used 2 extractions of acetonitrile/water/formic acid under ambient conditions. RMS notes the Applicant's statement, however, the RMS has further investigated extraction in the lab studies. The RMS has noted from representative chromatograms that in the Allen, 2003c study, Soxhlet extractions at 369 DAT accounted for 14.2 – 23.3% AR, with fluopicolide accounting for 9.7 – 17.6% AR in the Soxhlet extracts.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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			In the Allen, 2003b study, at 98 DAT Soxhlet extractions accounted for a further 5.4 – 6.1% AR as fluopicolide. Information relating to the amount of fluopicolide extracted with each successive ambient extraction in lab studies is not available. RMS considers that in light of this information, there is still some uncertainty over the suitability of the extraction methods for the field dissipation studies and that this should discussed by MS experts with a view to obtaining an appropriate resolution. Open Point: to be discussed at Expert Meeting.	
	Open point 4.6 RMS to clarify if half life values from field studies have been used for M01 in FOCUS exposure modelling as it is suggested in the list of end points. In case RMS confirms that these values should not be used in modelling then the LoEP needs to be amended. See reporting table 4(29).		RMS: RMS clarifies that the half life value for M01 used in FOCUSsw and FOCUSgw modelling was a normalised value derived from field dissipation studies. Whilst it has been observed that M01 leaches, the normalisation procedure attempted to take into account potential leaching of M01 below sampled horizons by adding amounts to a depth of up to 2m. Please see DAR Volume 3, section B.8.1.5.1 for further details. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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	Open point 4.7 MS experts to discuss the conceptual model used to derive the kinetic parameters used for modelling. In particular paying attention to: – the absence of a flow from the parent to the sink compartment and – the effect of normalization of degradation constants without the corresponding normalization of the formation constants. Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion. See reporting table 4(34).		RMS: RMS agrees with Applicant comment to this point. RMS believes that formation constants have been normalised by the process. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.8 MS experts to discuss in an experts meeting the kinetic evaluation of field dissipation studies. See reporting table 4(36).	BCS will prepare a position paper summarising and describing the kinetic evaluation of field dissipation studies, including documentation supplied to the rapporteur on the approach used by BCS to initial concentrations in modelling field data. This will be available in May 2007 and can be	RMS: Due to a combination of circumstances, the Notifier's position paper was not provided until Nov 2007. RMS will provide the subsequent evaluation before the PRAPeR 37 Expert meeting for on distribution on CIRCA prior to the meeting. However, MS should note that even if this is not	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled. New open point proposed, see open point 4.21

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		submitted upon request.	possible, a discussion of this open point is still possible. Open Point: to be discussed at Expert Meeting.	
	New open point 4.21: RMS to include in the LoEP the values from HS fitting presented in the addendum.		RMS December 2008: The LOEP have been amended as requested.	PRAPeR 37 (03. – 06.12.2007): Open point open. PRAPeR 62 (13 -17 10.2008): Open point fulfilled.
4.2	Data requirement Applicant to present the position paper with their evaluation of the accumulation studies. Applicant indicated to submit a position paper assessing the field accumulation studies (Kley, C; Mackenzie, E.; Report no. M-267721-01-1) by April 2007. See reporting table 4(41).	The position paper assessing the field accumulation studies of fluopicolide (Kley, C; Mackenzie, E.; Report no. M-267721-01-1) is available and will be submitted with the updated dossier	RMS: Applicant's position paper assessing the field accumulation studies has been submitted and is reported in RMS Addendum 1 (Nov 2007) and updated LoEP. RMS proposes that further expert discussion is needed over the general acceptability of this higher tier approach and over how best to use the results in deriving an overall conclusion. $PEC_{soil, accum}$ may need to be reassessed following this discussion. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Data requirement fulfilled.

