PEER REVIEW REPORT ON **FLUOPICOLIDE** 17 03 2009

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**REPORT OF PRAPeR EXPERT MEETING 36**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

## 1. Physical and Chemical Properties

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| Nov 2007 | UK | Fluopicolide addendum1 Vol3 (Nov 2007) phys-chem.doc |
| 12.11.2007 | UK | Fluopicolide evaluation table rev1-0 (2007-11-12) phys-chem.doc |
| 02.04.2007 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| Nov 2007 | UK | Fluopicolide rev addendum1 Vol4 (Nov 2007) cover page.doc |
| Nov 2007 | UK | Fluopicolide revised list of endpoints (Nov 2007) phys-chem.doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** AE F053616 06WG71 A1 & AE B066752 04 SC61 A1

5. **Classification and labelling:** Not discussed

**Recommended restrictions/conditions for use:** Not discussed

**Reference list:** Not discussed

**Areas of concern:** Possible relevant impurities

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 1. Physical and Chemical Properties

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 1.1 | Data requirement<br>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.<br><br>See reporting table 1(1). | Data requirement redundant.<br>New data gap.<br>Once full scale manufacturing is in progress then new 5 batch data must be provided. | Data requirement redundant.<br>New data requirement:<br>Once full scale manufacturing is in progress then new 5 batch data must be provided. |
| 1.6 | New data requirement identified at PRAPeR 36: | | Data requirement open. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Once full scale manufacturing is in progress then new 5 batch data must be provided. | | |
| | Open point 1.1<br>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.<br><br>See reporting table 1(5). | Open point fulfilled.<br>Message to tox and ecotox, is toluene a relevant impurity? | Open point fulfilled. |
| | Open Point 1.2<br>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. | The method separates the impurities open point fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | See reporting table 1(7). | | |
| | Open point 1.3<br>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.<br><br>See reporting table 1(8). | The issue was clarified. Open point fulfilled. | Open point fulfilled. |
| | Open point 1.4<br>The corrected formulation details should be given.<br><br>See reporting table 1(10). | The formulation details have been corrected and the open point is fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.5<br>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.<br><br>See reporting table 1(11). | The meeting accepted the rapporteur's explanation and the open point is fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.6<br>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 substance should be reported. These issues should be discussed in a meeting of experts.<br><br>See reporting table 1(16). | The meeting agreed with the comment of the RMS. Open point fulfilled. | Open point fulfilled. |
| | Open point 1.7<br>LOEP relative density the purity should be given..<br><br>See reporting table 1(24). | The list of end points has been amended and the open point is fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.8<br>It should state for the Log Pow that it is independent of pH.<br><br>See reporting table 1(27). | The list of end points has been amended and the open point is fulfilled. | Open point fulfilled. |
| | Open point 1.9<br>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.<br><br>See reporting table 1(29). | The list of end points has been amended and the open point is fulfilled. | Open point fulfilled. |
| | Open point 1.10<br>The endpoints should use the current agreed template.<br><br>See reporting table 1(33). | The list of end points has been amended and the open point is fulfilled. | Open point fulfilled. |
| | Open point 1.11<br>For melting point which sub method of A1 was used.<br><br>See reporting table 1(40). | DSC was used and the open point is fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.12<br>For the UV/VIS More detailed information about the measurement should be given, e.g. solvent, maximum absorbance.<br><br>See reporting table 1(44). | The requested information was provided and the open point is fulfilled. | Open point fulfilled. |
| 1.2 | Data requirement<br>Explosive properties mechanical sensitivity data should be provided.<br><br>[This should be considered as a technical data requirement as the study has already been submitted]<br><br>See reporting table 1(48). | The data was supplied data requirement fulfilled. | Data requirement fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 1.3 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (SC).]<br><br>See reporting table 1(59). | Storage stability data have been provided and the data requirement is fulfilled. | Data requirement fulfilled. |
| 1.4 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (WG).]<br><br>See reporting table 1(60). | Data accepted and the data requirement is fulfilled. | Data requirement fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.13<br>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 or corrigendum (WG).<br><br>See reporting table 1(62). | References amended open point fulfilled. | Open point fulfilled. |
| | Open point 1.14<br>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.<br><br>See reporting table 1(64). | References amended open point fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 1.5 | Data requirement<br>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.<br><br>See reporting table 1(66). | Data requirement reworded on whether M-01 (2,6-dichlorobenzamide) is considered toxicologically relevant.<br><br>The **new data requirment** would read as follows<br>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 been identified as a data gap.<br><br>**Message to tox**: Is M-01 (2,6-dichlorobenzamide) toxicologically relevant? | Data requirement reworded:<br><br>The new data requirment would read as follows<br>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.<br><br>Data requirement open. |
| | Open point 1.15<br>The LOQs should be given for each analyte in the list of end points.<br><br>See reporting table 1(72). | Open point fulfilled.<br><br>**New open point**: 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. | Open point fulfilled.<br><br>New open point, see open point 1.18 |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New open point 1.18:<br><br>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. | | Open point open. |
| | Open point 1.16<br>At least the linearity range should be given for all the residue methods.<br><br>See reporting table 1(78). | The clarification received was accepted open point fulfilled. | Open point fulfilled. |
| | Open point 1.17<br>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.<br><br>See reporting table 1(81). | Experts at the meeting were informed that the %RSDs were all less than 20%.<br>Open point fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New open point 1.19:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting. | The relevant impurities box should include 'open'<br>The molar extinction coefficient at the max absorbance should be given.<br>In the appearance box the purities should be stated.<br>Flammability should state not highly flammable.<br>In the heading of the summary of representative uses the name of the active should be stated.<br>The word 'Parent' should be deleted from the residue definitions | Open point open. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Section 1<br>Data requirements: ***5***<br>Open points: ***17*** | | | Section 1<br>Data requirements: ***2***<br>Open points: ***2*** |
| 1.1 | Data requirement<br>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.<br><br>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<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement redundant.<br>New data requirement:<br>Once full scale manufacturing is in progress then new 5 batch data must be provided. |
| 1.6 | New data requirement identified at PRAPeR 36:<br>Once full scale manufacturing is in progress then new 5 batch data must be provided. | | | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement open. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.1<br>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.<br><br>See reporting table 1(5). | BCS refer again to our comment made in the reporting tables.<br>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).<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open Point 1.2<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.3<br>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.<br><br>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).<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.4<br>The corrected formulation details should be given.<br><br>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.<br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.5<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.6<br>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 substance should be reported. These issues should be discussed in a | 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 accordingly. Therefore, although not initially, the results in the | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | meeting of experts.<br><br>See reporting table 1(16). | | end were generated using the correct response factor determined using an AE1050605 standard.<br><br><u>Retention times of active substance and impurities</u><br>**Method (a)**<br>Fluopicolide – 13.0 min<br>AEC636523 – 11.1 min<br>AC0553913 – 13.0 min<br>AEC639035 – 19.7 min<br>AEC648994 – 25.2 min<br>AE1050605 – 39.5 min<br><br>**Method (b)**<br>Fluopicolide - 21.3 min<br>M-01 - 4.6 min<br>AEC648995 – 6.5 min<br>AEF125577 – 18.4 min<br><br><u>Open Point</u>: to be discussed at Expert Meeting. | |
| | Open point 1.7<br>LOEP relative density the purity should be given..<br><br>See reporting table 1(24). | | RMS: Purity = 99.3%. However, relative density is no longer included in the current end points template.<br><br>Addressed | <u>PRAPeR 36 (27. – 30.11.2007):</u><br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.8<br>It should state for the Log Pow that it is independent of pH.<br><br>See reporting table 1(27). | | RMS: Agreed. Log Pow is independent of pH. The end points have been updated.<br><br>Addressed. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.9<br>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.<br><br>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.<br><br>Addressed. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.10<br>The endpoints should use the current agreed template.<br><br>See reporting table 1(33). | | RMS: The LOEP have been updated to the current template. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.11<br>For melting point which sub method of A1 was used.<br><br>See reporting table 1(40). | | RMS: Sub method 1.4.4.2<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.12<br>For the UV/VIS More detailed information about the measurement should be given, e.g. solvent, maximum absorbance.<br><br>See reporting table 1(44). | | RMS: The maximum absorbance is stated in B.2.1.10 as UV absorb 203 nm ($\varepsilon$ = 44159 l $mol^{-1}$ $cm^{-1}$), solvent was methanol<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| 1.2 | Data requirement<br>Explosive properties mechanical sensitivity data should be provided.<br><br>[This should be considered as a technical data requirement as the study has already been submitted]<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |
| 1.3 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (SC).]<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| 1.4 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (WG).]<br><br>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.<br><br>See also Open Point 1.13 below<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |
| | Open point 1.13<br>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 or corrigendum (WG).<br><br>See reporting table 1(62). | | RMS: See corrected text and reference in Section 2, Addendum 1.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.14<br>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.<br><br>See reporting table 1(64). | | RMS: References have been deleted from Section 2, Addendum 1.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| 1.5 | Data requirement<br>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.<br><br>See reporting table 1(66). | BCS refer again to our comment made in the reporting tables. | 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<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement reworded:<br><br>The new data requirment would read as follows<br>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.<br><br>Data requirement open. |
| | Open point 1.15<br>The LOQs should be given for each analyte in the list of end points.<br><br>See reporting table 1(72). | | RMS: LOQs are as follows:<br>Grape = 0.1 mg/kg<br>Wheat grain = 0.02 mg/kg<br>Potato = 0.02 mg/kg<br>Endpoints table have been updated.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled.<br><br>New open point, see open point 1.18 |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | New open point 1.18:<br><br>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. | | | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. |
| | Open point 1.16<br>At least the linearity range should be given for all the residue methods.<br><br>See reporting table 1(78). | | RMS: Linearity ranges are as follows;<br>Plant (Parent) = 0.01–1 µg/ml<br>Soil (Parent/M03) = 0.4–75 µg/l<br>Soil (M01/M02) = 0.4–100 µg/l<br>Water (Parent/M01/M02) = 0.2–25 µg/l<br>Air (Parent) = 0.01–1 µg/ml<br>Animal(Parent/M01/M02) = 0.1-10µg/ml<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.17<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
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| | New open point 1.19:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting. | | | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. |