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	Open point 4.9 MS experts to discuss the potential influence of photolysis on the results of the field studies and the use of field dissipation half lives for modelling environmental fate and behaviour (FOCUS SW and FOCUS GW). See reporting table 4(42).	See comment on data requirement 4.1	RMS: Further data (Kley, C; Mackenzie, E; Report no. MEF-06/495; M-286182-01-1) have been submitted on photolysis (see also data requirement 4.1). These data are reported in RMS Addendum 1 (Nov 2007) and updated LoEP. To assess the influence of photo-degradation in overall degradation of fluopicolide in soil under field conditions, the Applicant ran simulations in FOCUS PEARL both with and without taking into account photo-degradation in a 2mm soil surface layer. Depth profiles were presented for individual time points at FOCUS scenarios. There were no significant differences with or without additional photodegradation. RMS concluded that photolysis in soil did not appear to contribute significantly to the dissipation behaviour of fluopicolide in the field. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.10 MS experts to discuss whether the lysimeter study represents a worst case with respect to the formation of metabolites.		RMS: The RMS has re-checked the DAR for this point. EFSA's original comment stated that the relative rate of parent degradation in the Munster soil was not known. However, the DT50 of fluopicolide in the laboratory at 20˚C	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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	See reporting table 4(54).		and pF2 in the Munster soil was calculated by the RMS to be 249 days (please see DAR Volume 3, section B.8.1.1(c), Keirs, 2003a for details). This value is the third shortest value out of a range of six values ranging from 196 – 664 days. Thus, given parent degradation in this soil is relatively fast within the context of the fluopicolide database, formation of fluopicolide metabolites may be relatively high. Open Point: to be discussed at Expert Meeting.	
	Open point 4.11 RMS to update GAP table with 5d minimum application interval for potatoes. See reporting table 4(59).		RMS: The GAP table in the LOEPs has been amended. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.12 MS experts to discuss if the use of the 90th percentile is appropriate for PEC soil calculations. See reporting table 4(60).		RMS: RMS notes that this is a general point rather than being substance specific and refers to ongoing discussions between MS led by DE colleagues. The use of 90th percentile DT50 values in PECsoil calculations is one of the subjects discussed in the DE paper. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled. New open point proposed, see open point 4.22:

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	New open point 4.22: RMS to include the non normalised SFO DT50 values for parent used for their calculation of the accumulated PECsoil in the/a table in the LoEP.		RMS December 2008: The LOEPs have been amended as requested. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point open. PRAPeR 62 (13 -17 10.2008): Open point fulfilled.
	Open point 4.13 MS experts to discuss if FOCUS GW scenarios with normalized DT_{50} 's are appropriate for PEC soil calculation. See reporting table 4(61).		RMS: RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.14 MS to discuss whether the M01 half lives may be considered appropriate degradation half lives for modelling PEC soil. See reporting table 4(62).		RMS: RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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	Open point 4.15 MS experts to discuss which maximum amount formed of M01 should be considered for PEC soil calculations. 40.2 % comes form laboratory studies. It is doubtful that field studies are capable to identify the maximum formation of a metabolite. See reporting table 4(65).	**Comment BCS May 2008:** See comment on new open point 4.23.	RMS: RMS would like to make a comment on the EFSA statement, *'It is doubtful that field studies are capable to identify the maximum formation of a metabolite'*. In making this statement, EFSA are potentially ruling out the use of field studies as a way of better understanding the behaviour of metabolites under field conditions. Behaviour of parent substances is often very different from that observed under laboratory conditions, and it is often difficult to elucidate the reasons for this. Therefore it is logical that behaviour of metabolites in the field, both in terms of formation and decline, could be different to that seen in the lab. Provided that analytical techniques and sampling schedules are appropriate, field studies should be as sufficiently reliable to obtain information on maximum formation as lab studies. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled. New open point proposed, see open point 4.23.
	New open point 4.23: RMS to either recalculate the PEC soil for M01 and M02 or include a note what is the agreed value for formation percentage of M01and M02 in	**Comment BCS May 2008:** BCS agrees with the proposed maximum formation values for M01 and M02 in the field and have used these values in PECsoil calculations for new country submissions. Maximum formation values of the	RMS December 2008: The LOEPs have been amended as appropriate to reflect the discussions at the Expert Meeting in December 2007. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point open. PRAPeR 62 (13 -17 10.2008):

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	field.	metabolites M01 and M02 in field studies were detected at the Senas site. The maximum values were 11.9% on a mass basis for M01 and 9.6% for M02. These values are equivalent to 24.1% of the initial parent concentration for M01 and 16.4% for M02 (calculated in parent equivalents for the year 1999, excluding values from the second year).		Open point fulfilled.
	Open point 4.16 MS experts to discuss the different approaches taken for the PEC soil calculation. See reporting table 4(69).		RMS: RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point closed.
4.3	Data requirement Applicant to provide results with a second FOCUS model following the recommendations given in the PPR Opinion: **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.** For some of the metabolites it may not be confirmed that the	The reports are available (Kley, C; Ellrich, C; MEF-07/165 and Kley, C; Ellrich, C; MEF-07/166) and will be submitted with the updated dossier. Report MEF-07/165 refers to point 4 (81) in the reporting tables which was mentioned as a data requirement but is not explicitly mentioned in the evaluation table. **Comment BCS May 2008:** Two additional reports have been prepared (Kley, C & Ellrich, C; MEF-08/154, DART No. M-299223-01-1 and Kley, C & Ellrich, C; MEF-08/155, DART No. M-299231-01-1). New PECGW calculations with PEARL and PELMO modelling for vines assuming	RMS: The reports (Kley, C; Ellrich, C; MEF-07/165 and Kley, C; Ellrich, C; MEF-07/166) have been assessed in RMS Addendum 1 (Nov 2007) and updated LoEPs. New PEC_{GW} calculations have been submitted with a second FOCUS model (PEARL) and lower interception rate for vines (PEARL and PELMO). New PEC_{GW} calculations from PEARL and PELMO modelling have also been submitted for potatoes, assuming 3 application regimes (treatment every year, every 2 years and every 3 years).	PRAPeR 37 (03. – 06.12.2007): Data requirement maintained. The applicant is requested to submit a first Tier standard FOCUS PEARL modelling. However the data requirement may be re-classified as point of clarification by the applicant since the information required is limited to standard modelling recalculation using agreed input parameters. Alternatively the calculation may be provided directly by the RMS. PRAPeR 62 (13 -17 10.2008):

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	triggers of 0.75 µg/L and 10 µg/L are not exceeded in some scenarios. A second model is necessary to reduce the uncertainty and confirm the non relevance of the metabolites. Applicant indicated to submit new PEC GW calculations with a second model and lower interception rate for vines by May 2007. See reporting table 4(79).	application each year and for potatoes assuming application each year, every 2 years and every 3 years. The PEARL modelling has been conducted with and without kinetic sorption (as a lower tier assessment). The outcome of these modelling assessments is essentially the same as previous assessments. All metabolites remain within the current trigger values.	The PEARL modelling takes into account kinetic sorption parameters. Detailed calculation of the degradation rate for use with this kinetic sorption model is reported in Kley, C. 2004 (MEF-04/346) and Kley, C. 2004 (MEF-04/347). These studies were also summarised in the RMS Addendum 1 and appended for information. Based on the new PEC_{GW}, the following metabolites are predicted to exceed 0.1 µg/l in groundwater: M-01, M-03 (acidic soils), M-05, M-10, M-11, M-12 and M-13. M-02 and M-14 were predicted at concentrations less than 0.1 µg/l. For both the models, PEC_{GW} of M-01 following use on vines were between >0.75 µg/l and <10 µg/l. PEC_{GW} of the other metabolites simulated were all <0.75 µg/l. For both models, following use on potatoes, PEC_{GW} for all the metabolites simulated were <0.75 µg/l, apart from M-01 which was >0.75 µg/l and <10 µg/l at every scenario/ application regime, except Sevilla (PELMO, application every 1, 2 and 3 years which were <0.75 µg/l). M-11 was	Data requirement fulfilled.