**REPORT OF PRAPeR EXPERT MEETING 37**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**4. Fate and behaviour in the environment**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| Nov 2007 | UK | Fluopicolide addendum Fate Nov 2007 - field kinetics (Open Point 4.8).doc |
| Nov 2007 | UK | Fluopicolide addendum1 Vol3 B8-B9 (Nov 2007).doc |
| 19.11.2007 | UK | Fluopicolide evaluation table rev 1-0 (2007-11-19) fate.doc |
| 19.11.2007 | UK | Fluopicolide revised list of end points (2007-11-19) fate-ecotox.doc |
| 19.11.2007 | UK | Fluopicolide revised list of end points (2007-11-19) fate-ecotox.doc |
| 20.11.2007 | UK | FW Further documentation for PRAPeR 37 Experts' meeting on Fate and Behaviour Parma 03-06 12 2007.msg |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| None | | |

The conclusions of the meeting were as follows:

**4. Data on preparations:** AE F053616 06 WG 71 Al (vines); AE B066752 04 SC 61 Al (potatoes)

**5. Classification and labelling:** candidate for R53

**6. Recommended restrictions/conditions for use:** none identified

**7. Reference list:** not discussed

**Areas of concern:** leaching of a.s. and soil metabolites that require non-relevance assessment.

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 4. Fate and behaviour

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 4.1<br>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.<br>RMS to amend the list of end points accordingly.<br><br>MS experts to discuss if the half lives derived from the study dosed with M02 may however still be used for modelling.<br><br>See reporting table 4(6). | The information required for open point 4.1 is included in the separate addendum.<br>Metabolites were not seen at high levels in the route of degradation studies but they appeared in the lysimeter study requiring groundwater assessment.<br>In the assessment for metabolites a combination of DT50 coming from study with M02 or the metabolite under consideration dosed as parent was used.<br>There is an overlap in the soils that were used in the different studies. The meeting discussed whether the results of the same soils (replicates) should be averaged and then take the geomean or should one dataset be regarded as 'most reliable' and the other one be discarded.<br>The view of the meeting is that same soils in general should be seen as replicates and averaged (with geometric mean) before the geomean of the data is derived to be used for modelling. This approach is also supported in the case of fluopicolide however it seems there will be not much difference between the geomean derived in this way and the value derived now. The same number of values is obtained for each soil except for M14. The meeting agreed that in this case the geometric mean of all values is acceptable and the LoEP does not need to be amended. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | Open point 4.2<br>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 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.<br><br>See reporting table 4(10). | Clarification on the procedure is included in addendum 1 of November 2007.<br>There are some differences in the approach of normalisation between RMS and the applicant. It should be clear which values are derived when the guidance is strictly followed and the meeting agrees upon those provided by RMS in the LoEP. RMS included both their recalculated values and the values of the applicant as a footnote in the LoEP with a clarification in the addendum. However, the meeting found that the table collecting the data from filed studies would be more transparent if the names of the soils (and the year of the study when necessary) are included together with the soil texture. | Open point fulfilled |
| | Open point 4.3<br>MSs to discuss the effect of the applied high concentration on the soil degradation study with metabolite | The laboratory study where M01 was dosed as starting material used a very high application dose. In this particular lab study the DT50 was very long. It cannot be concluded from the data available that there is dose dependency. However, as the DT50 in the study was extrapolated way beyond study duration these are not considered very reliable.<br>There are field dissipation studies available from which DegT50 values for M01 were | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | M01 and the adequate DT50 for PECsoil and PECsw and PEC GW calculations.<br><br>See reporting table 4(12). | derived to be used in exposure assessment. The discussion on appropriate DT50 values will be held in later open points. | |
| 4.1 | Data requirement<br>Notifier to provide an estimation of soil photolysis half lives at other latitudes (i.e 40 ºN and 45 ºN).<br><br>Applicant indicated to submit a position paper (Report MEF-06/495) by April 2007.<br><br>See reporting table 4(14). | New calculation has been provided in addendum 1 from November 2007.<br>The applicant claimed the light energy in the original study (i.e. 456 W/$m^2$) was equivalent to what can be expected in Scotland. However, they also claim that the light energy in the study was higher than what may be expected in any other (southern) European location. In particular, they claim that the soil photolysis DT50's were calculated based on a solar energy of 68000 kJ/$m^2$*day, including an extrapolation to higher wavelength which seems not justified.<br>During the meeting a search of public available data revealed yearly average values for France of 400-550 W/$m^2$, depending on the latitude. This was taken as an indication that the value of 456 W/$m^2$ for Scotland in summer may not be considered an overestimation.<br>Then, the light energy from the original study (456 W/$m^2$) was recalculated based on the actual wavelengths irradiated and using the correct units conversion, taking into account that the energy in the original study was based on a 12 h day. This recalculation from the light intensity in original study would relate to solar energy of approx. 19000 kJ/$m^2$*day, comparable to a value between the scenario's Kremsmuenster and Sevilla that are reported in table 8.5 of the addendum (extracted form FOCUS GW scenarios data).<br><br>In conclusion the experts in the meeting agreed that the data requirement was not correctly addressed.<br>A new open point was set in the meeting; re-calculation of the $DT50_{soil\ photolysis}$ for various latitudes in Europe needs to be provided.<br>During the meeting an estimation of the $DT50_{photolysis}$ was made taking the mean solar energy for Sevilla from the FOCUS database. This value would be 47 days based on the DT50 of 62.5 days from the benzoyl label as calculated in the addendum (105 days Sevilla based on the 134 days for the pyridyl label, 83.5 days on average). | Data requirement still open<br><br>Calculation of $DT50_{photolysis}$ for adequate latitudes in Europe. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | | From the meeting discussion, photolysis might not be completely excluded as a process of degradation. The relevance of photolysis in soil with respect to the risk assessment was further discussed in relation with the field studies. | |
| | Open point 4.4<br>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.<br><br>See reporting table 4(17). | In the reporting table the question was raised that a ff of 0 for M14 was included for 1 soil in the study where M02 was dosed. In this soil M14 was not formed because at amounts that would have allowed to calculation of a reliable ff because the precursor appeared to be degrading slower that in the other two soils. The question arose weather if is correct to include a ff 0 in the arithmetic mean ff that is calculated? However, there is no guidance how deal with this situation. Should the mean of the 2 residual soils be taken or should the worst case value be used in the assessment?<br>The meeting agreed to use the worst case of the 2 remaining values for further assessment as is common for other parameters. A ff of 0.384 is to be used in modelling, as has been done in the new FOCUS GW assessment presented in the addendum. The geomean should be removed from the LoEP. | Open point fulfilled |
| | Open point 4.5<br>MS experts to discuss potential influence of the different extraction method employed on the respective results of the laboratory and field studies.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion. | There were some differences in the method of extraction for fluopicolide between the lab and field studies. For the laboratory studies an extraction step using Soxhlet was included which was not part of the extraction procedure employed in the field studies. With the Soxhlet about 10% extra fluopicolide was released.<br>Therefore, the more strongly sorbed part (non equilibrium domain) may have not be considered in the data obtained from the field studies and only degradation of the more easy available part is considered. The experts concluded that this raised concerns regarding the appropriateness of including considerations of non-equilibrium soil adsorption in the ground water modelling using FOCUS PEARL (see data requirement 4.3). The experts considered that this could imply that by assuming the non-equilibrium domain in the modelling the same phenomenon would have been counted twice. | Open point fulfilled |