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			>0.75 µg/l and <10 µg/l at Jokioinen (PELMO, application every year). The RMS welcomes MS expert consideration on whether the kinetic sorption model followed is an appropriate interpretation of how the PEARL model simulates non-equilibrium sorption and therefore whether it can be concluded to be a valid approach for use in PEARL.. Open Point: to be discussed at Expert Meeting. RMS December 2008: The Applicant has submitted additional GW calculations using PEARL but excluding aged adsorption considerations. This is described in Addendum 2 to the DAR, dated December 2008. The RMS considers that the calculations are acceptable. Addressed.	
4.4	Data requirement Applicant to repeat the FOCUS GW calculations following the GAP as reported in the Representative uses table.	See comment under data requirement 4.3 above.	RMS: Please see comment under data requirement 4.3 above. Open Point: to be discussed at Expert Meeting. RMS December 2008: Please see	PRAPeR 37 (03. – 06.12.2007): Data requirement fulfilled for PELMO. For PEARL: see data requirement 4.3.

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	Applicant indicated to submit repeated PEC GW calculations with a lower interception rate for vines by May 2007. See reporting table 4(80).		above for Data Requirement 4.3.	
	Open point 4.17 MS experts to discuss the approach taken by the RMS to calculate the amount of M02 formed in field See reporting table 4(84).		RMS: RMS has no further comment to make in relation to this open point. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point closed.
	Open point 4.18 RMS to indicate in the LoEP box “relevant metabolites” in soil the max. amount of M02 (with respect to applied fluopicolide) found in field studies (at this stage this value is 21.3 %). See reporting table 4(84).		RMS: RMS proposes that this open point be dealt with after discussion proposed at open point 4.17. Open Point: to be discussed at Expert Meeting. RMS December 2008: The LOEPs have been amended as appropriate. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point still open. PRAPeR 62 (13 -17 10.2008): Open point fulfilled.

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	Open point 4.19 RMS to clarify in the LoEP which DT_{50} field values are actually used in modelling (e.g. values not all values for M01 are to be used). See reporting table 4(88).		RMS: LoEP has been amended in relation to input parameters used in modelling. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.20 RMS to present the complete assessment for the relevance of ground water metabolites in and addendum. Special attention should be paid to the fact that at this stage for metabolites M01, M05 and M10 the trigger of 0.75 µg/L is also exceeded either in the lysimeter or the FOCUS modelling. See reporting table 4(92).		RMS: Following the submission of new FOCUS groundwater modelling a completely revised Relevance of Metabolites in Groundwater assessment (following EU Guidance Document - Sanco/221/200-rev 10, 25 February 2003) has been presented for all those metabolites that exceed 0.1 µg/l (in either the original DAR or the addendum). See Section B.6.1.4.1, Addendum 1 (Nov 2007). This includes a refined risk assessment for those metabolites found to be above 0.75 µg/l (M-01, M-05, M-10 and M-11) in either consideration. Open Point: to be discussed at Expert Meeting.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.

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	New open point 4.24: RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting.		RMS December 2008: The LOEPs have now been amended as appropriate. Addressed.	PRAPeR 37 (03. – 06.12.2007): Open point open. PRAPeR 62 (13 -17 10.2008): Open point fulfilled.

5. Ecotoxicology

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	Section 5 Data requirements: **-** Open points: ***12***			Section 5 Data requirements: **-** Open points: ***4***
	Open point 5.1 RMS to clarify in an addendum how the MAF for different vegetation was calculated and used in the assessment of risk to birds. Note: This open point was set after a comment on the reporting table during the written procedure. See reporting table 5(9).		RMS: See Addendum 1 (Nov 2007). MAF 1.8 (as specified in SANCO 4145/2000) now used (Table B.9.1) in bird & mammal risk assessment for EXP 11120A use on potato. Low risk indicated. Point addressed.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.2 RMS to include the corrected calculations and the refined RA in an addendum. List of endpoints has been amended. No discussion in expert meeting required unless required by MS. See reporting table 5(15).		RMS: See Addendum 1 (Nov 2007) Revised refined dietary risk taken account of canopy interception to herbivorous mammals following EXP 11074B use on vine presented (Table B.9.1.3). Low risk indicated. Point addressed.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled. Two new open point proposed, see open point 5.13 and 5.14