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| | See reporting table 4(26). | | |
| | Open point 4.6<br>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.<br><br>See reporting table 4(29). | It was confirmed that field half life has been used in FOCUS exposure modelling.<br>The justification of the correct half life to be used in FOCUS exposure modelling is discussed later on in another open point. | Open point fulfilled |
| | Open point 4.7<br>MS experts to discuss the conceptual model used to derive the kinetic parameters used for modelling. In particular paying attention to:<br>– the absence of a flow from the parent to the sink compartment and | There was no flow to sink included. The DAR was written before new FOCUS kinetic guidance and did not exactly follow this guidance. Including a sink would influence the ff of metabolites and the DT50. However in this case the values that are used in modelling are considered acceptable. The conceptual model is the same as used for groundwater modelling.<br><br>The normalisation of the DT50 included the normalisation of formation rates.<br>The experts agree with RMS conclusion on the statement of the applicant in the reporting table. It must however be clear that the normalised DT50 of M01 as shown in the LoEP is only valid in combination with a ff of 1. This should be clarified in the LoEP. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | – the effect of normalization of degradation constants without the corresponding normalization of the formation constants.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion.<br><br>See reporting table 4(34). | | |
| | Open point 4.8<br>MS experts to discuss in an experts meeting the kinetic evaluation of field dissipation studies.<br><br>See reporting table 4(36). | The information supplied is included in the separate addendum.<br>The information did not change very much what was already presented in the DAR. HS fit seems to have better fit to the non normalised data. At the moment in the LoEP the values from the addendum are not included. The meeting agreed that the non-normalised HS actual DT50 and DT90 are the most appropriate values and are to be included in the LoEP.<br><br>New open point: RMS to include in the LoEP the values from HS fitting presented in the addendum. | Open point fulfilled<br><br>New open point: RMS to include in the LoEP the values from HS fitting presented in the addendum. |
| | New open point 4.21:<br><br>RMS to include in the LoEP the values from HS fitting presented in the addendum. | | Open point open. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| 4.2 | Data requirement<br>Applicant to present the position paper with their evaluation of the accumulation studies.<br><br>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.<br><br>See reporting table 4(41). | Applicant did not agree on the evaluation of field accumulation behaviour by RMS in the original DAR, that the plateau has not been reached.<br>Applicant provided a position paper with regard to accumulation studies which is evaluated in addendum 1 of November 2007.<br>RMS evaluated what has been presented by the applicant but the final outcome remains that a plateau was not reached in at least some of the field accumulation studies provided.<br>The original conclusion is therefore still supported and there is no need for a change of the assessment.<br>There is no need to change the LoEP. | Data requirement fulfilled |
| | Open point 4.9<br>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).<br><br>See reporting table 4(42). | The meeting estimated a $DT50_{photolysis}$ of 83.5 days based on a year mean light intensity for Sevilla.<br>According to the LoEP the normalised DT50's are SFO and not bi-phasic. In that case photolysis would not play a role. However, there is no time step normalised visual fits presented to give a clearer view. From the fits that are presented it seems that there is a faster decline seen at the beginning which can be caused by photolysis, but also by non-equilibrium sorption (as applicant says). Another alternative explanation to the apparent rapid decline at the beginning of the field studies (first 5 -14 d) could also be caused due to a deficient homogenization in soil at the beginning of the studies. This has to do with the experimental set up for field studies and is not unusual. This last explanation was the most supported by the experts in the meeting (in fact initial concentration in some of the field studies is far to the nominal and to the calibrated applied concentrations). At some trial sites (Valencia, Apilly, Roedelsee) the hinge point is later in the studies. In those cases photolysis or aged sorption may have played a role on the biphasic behaviour.<br>The experts are of the opinion that the results of the field studies can be used to derive DT50 forFOCUS exposure modelling. One suggestion was the data from the first few sampling points in the rapid phase should be excluded to derive a conservative DegT50 | Open point fulfilled |

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| | | for modelling. However no consensus was reached on what would be the best approach to consider the possible effect of deficient soil homogenization at the first sampling points. | |
| | Open point 4.10<br>MS experts to discuss whether the lysimeter study represents a worst case with respect to the formation of metabolites.<br><br>See reporting table 4(54). | RMS made a comment in the evaluation table. The soil used in the lysimeter was also used in one of the laboratory aerobic degradation experiments. The parent was degraded rather fast in this soil. Therefore it can be considered representative but not necessarily worst case with regard to metabolite formation. The study duration was probably just long enough (3 yr) to detect all significant metabolites. However it may have been too short to identify the maximum annual average concentration for all of them. | Open point fulfilled |
| | Open point 4.11<br>RMS to update GAP table with 5d minimum application interval for potatoes.<br><br>See reporting table 4(59). | LoEP has been updated | Open point fulfilled |
| | Open point 4.12<br>MS experts to discuss if the use of the 90$^{th}$ percentile is appropriate for PEC soil calculations.<br><br>See reporting table 4(60). | This open point is related to the next open point. The 90$^{th}$ percentile value was used in the PECgw scenario used for PECsoil calculation by the applicant.<br>RMS is not in favour of using the 90$^{th}$ percentile and the approach using FOCUSgw scenario's for calculating the accumulated PECsoil. For potatoes the results provided by the applicant were included as these were more conservative. For vines RMS recalculated using the longest non normalised SFO field DT50 values both for the parent substance and M01.<br>It was agreed that for potatoes the values provided by the applicant were accepted using the 90$^{th}$ percentile and the GW scenario's as they were more conservative than the ones derived by the RMS using the worst case DT50.<br>The meeting agrees on using the SFO DT50 of 290 days for the parent and 315 days for M01. The DT50 selected for the parent results in a DT90 close to the highest DT90 of the | Open point fulfilled.<br><br>New open point proposed, see open point 4.22 |

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| | | HS fitting.<br>New open point: 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. | |
| | New open point 4.22:<br>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. | | Open point open. |
| | Open point 4.13<br>MS experts to discuss if FOCUS GW scenarios with normalized $DT_{50}$ 's are appropriate for PEC soil calculation.<br><br>See reporting table 4(61). | This open point relates to the previous open point.<br>RMS in not in favour of using the approach using FOCUSgw scenario's for calculating the accumulated PECsoil.<br>For potatoes the results provided by the applicant where included as these were more conservative. For vines RMS recalculated using the longest non normalised SFO field DT50 values, both for the parent substance and M01. This approach was accepted by the meeting who agreed RMS position (see open point 4.12). | Open point fulfilled |
| | Open point 4.14<br>MS to discuss whether the M01 half lives may be considered appropriate degradation half lives for modelling PEC soil.<br><br>See reporting table 4(62). | This open point relates to the previous open points.<br>Since the general approach is not accepted there was no further discussion on the specific input parameters. The results of the calculations were included and accepted by the meeting for potatoes as discussed in open point 4.12 and 4.13. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | Open point 4.15<br>MS experts to discuss which maximum amount formed of M01 should be considered for PEC soil calculations.<br><br>40.2 % comes form laboratory studies. It is doubtful that field studies are capable to identify the maximum formation of a metabolite.<br><br>See reporting table 4(65). | The max amount formed in the field was selected from a field study where the substance was applied two years in sequence. The highest value appears in the second year. Notifier considers it not justified to use this value. It is more appropriate to use the value from the first year of application. In that case the value would go down from 14.6% on mass basis to 11.9%.<br>To account for leaching the mass over all soil layers was taken into account in all cases.<br>The max. amount formed is related to the max amount of parent present in the soil.<br>In fact it is not correct to use the maximum formation percentage from the second year of the Senas 2000 study as there was an application in the previous year and there will be residues left from both parent and M01 and therefore the formed amount is not just related to formation from an application. The value from the first year can be used (Senas 1999). The first year of the accumulation study can be considered a soil dissipation study.<br>The meeting agreed that the value of 11.9% on mass basis is the correct value. In principle revised PEC calculations should be performed. However, there won't be an influence on the RA. The same issue is pertinent for M02. RMS to decide if a recalculation is performed or a remark is included in the LoEP, which is the correct value for formation and from which field study is was derived.<br>The experts agreed that in the Senas 1999 field study the maximum of the metabolite has been identified adequately.<br>New open point: 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 field. | Open point fulfilled.<br><br>New open point proposed, see open point 4.23 |
| | New open point 4.23:<br><br>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 field. | | Open point open. |
| | Open point 4.16<br>MS experts to discuss | See discussion on previous open points. | Open point closed |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | the different approaches taken for the PEC soil calculation.<br><br>See reporting table 4(69). | | |
| 4.3 | Data requirement<br>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.**<br><br>For some of the metabolites it may not be confirmed that the 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 | Notifier provided what was claimed to be higher tier modelling with a second model in line with the PPR opinion.<br>PEARL modelling was provided using the approach of non equilibrium sorption. The approach is evaluated in detail in the addendum 1 of November 2007.<br>In addendum 1 of November 2007 the approach for deriving the non equilibrium sorption parameters as submitted by the applicant was presented as was the new PECgw calculation.<br>The PELMO calculation is in principle the same as presented in the DAR only using a GAP for potatoes of application every 1 and 2 years and the highest formation fraction for M14. The other input parameters are the same. For M01 a formation fraction equivalent to 100% was used.<br>For the non equilibrium sorption approach used in PEARL the following reservations were made by the meeting:<br>• The measured field values were used to derive the degradation in the equilibrium phase. The extraction method without soxhlet may have influenced the measured value. A proportion of substance present in the non equilibrium compartment may not have been extracted, which could lead to the fact that this phase may be accounted twice in the modelling, i.e"double counted" . Another question is whether one extraction with calcium chloride is enough to describe the fraction in the equilibrium domain in sorption studies.<br>• The mean value for $k_d$ and fne derived from the sorption studies was used for the field sites Appilly and Valencia. There was a comment that it is not possible to use mean values for $k_d$ and fne to derive $k_t$ for the field studies as the non equilibrium parameters are related to each other and to the soil where these were derived. Using just the four field soils would result in a DT50 that is slightly lower to be used in PEARL and therefore will not influence the RA.<br>• There are 4 experimental data in the aged sorption / degradation studies. | Data requirement maintained. The applicant is requested to submit a first Tier standard FOCUS PEARL modelling.<br><br>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. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | and confirm the non relevance of the metabolites.<br><br>Applicant indicated to submit new PEC GW calculations with a second model and lower interception rate for vines by May 2007.<br><br>See reporting table 4(79). | However, the $C_0$ was not actually measured but estimated from the applied amount. Therefore the model fits 3 parameters to 3 actually measured data points which makes the fit unreliable (too few degrees of freedom).<br>• The aged sorption approach should only be applied to field studies that are regarded adequate to derive a DegT50 (other dissipation processes are excluded, e.g. in this case question about photolysis).<br>• If the simple approach of SFO kinetics clearly applies to the normalised data there is in principle no justification to use the non equilibrium approach as there is no time dependent process included in the SFO model.<br>• It is not clear how the 1/n that was used for the $f_{des,neq}$ in the fitting was derived from the original study and if this can be considered correct.<br>In conclusion the non equilibrium approach used in the PEARL modelling was not accepted by the meeting, although one of the MS experts disagreed on the data requirement set. The experts noted that there was little guidance available on experimental methodologies required to derive non-equilibrium sorption parameters. This is an important issue as this higher approach appears to be used in an increasing number of in leaching modelling assessments. | |
| 4.4 | Data requirement<br>Applicant to repeat the FOCUS GW calculations following the GAP as reported in the Representative uses table.<br><br>Applicant indicated to submit repeated PEC GW calculations with a lower interception rate for vines by May 2007.<br><br>See reporting table 4(80). | The PELMO calculation is in principle the same as presented in the DAR only using a GAP for potatoes of application every 2 years. This is agreed upon. | Data requirement fulfilled for PELMO. For PEARL: see data requirement 4.3. |

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| | Open point 4.17<br>MS experts to discuss the approach taken by the RMS to calculate the amount of M02 formed in field<br><br>See reporting table 4(84). | See open point 4.15. | Open point closed |
| | Open point 4.18<br>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 %).<br><br>See reporting table 4(84). | As a result of the open point 4.15 and 4.17 this has to be amended by the rapporteur.<br>The open point remains open. | Open point remains open. |
| | Open point 4.19<br>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).<br><br>See reporting table 4(88). | A comment was made that in some of the field studies the amount that leached to deeper layers was summed to derive the DegT50 for the top soil. Some MS questioned if this can be considered a correct procedure. In general it is not best practice to derive DegT50 from field studies if leaching is demonstrated (FK checklist!). This is especially important if residues are detected in the lowest soil layer sampled. However in this particular case a correction was made for movement to deeper layers. Furthermore, disregarding these fields does not lead to a difference in the RA and was therefore accepted in this case. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | Open point 4.20<br>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.<br><br>See reporting table 4(92). | A full relevance assessment was provided in paragraph 8.6.2 and in addendum 1 from November 2007.<br>The final conclusion will depend on the outcome of the toxicology meeting. | Open point fulfilled |
| | Residue definition agreed upon | Residues that need further assessment or are assessed during evaluation<br><br>Soil:fluopicolide and metabolites M-01, M-02 and M-03<br>Surface Water:fluopicolide and soil metabolites M-01, M-02 and M-03<br>Sediment:fluopicolide and soil metabolites M-01, M-02 and M-03<br>Ground water:fluopicolide and metabolites M-01, M-02, M-03, M-05, M-10, M-11, M-12, M13, M-14 and M-15 (0.095 μg/L in the last year of the lysimeter study)<br>Air: fluopicolide by default | |
| | New open point 4.24: | • M14 ff: the geomean should be removed from the LoEP.<br>• Clarify in the LoEP that DT50 of M01 is with ff of 1. | Open point open. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting. | • RMS to include the values from HS fitting from the addendum in the LoEP<br>• 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.<br>• 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 field.<br>• Add the location of the field study to the LoEP next to the soil type<br>• It is noted that in the ecotox LoEP the results of the relevance assessment are not mentioned. (message to ecotox)<br>• Box ready biodegradability: just 'no' is sufficient. Any consequences for labelling could be discussed in the labelling box. The *degradation* mentioned should be changed to *mineralisation*, since study was conducted acc. to OECD301b so mineralisation was measured. The sentence 'failing the 10-day window but passes 70 % within 28 days' could be added to the labelling box.<br>• The PECsoil for M01 in potatoes now refers to footnote 3, this should probably be 1 and 2, RMS to check. (refers to soil depth used for PEC calculation)<br>• For M03, it could be indicated in the LoEP from which field study the DT50 of 55 days is derived (one German loamy sand site, RMS please specify) | |
| | | The meeting noted that there is no clear guidance or agreed protocol how to perform studies on aged sorption that lead to the results required in the PEARL modelling. | |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | Section 4<br>Data requirements: ***4***<br>Open points: ***20*** | | | Section 4<br>Data requirements: ***2***<br>Open points: ***4*** |
| | Open point 4.1<br>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.<br>RMS to amend the list of end points accordingly.<br><br>MS experts to discuss if the half lives derived from the study dosed with M02 may however still be used for modelling.<br><br>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.<br><br>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.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.2<br>RMS to clarify normalized laboratory DT50's values for fluopicolide and metabolites. I.e for fluopicolide in LoEP | | RMS: Please see RMS Addendum 1 (Nov 2007), and updated LoEP.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

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| | the range is 194 – 333 d when for 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.<br><br>See reporting table 4(10). | | | |
| | Open point 4.3<br>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.<br><br>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.<br>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.<br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| 4.1 | Data requirement<br>Notifier to provide an estimation of soil photolysis half lives at other latitudes | 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 | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement still open. |

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| | (i.e 40 ºN and 45 ºN).<br><br>Applicant indicated to submit a position paper (Report MEF-06/495) by April 2007.<br><br>See reporting table 4(14). | degradation studies and contains in the appendix a calculation of soil photolysis half lives at other latitudes. The report will be submitted with the updated dossier. | updated LoEP.<br>RMS concludes that soil photolysis at 40ºN and 45ºN is unlikely to significantly influence the degradation of fluopicolide in soil.<br>Addressed. | Calculation of $DT50_{photolysis}$ for adequate latitudes in Europe. |
| | Open point 4.4<br>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.<br><br>See reporting table 4(17). | | RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.5<br>MS experts to discuss potential influence of the different extraction method employed on the respective results of the laboratory and field studies.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion. | | 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.<br><br>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 | PRAPeR 37 (03. – 06.12.2007):<br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | See reporting table 4(26). | | 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.<br>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.<br>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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.6<br>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. | | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

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| | See reporting table 4(29). | | B.8.1.5.1 for further details.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.7<br>MS experts to discuss the conceptual model used to derive the kinetic parameters used for modelling. In particular paying attention to:<br>– the absence of a flow from the parent to the sink compartment and<br>– the effect of normalization of degradation constants without the corresponding normalization of the formation constants.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.8<br>MS experts to discuss in an experts meeting the kinetic evaluation of field dissipation studies. | 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 | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.21 |

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| | See reporting table 4(36). | by BCS to initial concentrations in modelling field data. This will be available in May 2007 and can be submitted upon request. | Expert meeting for on distribution on CIRCA prior to the meeting. However, MS should note that even if this is not possible, a discussion of this open point is still possible.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | New open point 4.21:<br><br>RMS to include in the LoEP the values from HS fitting presented in the addendum. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |
| 4.2 | Data requirement<br>Applicant to present the position paper with their evaluation of the accumulation studies.<br><br>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.<br><br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement fulfilled. |
| | Open point 4.9<br>MS experts to discuss the | See comment on data requirement 4.1 | RMS: Further data (Kley, C; Mackenzie, E; Report no. MEF-06/495; | PRAPeR 37 (03. – 06.12.2007): |

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| | 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).<br><br>See reporting table 4(42). | | 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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | Open point fulfilled. |
| | Open point 4.10<br>MS experts to discuss whether the lysimeter study represents a worst case with respect to the formation of metabolites.<br><br>See reporting table 4(54). | | 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 and pF2 in the Munster soil was calculated by the RMS to be 249 days | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

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| | | | (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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.11<br>RMS to update GAP table with 5d minimum application interval for potatoes.<br><br>See reporting table 4(59). | | RMS: The GAP table in the LOEPs has been amended.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.12<br>MS experts to discuss if the use of the 90$^{th}$ percentile is appropriate for PEC soil calculations.<br><br>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 90$^{th}$ percentile DT50 values in PECsoil calculations is one of the subjects discussed in the DE paper.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.22: |
| | New open point 4.22:<br>RMS to include the non | | | PRAPeR 37 (03. – 06.12.2007): |

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| | normalised SFO DT50 values for parent used for their calculation of the accumulated PECsoil in the/a table in the LoEP. | | | Open point open. |
| | Open point 4.13<br>MS experts to discuss if FOCUS GW scenarios with normalized $DT_{50}$ 's are appropriate for PEC soil calculation.<br><br>See reporting table 4(61). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.14<br>MS to discuss whether the M01 half lives may be considered appropriate degradation half lives for modelling PEC soil.<br><br>See reporting table 4(62). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.15<br>MS experts to discuss which maximum amount formed of M01 should be considered for PEC soil calculations.<br><br>40.2 % comes form laboratory studies. It is doubtful that field studies are capable to identify the maximum formation of a | | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.23. |

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| | metabolite.<br><br>See reporting table 4(65). | | 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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | New open point 4.23:<br><br>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 field. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |
| | Open point 4.16<br>MS experts to discuss the different approaches taken for the PEC soil calculation.<br><br>See reporting table 4(69). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point closed. |
| 4.3 | Data requirement<br>Applicant to provide results with a second FOCUS model following 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. | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement maintained. The applicant is requested to submit a first Tier |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | 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.**<br><br>For some of the metabolites it may not be confirmed that the 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.<br><br>Applicant indicated to submit new PEC GW calculations with a second model and lower interception rate for vines by May 2007.<br><br>See reporting table 4(79). | 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. | updated LoEPs.<br><br>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).<br><br>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.<br><br>Based on the new $PEC_{GW}$, the following metabolites are predicted to exceed<br>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.<br><br>For both the models, $PEC_{GW}$ of M-01 | standard FOCUS PEARL modelling.<br><br>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. |