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	New open point 5.13: RMS to include a note in the LoEP for the long-term risk assessment for herbivours mammals with the explanations, that the current risk assessment of mammals covers only one out of three applications in vineyards during early growth stages (up to BBCH 57).		RMS (December 2008): See revised LOEPs. Revised long term TERs for the risk to herbivorous mammals from consuming contaminated sub canopy ground vegetation in vines were calculated assuming 60-80% canopy interception. Fluopicolide is applied to vine between growth stages BBCH 53-81. For applications BBCH>57 (full canopy developed) with >70% interception, the TERs indicate low risk. However, for earlier applications (GS53-57) the TERs indicate that if the canopy is less than fully developed (60% interception is assumed), then reduction in the number of applications and/or increased spray interval may need to be considered. RMS (February 2009): Refined risk in Addendum 3 and LOEPs amended accordingly. Open point fulfilled.	PRAPeR 38 (03 – 07 12.2007): Open point open. PRAPeR 63 (12. – 16.01.2009) Open point open. RMS to update the list of end points according to the current standard format.
	New open point 5.14: RMS to revise LoEP with correct short-term bird endpoint.		RMS (December 2008): See revised LOEPs. The short term avian (*C.virginianus*) LDD50 was amended to >1744 mg a.s./kg bw /d. (+ one minor amendment to a TER). No effect on risk assessment.	PRAPeR 38 (03 – 07 12.2007): Open point open. PRAPeR 63 (12. – 16.01.2009) Open point fulfilled.

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			Open point fulfilled.	
	Open point 5.3 RMS to include the information on Log Pow values for the metabolites in an addendum (only data for M02 and M03 are available in Vol.B.2.1 of the DAR. No discussion in an experts meeting is required. See reporting table 5(21).		RMS: See Addendum1 Further consideration and discussion with respect to log Pow and low bioconcentration potential of fluopicolide metabolites presented (B.9.2). Point addressed.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.4 RMS to include the correction in a corrigendum and to update the list of endpoint. Since trigger values are different for algae and fish/invertebrates we would prefer to have TER values also for fish and invertebrates in the list of endpoints even if algae was the most sensitive organism group. See reporting table 5(25).		RMS: See Addendum1 A corrected aquatic spray drift risk assessment presented for EXP 11120A for vine use (Table B.9.2.1). Low risk indicated with 5m buffer zone. (LOEPs also corrected). Point addressed.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.5 RMS to include the information and argumentation regarding the ecotoxicological relevance of		RMS: See Addendum1 Aquatic risk of groundwater metabolites presented (Tables 9.2.2 and 9.2.3). Low aquatic risk indicated. Ecotoxicological relevance of GW	PRAPeR 38 (03 – 07 12.2007): Open point still open.

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	GW metabolites presented in column 3 in an addendum for the sake of completeness. We agree that since the TER for M05 is >18519 (vine) and >58824 (potato) for algae and this metabolite is the one of highest concentration in the $FOCUS_{gw}$ modelling, apart from M01, the risk from M10, M11, M12 and M13 to aquatic organisms can be considered to be low. The information presented is however of value for the assessment of "pesticidal activity". No discussion in an experts meeting is required. See reporting table 5(27).		metabolites discussed. GW metabolites considered ecotoxicologically not relevant Point addressed. (also addresses Open pt. 5.12) RMS (December 2008): The RMS has reassessed the aquatic risk posed by groundwater metabolites formed >0.1ug/L using revised PECgw values (see Addendum 2, 2008) and included a table in the LOEPs. No risk to aquatic organisms is indicated. Other conclusions with respect to biological activity of the metabolites and the overall absence of relevance of fluopicolide GW metabolites from an ecotoxicological perspective remain as presented in Addendum 1, 2007. RMS (February 2009): Revised fluopicolide GW metabolite aquatic risk assessment in Addendum3. LOEPs amended accordingly. Open point fulfilled.	PRAPeR 63 (12. – 16.01.2009) Open point open. RMS to update the LoE according to the standard format and to include the revised risk assessment for the aquatic relevant metabolites in an addendum.
	Open point 5.6 RMS to correct the list of endpoint with exact %-age effect on fecundity instead of		RMS: See Addendum1 NTA effects listed in more detail in Table B.9.5.1. All in-field and off-field HQs indicate low risk to NTAs from	PRAPeR 38 (03 – 07 12.2007): Open point still open: RMS to revise LoEP