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| | | | 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.<br><br>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 >0.75 µg/l and <10 µg/l at Jokioinen (PELMO, application every year).<br><br>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..<br><br>Open Point: to be discussed at Expert Meeting. | |
| 4.4 | Data requirement<br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>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.<br><br>See reporting table 4(80). | | | |
| | Open point 4.17<br>MS experts to discuss the approach taken by the RMS to calculate the amount of M02 formed in field<br><br>See reporting table 4(84). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point closed. |
| | Open point 4.18<br>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 %).<br><br>See reporting table 4(84). | | RMS: RMS proposes that this open point be dealt with after discussion proposed at open point 4.17.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point still open. |
| | Open point 4.19<br>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). | | RMS: LoEP has been amended in relation to input parameters used in modelling.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

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| | See reporting table 4(88). | | | |
| | Open point 4.20<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | New open point 4.24:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |

**REPORT OF PRAPeR EXPERT MEETING 38**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**5. Ecotoxicology**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| Nov 2007 | UK | Fluopicolide addendum1 Vol3 B8-B9 (Nov 2007).doc |
| 19.11.2007 | UK | Fluopicolide evaluation table rev 1-0 (2007-11-19) ecotox.doc |
| 02.04.2007 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| 19.11.2007 | UK | Fluopicolide revised list of end points (2007-11-19) fate-ecotox.doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

**4. Data on preparations:** EXP 11074B (vine), EXP 11120A (potato)

**5. Classification and labelling:** N, R50/53

**8. Recommended restrictions/conditions for use:** current risk assessment of mammals covers only one out of three applications in vineyards during early growth stages (up to BBCH 57). Add

**9. Reference list:** xxx

**Areas of concern:** mammals, aquatic organisms (vine)

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 5. Ecotoxicology

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.1<br>RMS to clarify in an addendum how the MAF for different vegetation was calculated and used in the assessment of risk to birds.<br><br>Note: This open point was set after a comment on the reporting table during the written procedure.<br><br>See reporting table 5(9). | RMS used a wrong MAF value in the DAR. This has been corrected in the addendum. No change in outcome of RA. Open point fulfilled. | Open point fulfilled. |
| | Open point 5.2<br>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.<br><br>See reporting table | RMS explained in the addendum why 70% interception was assumed (sort of average between 60% and 85%, reflecting the growth of the crop during the application period).<br>It seems that the first two of the three applications are done at a crop stage with 60% interception. Therefore, should 60% interception be used? Depends on the timing. The minimum timespan of application is 30 days.<br>Futhermore, the MAF-value seems to be wrong (should be 1.8 instead of 1.5 as used in the calculations).<br>With 60% interception and a MAF of 1.8, TER is below 5.<br>TER calculation could also reflect the growth of the crop, so first two applications with interception 60% and one with 85%.<br><br>It was suggeste to provide a range of TER calculations in the LoEP, for MS to decide | Open point fulfilled.<br><br>Two new open point proposed, see open point 5.13 and 5.14 |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | 5(15). | which is most relevant for their country. This was not supported.<br><br>The meeting agreed that a note should be added to the LoEP and in the conclusion report 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). The other two applications should be at later growth stages (up to BBCH 81) where the interceptions is higher than 60%.<br>Open point closed,<br>New open point: 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).<br><br>The short-term bird endpoint presented in the LoEP is not correct, It should be changed from >2064 to 1144 mg/kg bw/day. RMS to revise. New open point: RMS to revise LoEP with correct short-term bird endpoint. | |
| | New open point 5.13:<br>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). | | Open point open. |
| | New open point 5.14:<br>RMS to revise LoEP with correct short-term bird endpoint. | | Open point open. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.3<br>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.<br><br>See reporting table 5(21). | This was done (page 84 of the addendum).<br>No comments. Open point fulfilled. | Open point fulfilled. |
| | Open point 5.4<br>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.<br><br>See reporting table 5(25). | This was done. Open point fulfilled. | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.5<br>RMS to include the information and argumentation regarding the ecotoxicological relevance of GW metabolites presented in column 3 in an addendum for the sake of completeness.<br><br>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".<br><br>No discussion in an experts meeting is required. | This was done (page 86-90).<br>The PECs,gw presented in Table B.9.2.4 were not accepted by the fate meeting. However, with revised calculations the outcome of the conclusion for the groundwater metabolites will probably not change much.<br>RMS argued that the PECs,gw will be lower than calculated with the model, because interception will occur (page 89: 'for vine application a correction for 60% canopy interception would also have further reduced potential exposure'). However, this interception is already included in the groundwater modelling.<br>The 'dilution' argument of the RMS (10-fold dilution from groundwater to surface water) is accepted. New PECs,gw must be awaited before a final conclusion can be drawn. It seems that they will have to increase with one order of magnitude to reach a risk for the metabolites. Open point still open.<br><br>What about ecotoxicological relevance, which is important for monitoring?<br>For M01 and M05, data show that they are not ecotoxicologically relevant.<br>For the other metabolites, a tenfold toxicity compared to parent was assumed but no data are available. What could be the trigger value assumed for groundwater relevance? Until this is addressed with data, relevance must be assumed (and the trigger value of 0.5 ug/L for sum of active and relevant compounds must be used). | Open point still open. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | See reporting table 5(27). | | |
| | Open point 5.6<br>RMS to correct the list of endpoint with exact %-age effect on fecundity instead of <50%. Note that highest conc. with effects <50% for *A. rhopalosiphi* was 2 L/ha<br><br>See reporting table 5(38). | This was done. Open point still open to revise the LoEP according to these comments to LoEP, NTA part:<br>- all endpoints should be presented in the same units<br>- check endpoint T.pyri (EXP11120A)<br>- include mortality data in extended labstudies | Open point still open: RMS to revise LoEP |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.7<br>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.<br><br>Corrected calculations should be included in a corrigendum.<br><br>See also the comment from the applicant on the reporting table to be discussed in an experts meeting.<br><br>See reporting table 5(39). | Explanations about correction should also be made for the long-term. Open point still open. | Open point still open. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | Open point 5.8<br>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.<br><br>See reporting table 5(45). | Fate: no revised PECs. Open point fulfilled. | Open point fulfilled. |
| | Open point 5.9<br>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.<br><br>See reporting table 5(47). | Fate: no revised PECs. Open point fulfilled. | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.10<br>RMS to include the argumentation for why no 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.<br><br>See reporting table 5(48). | This was done (page 95 addendum). No comments. Open point fulfilled. | Open point fulfilled. |
| | Open point 5.11<br>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.<br><br>See reporting table 5(49). | This was done (page 95 addendum). No comments. Open point fulfilled. | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.12<br>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.<br><br>See reporting table 5(53). | See o.p. 5.5. Open point closed. | Open point closed. |
| | Message from phys/chem: | Is toluene considered a relevant impurity?<br><br>Toxicity of toluene to aquatic organisms might be found on the MSDS. New data gap: notifier to address the ecotoxicological relevance of toluene in the technical material.<br><br>See also general report. | New data gap: notifier to address the ecotoxicological relevance of toluene in the technical material. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | Section 5<br>Data requirements: **-**<br>Open points: ***12*** | | | Section 5<br>Data requirements: **-**<br>Data gaps: ***1***<br>Open points: ***5*** |
| | Open point 5.1<br>RMS to clarify in an addendum how the MAF for different vegetation was calculated and used in the assessment of risk to birds.<br><br>Note: This open point was set after a comment on the reporting table during the written procedure.<br><br>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.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.2<br>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.<br><br>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.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled.<br><br>Two new open point proposed, see open point 5.13 and 5.14 |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | New open point 5.13:<br>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). | | | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point open. |
| | New open point 5.14:<br>RMS to revise LoEP with correct short-term bird endpoint. | | | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point open. |
| | Open point 5.3<br>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.<br><br>See reporting table 5(21). | | RMS: See Addendum1<br>Further consideration and discussion with respect to log Pow and low bioconcentration potential of fluopicolide metabolites presented (B.9.2).<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.4<br>RMS to include the correction in a corrigendum and to update the list of endpoint. Since trigger values are different for algae and | | RMS: See Addendum1<br><br>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). | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | 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.<br><br>See reporting table 5(25). | | Point addressed. | |
| | Open point 5.5<br>RMS to include the information and argumentation regarding the ecotoxicological relevance of GW metabolites presented in column 3 in an addendum for the sake of completeness.<br><br>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".<br><br>No discussion in an experts meeting is required. | | RMS: See Addendum1<br>Aquatic risk of groundwater metabolites presented (Tables 9.2.2 and 9.2.3).<br>Low aquatic risk indicated.<br>Ecotoxicological relevance of GW metabolites discussed.<br>GW metabolites considered ecotoxicologically not relevant<br><br>Point addressed.<br>(also addresses Open pt. 5.12) | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | See reporting table 5(27). | | | |
| | Open point 5.6<br>RMS to correct the list of endpoint with exact %-age effect on fecundity instead of <50%. Note that highest conc. with effects <50% for *A. rhopalosiphi* was 2 L/ha<br><br>See reporting table 5(38). | | RMS: See Addendum1<br>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 proposed uses.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open: RMS to revise LoEP |
| | Open point 5.7<br>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.<br><br>Corrected calculations should be included in a corrigendum.<br><br>See also the comment from the applicant on the reporting table to be discussed in an experts meeting.<br><br>See reporting table 5(39). | | RMS: See Addendum1<br>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.<br><br>Point addressed | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open. |
| | Open point 5.8 | BCS refers to the corresponding comment made on the reporting tables | RMS: The Env fate endpoints are pending discussion and have not | PRAPeR 38 (03 – 07 12.2007): |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | 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.<br><br>See reporting table 5(45). | 5.(45) | currently been amended. Therefore, no ecotox action has been taken.<br><br>Open Point: to be discussed at Expert Meeting. | Open point fulfilled. |
| | Open point 5.9<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.10<br>RMS to include the argumentation for why no 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.<br><br>See reporting table 5(48). | | RMS: See Addendum1<br>Further discussion presented (B.9.8) concluding likely insignificant effects of M03 on soil microbial activity in the absence of data.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.11<br>RMS to include the argumentation regarding risk to non-target plants from | | RMS: See Addendum1<br>Further discussion presented (B.9.9) concluding insignificant effects of M01 on off-field non-target plants. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | exposure to M 01 in an addendum for the sake of completeness. No discussion in an expert meeting is required.<br><br>See reporting table 5(49). | | Point addressed. | |
| | Open point 5.12<br>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.<br><br>See reporting table 5(53). | | RMS: Ecotoxicological relevance of GW metabolites discussed in Addendum 1 (Nov 2007). RMS considers the GW metabolites to be ecotoxicologically not relevant.<br>(see also Open pt. 5.5)<br>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 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.<br><br>Point addressed.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point closed; see open point 5.5 |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| 5.1 | Data gap identified at PRAPeR 38:<br><br>Notifier to address the ecotoxicological relevance of toluene in the technical material. | | | PRAPeR 38 (03 – 07 12.2007):<br><br>Data gap open. |

**Report of PRAPeR Expert MEETING 39**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**2. Mammalian Toxicology**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| Nov 2007 | UK | Fluopicolide addendum1 Vol3 B2-B6-B8-B9 (Nov 2007).doc |
| 23.11.2007 | UK | Fluopicolide evaluation table rev 1-0 (2007-11-23) tox.doc |
| 02.04.2007 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| 19.11.2007 | UK | Fluopicolide revised list of end points (2007-11-19).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** SC: “EXP 11120A”; WG: “EPX 11074B”

5. **Classification and labelling:** none proposed

6. **Recommended restrictions/conditions for use:** none proposed

7. **Reference List:** not discussed

| **Areas of concern:** Toxicological relevance of groundwater metabolite M 01 |
|---|

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 2. Mammalian toxicology

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 2.1<br>The relevance of the liver weight increase in the 90 day study in dog to be agreed on in an experts' meeting<br><br>See reporting table 2(3). | The RMS reported that additional information on the 90-day dog study had been provided in an addendum to the DAR.<br>Regarding the 90-day study it was pointed out that the pronounced increases in liver weights observed had to be considered as being adverse and the experts confirmed to set the NOAEL in this study at 70 mg/kg bw/d. | Open point fulfilled.<br>The NOAEL of 70 mg/kg bw/d in the 90-day dog study was confirmed. |
| | Open point 2.2<br>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<br><br>See reporting table 2(6). | The RMS referred to Table 6.93 in the addendum to the DAR where it could be seen that in mice next to other liver effects increased hepatocellular adenomas were observed at the highest dose level of 3.200 ppm, while no tumours had been seen at the next lower dose of 400 ppm. And whereas in the chronic rat study liver toxicity has as well been observed (see DAR, Vol.3, B.6, p.291) no tumours had been detected.<br><br>The experts meeting agreed that these findings do not trigger classification for carcinogenicity.<br><br>In addition to the parent compound carcinogenicity of the metabolite M01 has been discussed. This metabolite is occurring in the ground water. With M01 a chronic rat study was carried out in which adenomas were found at a dose exceeding the MTD.<br>One member state pointed out clearly that for risk assessment purposes the tumours (5 adenomas, only in females, n = 35) could be easily considered as non-relevant. But when looking at the criteria for carcinogenicity of Dir. 67/548/EEC the data might trigger classification as Carc. Cat. 3 R40. Even the fact that the tumours were observed above MTD level and the metabolite had no genotoxic potential might not be of much help.<br>The RMS added that the tumours did not reach statistical significance and it was not | Open point fulfilled.<br>Neither for fluopicolide nor for metabolite M01 was a classification for carcinogenicity proposed. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | | clear if they were really treatement related. They occurred only at the highest dose and consequently a dose-response curve could not be established. Probably the tumours were just a secondary effects of liver toxicity. Moreover the parent compound was not carcinogenic either.<br>The experts agreed not to propose a classification for carcinogenicity for metabolite M01. | |
| | Open point 2.3<br>The amount of bioavailable fluopicolide after oral administration to be agreed on in an experts' meeting<br><br>See reporting table 2(8). | The RMS reported that different biliary excretion values are reported for the pyridyl (62%) and for the the phenyl (80%) radiolabel. That was described in detail also in the addendum to the DAR on page 23. The experts confirmed the RMS' proposal and agreed that the value of 62% has to be used for oral absorption. | Open point fulfilled. Value of 62% for oral absorption was confirmed. |
| | Open point 2.4<br>The need for setting an ARfD, and the most relevant study to be considered, to be discussed in an experts' meeting<br><br>See reporting table 2(12). | The meeting agreed to the RMS' proposal to set the ARfD at 0.18 mg/kg bw based on the NOAEL derived in the 28-d study in rats applying a safety factor of 100.<br>This reference value is further supported by the results of the developmental rabbit study. | Open point fulfilled.<br><br>ARfD: 0.18 mg/kg bw |
| 2.1 | Data requirement<br>Applicant to provide a GLP revision of the acute dermal study (Krotlinger 2003)<br><br>The applicant announced in the written procedure that the report M-220872-02-1 (Krotlinger 2003) is available and can be submitted immediately.<br><br>See reporting table 2(16). | The required information was submitted and is presented in the addendum to the DAR. | Data requirement fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 2.5<br>RMS to provide further details on the results of the *in vivo* dermal absorption study (see comment by NL) in an addendum<br><br>See reporting table 2(18). | Further information and a discussion of the in vivo dermal absorption study presented in the DAR has been provided in the addendum and was endorsed by the experts at the meeting. | Open point fulfilled. |
| | Open point 2.6<br>Dermal absorption to be discussed in a meeting of experts<br><br>See reporting table 2(19). | The experts agreed to the values (0.24% for the concentrate and 2.75% for the diluted product) forwarded by the RMS. | Open point fulfilled. |
| | Open point 2.7<br>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.<br><br>See reporting table 2(21). | The experts agreed to the default values given by the RMS. | Open point fulfilled. |
| | Open point 2.8<br>The experts to agree on the operator exposure assessment for fluopicolide.<br><br>It is noted that the EUROPOEM is not yet validated for use in the regulatory risk assessment; the EUROPOEM group | The RMS is referred to the relevant chapters in the DAR (pp. 507) adding that exposure assessment had been conducted according to the German Model, POEM and EUROPOEM and that a safe use is given for all models (in POEM only with gloves). The experts agreed to the exposure assessment as provided by the RMS. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | highlighted in the final report some drawbacks still to be clarified.<br><br>See reporting table 2(22). | | |
| 2.2 | New data requirement<br>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<br><br>See reporting table 2(24). | The information has been submitted and the RMS summarised it in an addendum to Vol.4.<br>The meeting considered the batches used in the toxicological studies equivalent to technical specification. | Data requirement fulfilled. |
| | New open point 2.9<br>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.<br><br>See reporting table 2(24). | See 2.2. | See 2.2 |
| | Open point 2.10<br>RMS to present the complete assessment for the relevance of ground water metabolites in an | EFSA reported that new FOCUS estimates had been submitted with the addendum to the DAR. A representative from the Fate Group reported that some of the new estimates have been rejected. However, that did not change the overall picture on the issue of toxicological relevance of those metabolites.<br>The RMS referred to the the addendum to the DAR where an evaluation of the | Open point fulfilled.<br>Data gap identified, see data gap 2.3. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | 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.<br><br>See reporting table 2(25). | studies available for the groundwater metabolites M01, M02, M03, M04, M05, M10, M11, M12, M13 and M14 had been provided. M 01 was found in groundwater at levels of up to 6.26 μg/L.<br>Negative in vivo and in vitro genotoxicity studies were available. The LD50 (rat) was between 500 and 2000 mg/kg bw/day. A 90-day study in rats showed that it had a similar toxicity profile in terms of severity of the findings as the parent.<br>In a 2-year rat study with M01 a NOAEL of 5.7 mg/kg bw/d was derived (adenomas were found in males at the highest dose), a value in a similar range as that obtained in a 2-year rat study with fluopicolide, where the NOAEL was 8.4 mg/kg bw/day (based on different findings). Although there were concerns with regard to the validity of that study it was considered acceptable. Also an evaluation report of with M 01 was available from the U.S. EPA and also there the poor quality of some of the study was reported. The toxicological relevance of M01 was then discussed intensely.<br><br>The experts considered the overall available data package both of the metabolite and the parent compound.<br><br>It was noted that that using the ADI of the parent compound would cover the adenomas found with M 01 (in males) in the 2-year study with a margin of safety of 262. Some experts noted that such a margin of safety should be significantly higher (>1000).<br><br>The systemic toxicity of M 01 was higher than that of the parent. The experts agreed that the chronic study was of limited validity and that it was not clear whether all parameters had been investigated.<br><br>Comparing the toxicity of the parent and the metabolite the RMS noted that the MTD was exceeded in both 2-year studies (2500 ppm with fluopicolide and 500 ppm with M01). The NOAELs obtained in the 90-day and the 2-year studies were in the same range. The outstanding issue was the uncertainty in histopathology with the metabolite and the low margin of safety if the ADI of the parent was used to cover the effects observed with the metabolite.<br><br>The metabolite M 01 was considered relevant unless the non-relevance was proven. Therefore the experts agreed to set a data gap. If the notifier disagreed further | |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | | information supporting the non-relevance of M01 should be provided.<br><br>The RMS went then through the assessment of the other metabolites occurring in groundwater that was presented in an addendum to the DAR M02, M05, M010 and M14.<br><br>The experts agreed that none of these metabolites should be considered as toxicologically relevant. | |
| 2.3 | Data gap identified at PRAPeR 39:<br>Notifier to provide further information on M01 if deemed necessary. | | Data gap open. |
| | Open point 2.11<br>Some metabolites are found in rotational crops. Their toxicity should be discussed compared to the toxicological properties of the parent.<br><br>See reporting table 2(26). | In the addendum to the DAR an assessment of the crop metabolites M 04, M08 and M09 was presented. The experts agreed that the toxicity profile of these metabolites was lower than that of the parent compound. | Open point fulfilled. |
| | **Message from Phys Chem to Tox and Ecotox:** Is toluene a relevant impurity? | Toluene should be considered as a relevant impurity, based on hazard considerations. The experts agreed that the amount of 5g/kg is not expected to be of toxicological concern. | |
| | **Message from Phys Chem to Tox:** Is M-01 (2,6-dichloro benzamide) toxicologically relevant? | See open point 2.10 | |