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	<50%. Note that highest conc. with effects <50% for *A. rhopalosiphi* was 2 L/ha See reporting table 5(38).		proposed uses. Point addressed. RMS (December 2008): The LOEPs has been revised to include actual dose-related % repro effects in extended laboratory studies for EXP11120A, where a safe use at 2.0L is indicated. Though it should be noted that since all HQ values with Tier 1 indictor NTA spp. are <2 indicating acceptable risk. Open point fulfilled.	 PRAPeR 63 (12. – 16.01.2009) Open point fulfilled.
	Open point 5.7 RMS to update the list of endpoints for earthworms. It is still not clear if the values for the formulation are based on a.s. or formulation concentrations. Furthermore, values should be given as mg/kg DS. Corrected calculations should be included in a corrigendum. See also the comment from the applicant on the reporting table to be discussed in an		RMS: See Addendum1 Revised list of earthworm fluopicolide and soil metabolite endpoints corrected for log Pow/soil OM, as appropriate, along with amended risk assessment presented (Table B.9.6.1). LOEPs also amended. Point addressed RMS (December 2008): The soil macroorganism LOEPs has been revised and are expressed as mg/kg d.wt. soil and to clarify where correction for logPow and soil organic matter is appropriate. Some TERs	PRAPeR 38 (03 – 07 12.2007): Open point still open. PRAPeR 63 (12. – 16.01.2009) Open point open: RMS to update the LoE with the endpoint for earthworm in mg a.s./kg soil. A clarification on the endpoint for earthworm reported in the LoE is also nessessary.

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	experts meeting. See reporting table 5(39).		have been also been amended (see Open pt. 5.8). No change in low risk conclusion. RMS (February 2009): Further clarification provided in LOEPs. Open point fulfilled.	
	Open point 5.8 Pending on the discussion on the PECsoil in the section on Fate and behaviour, a revision of the risk assessment for soil organisms might be necessary. See reporting table 5(45).	BCS refers to the corresponding comment made on the reporting tables 5.(45)	RMS: The Env fate endpoints are pending discussion and have not currently been amended. Therefore, no ecotox action has been taken. Open Point: to be discussed at Expert Meeting. RMS (December 2008): See Open pt. 5.8	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.9 Pending on the discussion on the PECsoil in the section on Fate and behaviour, a revision of the risk assessment for soil organisms might be necessary. See reporting table 5(47).		RMS: The Env fate endpoints are pending discussion and have not currently been amended. Therefore, no ecotox action has been taken. Open Point: to be discussed at Expert Meeting.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.10 RMS to include the argumentation for why no		RMS: See Addendum1 Further discussion presented (B.9.8) concluding likely insignificant effects of	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.

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	studies with soil micro-organisms are required with M 03 in an addendum for the sake of completeness. No discussion in an expert meeting is required. See reporting table 5(48).		M03 on soil microbial activity in the absence of data. Point addressed.	
	Open point 5.11 RMS to include the argumentation regarding risk to non-target plants from exposure to M 01 in an addendum for the sake of completeness. No discussion in an expert meeting is required. See reporting table 5(49).		RMS: See Addendum1 Further discussion presented (B.9.9) concluding insignificant effects of M01 on off-field non-target plants. Point addressed.	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.12 RMS to present the complete assessment for the relevance of ground water metabolites in and addendum. Special attention should be paid to the fact that at this stage for metabolites M01, M05 and M10 the trigger of 0.75 µg/L is also exceeded either in the lysimeter or the FOCUS modelling.		RMS: Ecotoxicological relevance of GW metabolites discussed in Addendum 1 (Nov 2007). RMS considers the GW metabolites to be ecotoxicologically not relevant. (see also Open pt. 5.5) Following the submission of new FOCUS groundwater modelling a completely revised Relevance of Metabolites in Groundwater assessment (following EU Guidance Document - Sanco/221/200-rev 10, 25	PRAPeR 38 (03 – 07 12.2007): Open point closed; see open point 5.5