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|---|---|---|---|---|
| | Section 2<br>Data requirements: ***2***<br>Open points: ***11*** | | | Section 2<br>Data requirements: ***1***<br>Data gaps: ***1***<br>Open points:***0*** |
| | Open point 2.1<br>The relevance of the liver weight increase in the 90 day study in dog to be agreed on in an experts' meeting<br><br>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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br>The NOAEL of 70 mg/kg bw/d in the 90-day dog study was confirmed. |
| | Open point 2.2<br>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<br><br>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.<br>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.<br><br>Carcinogenic Potential of Fluopicolide:<br>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 ppm a dose level at which the | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br>Neither for fluopicolide nor for metabolite M01 was a classification for carcinogenicity proposed. |

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| | | 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. | 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.<br><br>The Notifier provided a position paper (Virginie Payraudeau 2/11/2006 – See | |

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| | | | 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.<br><br><u>Carcinogenic Potential of M-01 (BAM)</u><br>The key elements of the RMS assessment the following:<br><br>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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| | | | ii. There was no indication of progression from adenomas to carcinomas.<br><br>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.<br><br>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 carcinogen. | |

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| | | | 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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 2.3<br>The amount of bioavailable fluopicolide after oral administration to be agreed on in an experts' meeting<br><br>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.<br><br>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 correction factor of 0.62 was allowed to account for the extent of oral | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. Value of 62% for oral absorption was confirmed. |

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| | | | 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."<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 2.4<br>The need for setting an ARfD, and the most relevant study to be considered, to be discussed in an experts' meeting<br><br>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.<br><br>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.<br>Open Point: to be discussed at Expert | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br><br>ARfD: 0.18 mg/kg bw |

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| | | | Meeting. | |
| 2.1 | Data requirement<br>Applicant to provide a GLP revision of the acute dermal study (Krotlinger 2003)<br><br>The applicant announced in the written procedure that the report M-220872-02-1 (Krotlinger 2003) is available and can be submitted immediately.<br><br>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.<br><br>Addressed. | PRAPeR 39 (10– 13 12.2007):<br><br>Data requirement fulfilled. |
| | Open point 2.5<br>RMS to provide further details on the results of the *in vivo* dermal absorption study (see comment by NL) in an addendum<br><br>See reporting table 2(18). | | RMS: Further details are presented in Addendum 1 (Nov 2007). See Section B.6.12.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| | Open point 2.6<br>Dermal absorption to be discussed in a meeting of experts<br><br>See reporting table 2(19). | | See Open Point 2.2 above.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| | Open point 2.7<br>The experts to consider whether the default given by | | RMS: It is the RMSs view that although the maximum proposed application volume for the use of EXP 11074B (the | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |

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| | the UK POEM model for high-volume broadcast air-assisted sprayers (500 l/ha) is representative for the real scenarios.<br><br>See reporting table 2(21). | | 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).<br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 2.8<br>The experts to agree on the operator exposure assessment for fluopicolide.<br><br>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.<br><br>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 75$^{th}$ 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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| 2.2 | New data requirement<br>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 | 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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Data requirement fulfilled. |

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| | See reporting table 2(24). | | | |
| | New open point 2.9<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>see data requirement 2.2 |
| | Open point 2.10<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br><br>New data gap identified, see 2.3 |

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| 2.3 | Data gap identified at PRAPeR 39:<br>Notifier to provide further information on M01 if deemed necessary. | | | PRAPeR 39 (10– 13 12.2007):<br><br>Data gap open. |
| | Open point 2.11<br>Some metabolites are found in rotational crops. Their toxicity should be discussed compared to the toxicological properties of the parent.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |

**REPORT OF PRAPeR EXPERT MEETING 40**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

## 3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| 23.11.2007 | UK | Fluopicolide evaluation table rev 1-0 (2007-11-23) residues.doc |
| 02.04.2007 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| 19.11.2007 | UK | Fluopicolide revised list of end points (2007-11-19).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** None

5. **Classification and labelling:** Not discussed

6. **Recommended restrictions/conditions for use:** None

7. **Reference List:** Not discussed

| **Areas of concern:** None |
|---|

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 3. Residues

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 3.1<br>Residue definition for risk assessment in rotational crops to be discussed in an expert meeting<br><br>See reporting table 3(10). | The RMS proposes to include the metabolite M01 in the residue definition for risk assessment because it should be considered as toxic as the parent compound. Based on this RMS conclusion the meeting now also considers the necessity to set conversion factors for risk assessment. For grapes, it is decided that no conversion factor is required because the residue levels of M01 in grapes are negligible compared to the residue levels of the parent. For potatoes and rotational crops, it is also proposed not to set conversion factors for risk assessment because the findings in the potato trials and the rotational crop trials are all below the LOQ. In addition, for potatoes, the metabolism studies indicate that the levels of metabolite M01 are lower than the levels of the parent compound. In the future it may however be considered to set conversion factors for other crops when further uses are supported. | Open point fulfilled.<br><br>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. |
| | Open point 3.2<br>MS to consider whether rotational crop studies are sufficient for drawing final conclusions and whether restrictions are needed in an expert meeting.<br><br>See reporting table 3(23). | For the cold rotational crops studies, the sum of parent compound and metabolite M01 were observed in wheat straw only. In cabbage, minor amounts of the metabolite M01 were identified. For the risk assessment, the meeting agrees to consider a level of 0.04 mg/kg for all leafy vegetables which results in an increase of less than 1 % of the ADI in the chronic exposure. | Open point fulfilled. |
| | Open point 3.3<br>MRL proposal on grapes to be discussed in an expert meeting (validity of the trials with 4 applications, | According to the RMS there is no significant difference between the residue trials with 3 applications and residue trials with 4 applications. It is also believed by the RMS that this will not influence the overall conclusion and the overall MRL proposal. The meeting agrees to keep these northern trials with 4 applications in the overall risk assessment, because the highest residue values were anyway observed in the southern residue trials. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | considering the persistency of the compound)<br>RMS to provide the meeting with statistical analysis of the results.<br><br>See reporting table 3(28). | | |
| | Open point 3.4<br>MS to discuss the approach for risk assessment depending on final decision on residue definition for risk assessment in rotational crops<br><br>See reporting table 3(33). | The residue levels of M01 in rotational crops have been included in the risk assessment for the consumer (see open point 3.2). | Open point fulfilled. |
| | Open point 3.5<br>RMS to check if balance data allow %ages of transference to be calculated<br><br>See reporting table 3(39). | It is noted by the meeting that the different types of wine were put together for the interpretation of the processing trial results. When reporting results of processing studies for wine it is advisable to make distinction between white wine, red wine and heated red wine since these production processes are very different from one another. Consequently the type of wine produced may influence the transference very significantly. In this case the meeting agrees that the type of wine has very little influence on the transference factors for fluopicolide, but in the future it would be advisable to report results for the different types of wine separately. | Open point fulfilled. |
| | Open point 3.6<br>RMS to present the complete assessment for the relevance of ground water metabolites in and | According to the fate and behaviour section, metabolite M01 exceeds 0.75 μg/L and this metabolite is also considered relevant by the mammalian toxicology section. Performing a consumer risk assessment for this ground water metabolite would therefore not influence the outcome of the global peer review (according to guidelines a relevant ground water metabolite is not allowed to exceed 0.75 μg/L in any case). The other metabolites are not considered relevant by the mammalian toxicology section and according to the fate and | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
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| | 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.<br><br>See reporting table 3(40). | behaviour section they are not expected to exceed the trigger value of 0.75 µg/L. Therefore no risk assessment for the consumer is required.<br><br>In conclusion, for the time being a consumer risk assessment for the ground water metabolites is not required. | |
| | New open point | It is noted that the dietary burden intake calculation was not performed considering the grape pomace. According to the present guidelines grape pomace is not to be included in the dietary burden calculation, but in the future this might be required when considering the future OECD guidelines. In the meantime the meting agrees that it is not necessary to include it. | New open point fulfilled. |
| | New open point 3.6:<br>RMS to amend the list of end points according to the discussions during the PRAPeR 40 meeting. | LOEP to be revised considering the above discussions. | Open point open. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Section 3<br>Data requirements: **-**<br>Open points: ***6*** | | | Section 3<br>Data requirements: **-**<br>Open points: ***1*** |
| | Open point 3.1<br>Residue definition for risk assessment in rotational crops to be discussed in an expert meeting<br><br>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.<br>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.<br>Therefore for the above reasons, M01 should not be included in the residues definition for monitoring.<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled.<br><br>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. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
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| | Open point 3.2<br>MS to consider whether rotational crop studies are sufficient for drawing final conclusions and whether restrictions are needed in an expert meeting.<br><br>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).<br><br>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).<br><br>To conclude, a sufficient variety of crops have been looked at with | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | | | sufficient residues data (8 trials on each rotational crop) to conclude that residues in rotational crops will not be significant and restrictions are not needed.<br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 3.3<br>MRL proposal on grapes to be discussed in an expert meeting (validity of the trials with 4 applications, considering the persistency of the compound)<br>RMS to provide the meeting with statistical analysis of the results.<br><br>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).<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
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| | Open point 3.4<br>MS to discuss the approach for risk assessment depending on final decision on residue definition for risk assessment in rotational crops<br><br>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).<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |
| | Open point 3.5<br>RMS to check if balance data allow %ages of transference to be calculated<br><br>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.<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |
| | Open point 3.6<br>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: 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. | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | See reporting table 3(40). | | Open Point: to be discussed at Expert Meeting. | |
| | New open point 3.6:<br>RMS to amend the list of end points according to the discussions during the PRAPeR 40 meeting. | | | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point open. |