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	See reporting table 5(53).		February 2003) has also been presented for all those metabolites that exceed 0.1 µg/l (in either the original DAR or the addendum). See Section B.6.1.4.1, Addendum 1 (Nov 2007). This includes a refined risk assessment for those metabolites found to be above 0.75 µg/l (M-01, M-05, M-10 and M-11) in either consideration. Point addressed. Open Point: to be discussed at Expert Meeting.	
5.1	Data requirement identified at PRAPeR 38: Notifier to address the ecotoxicological relevance of toluene in the technical material.	**Comment BCS May 2008:** A report to address this point was prepared and submitted: Pross, S. (2008) Eco-toxicological relevance of toluene as impurity in Fluopicolide technical material. Study report N° M-300968-01-01, Bayer CropScience AG, Monheim, Germany Conclusion: Since toluene was present (1.0 – 4.06 g/kg which is 0.1 – 0.406 %) in the fluopicolide batches used for the ecotoxicological studies it is considered to have been adequately tested for its ecotoxicological effects. It is also covered by the risk assessment for fluopicolide up to the specified concentration limit of 0.5%. A review of the literature shows that the	RMS (December 2008): The RMS has considered the case proposed the Notifier (Pross, 2008). Ecotoxicological testing was undertaken using fluopicolide technical material (batches OP2050046, OP2050190, OP2350005, R001737, OP20500045) containing 0.1-0.4% w/w toluene (AEF125577) (see DAR Vol 4,Table C.1). Therefore the ecotoxicological risk assessment for technical fluopicolide essentially encompasses the risk from toluene in technical material (max. <0.5%w/w pilot plant; <0.3%w/w manufacturing plant – Volume 4, Addendum 2, C 2.2). Furthermore, the ecotoxicological profile of “pure” toluene shows it not to be more toxic than fluopicolide	PRAPeR 38 (03 – 07 12.2007): Data requirement open. PRAPeR 63 (12. – 16.01.2009) Data requirement fulfilled. New open point proposed, see below.

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		toxicology and ecotoxicology of "pure" toluene is well described and documented. The ecotoxicological profile of toluene as evaluated in the EU Risk Assessment demonstrates than it is not more toxic than the TGAS. This resulted in a "no classification" for the environment within the EU legally binding classification and labelling system. From a risk assessment for toluene using a worst case PECi approach the TERs are well in excess of EU 91/414 Annex VI triggers for all species. Therefore, it can be concluded that the presence of toluene at the specified level does not lead to an unacceptable risk. In an overall conclusion the impurity toluene, at the specified maximum concentration limit of 0.5% in technical fluopicolide is considered not of ecotoxicological relevance.	technical. A risk assessment using worse case toluene PECsoil (0.0009 mg/kg) and PECsw (0.000046 mg/L) initial values based on theoretical toluene content in fluopicolide PECs generate respective TERs of 16667, 16087 and 76087 with worse toxic toluene endpoints for worm(28dNOEC=15 mg/kg d.wt soil), Daphnia (96hEC50=3.5 mg/L) and Ceriodaphnia (7dNOEC=0.74 mg/L). The TERs clearly exceed relevant Annex VI EU 91/414 thresholds indicating low risk. Toluene also has low bioaccumulation potential (BCF=90). Thus all evidence indicates that environmental toluene derived from fluopicolide technical use in PPPs will not cause concern from an ecotoxicological perspective. Data requirement closed. Point addressed.	
	New open point 5.15: RMS to include in an addendum a summary of the applicant.		RMS February 2009: RMS summary of risk assessment as at 5.1 above provided in Confidential Addendum (Vol4). Open point fulfilled	PRAPeR 63 (12. – 16.01.2009) Open point open.