**REPORT OF PRAPeR EXPERT MEETING 61**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**1. Physical and Chemical Properties**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| December 2008 | UK | Fluopicolide addendum 2 Vol 4 (December 2008).doc |
| 16-12-2008 | UK | Fluopicolide evaluation table rev1-2 (16-12-2008).doc |
| 2007-04-02 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| November 2008 | UK | Fluopicolide updated list of endpoints (November 2008).doc |

3. Documents tabled at the meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** AE F053616 06WG71 A1 & AE B066752 04 SC61 A1

5. **Classification and labelling:** Not discussed

**6. Recommended restrictions/conditions for use:** Not discussed

**7. Reference list:** Not discussed

| **Areas of concern:** Possible relevant impurities |
|---|

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 1. Physical and Chemical Properties

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 1.1 | Data requirement<br>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.<br><br>See reporting table 1(1).<br><br><u>PRAPeR 36 (27. – 30.11.2007):</u> | Data requirement redundant as a new data requirement has already been proposed during the PRAPeR 36 meeting. | Data requirement redundant, see new data requirement 1.6. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Data requirement redundant.<br>see new data requirement 1.6 | | |
| 1.6 | New data requirement identified at PRAPeR 36:<br>Once full scale manufacturing is in progress then new 5 batch data must be provided.<br><br><u>PRAPeR 36 (27. – 30.11.2007):</u><br><br>Data requirement open. | The RMS indicated that new 5-batch and QC data has been presented in the Addendum 2 to Volume 4 (December 2008). It was noted by the meeting that in the table on page 12 that the statistical analysis is incorrect. It was agreed that this had no implications on the acceptance of the specification.<br><br>The revised proposed specification as given by the applicant on page 13 was agreed by the meeting. It was also accepted that the applicant was going to blend any batches outside the specification. | Data requirement fulfilled |
| 1.5 | Data requirement<br>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. | This data requirement is dependent on whether the toxicology meeting considers that this impurity is relevant.<br><br>Message to tox and ecotox to confirm the relevance of 2,6-dichlorobenzamide (BAM or M01) and to confirm the maximum level. | Data requirement open and pending on the discussions during the meeting on mammalian toxicology and ecotoxicology. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | See reporting table 1(66).<br><br><u>PRAPeR 36 (27. – 30.11.2007):</u><br><br>Data requirement reworded:<br><br>The new data requirement would read as follows<br>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.<br><br>Data requirement open. | | |
| | New open point 1.18:<br><br>The wording in the end points should be clarified. The ranges given in the list of end points should be changed to specific | The RMS confirmed that the LOEPs have been updated and the meeting agreed.. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | LOQs for each matrix.<br><br>PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. | | |
| | New open point 1.19:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting.<br><br>PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. | The RMS confirmed that the LOEPs have been updated and the meeting agreed. | Open point fulfilled. |
| | New open Point 1.20:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 61 meeting. | The list offend points has to be amended:<br><br>The sentence ‘based on pilot plant production’ should be deleted.<br>The box on relevant impurities should be left ‘open’. | Open point open. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Section 1<br>Data requirements: ***5***<br>Open points: ***17*** | | | Section 1<br>Data requirements: ***1***<br>Open points: ***1*** |
| 1.1 | Data requirement<br>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.<br><br>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<br><br>Addressed<br><br>RMS (Dec 2008): See 1.6 below. | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement redundant.<br>New data requirement:<br>Once full scale manufacturing is in progress then new 5 batch data must be provided.<br><br>PRAPeR 61 (13 – 16 January 2009):<br><br>Data requirement redundant, see new data requirement 1.6. |
| 1.6 | New data requirement identified at PRAPeR 36:<br>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 | 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 | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement open.<br><br>PRAPeR 61 (13 – 16 January 2009): |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | | incorporate the results into an addendum to the DAR. The report can be made available upon request. | 2008). To be discussed at an Expert Meeting. | Data requirement fulfilled. |
| | Open point 1.1<br>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.<br><br>See reporting table 1(5). | BCS refer again to our comment made in the reporting tables.<br>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).<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open Point 1.2<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.3<br>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.<br><br>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).<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.4<br>The corrected formulation details should be given.<br><br>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.<br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.5<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.6<br>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 substance should be reported. These issues should be discussed in a | 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 accordingly. Therefore, although not initially, the results in the | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | meeting of experts.<br><br>See reporting table 1(16). | | end were generated using the correct response factor determined using an AE1050605 standard.<br><br>Retention times of active substance and impurities<br>**Method (a)**<br>Fluopicolide – 13.0 min<br>AEC636523 – 11.1 min<br>AC0553913 – 13.0 min<br>AEC639035 – 19.7 min<br>AEC648994 – 25.2 min<br>AE1050605 – 39.5 min<br><br>**Method (b)**<br>Fluopicolide - 21.3 min<br>M-01 - 4.6 min<br>AEC648995 – 6.5 min<br>AEF125577 – 18.4 min<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 1.7<br>LOEP relative density the purity should be given..<br><br>See reporting table 1(24). | | RMS: Purity = 99.3%. However, relative density is no longer included in the current end points template.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.8<br>It should state for the Log Pow that it is independent of pH.<br><br>See reporting table 1(27). | | RMS: Agreed. Log Pow is independent of pH. The end points have been updated.<br><br>Addressed. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.9<br>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.<br><br>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.<br><br>Addressed. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.10<br>The endpoints should use the current agreed template.<br><br>See reporting table 1(33). | | RMS: The LOEP have been updated to the current template. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.11<br>For melting point which sub method of A1 was used.<br><br>See reporting table 1(40). | | RMS: Sub method 1.4.4.2<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.12<br>For the UV/VIS More detailed information about the measurement should be given, e.g. solvent, maximum absorbance.<br><br>See reporting table 1(44). | | RMS: The maximum absorbance is stated in B.2.1.10 as UV absorb 203 nm ($\varepsilon$ = 44159 l $mol^{-1}$ $cm^{-1}$), solvent was methanol<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| 1.2 | Data requirement<br>Explosive properties mechanical sensitivity data should be provided.<br><br>[This should be considered as a technical data requirement as the study has already been submitted]<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |
| 1.3 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (SC).]<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| 1.4 | Data requirement<br>A 2 year storage stability study in the commercial packaging.<br><br>[This should be regarded as a technical data requirement as it is noted that a study has already been provided (WG).]<br><br>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.<br><br>See also Open Point 1.13 below<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled. |
| | Open point 1.13<br>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 or corrigendum (WG).<br><br>See reporting table 1(62). | | RMS: See corrected text and reference in Section 2, Addendum 1.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.14<br>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.<br><br>See reporting table 1(64). | | RMS: References have been deleted from Section 2, Addendum 1.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| 1.5 | Data requirement<br>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.<br><br>See reporting table 1(66). | BCS refer again to our comment made in the reporting tables.<br><br>**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.<br>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 (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 | 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<br><br>Addressed<br><br>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 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 | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement reworded:<br><br>The new data requirement would read as follows<br>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.<br><br>Data requirement open.<br><br>PRAPeR 61 (13 – 16 January 2009):<br><br>Data requirement open and pending on the discussions during the meeting on mammalian toxicology and ecotoxicology. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | | 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. | can be addressed at member state level | |
| | Open point 1.15<br>The LOQs should be given for each analyte in the list of end points.<br><br>See reporting table 1(72). | | RMS: LOQs are as follows:<br>Grape = 0.1 mg/kg<br>Wheat grain = 0.02 mg/kg<br>Potato = 0.02 mg/kg<br>Endpoints table have been updated.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled.<br><br>New open point, see open point 1.18 |
| | New open point 1.18:<br><br>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):<br><br>Open point open.<br><br>PRAPeR 61 (13 – 16 January 2009):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 1.16<br>At least the linearity range should be given for all the residue methods.<br><br>See reporting table 1(78). | | RMS: Linearity ranges are as follows;<br>Plant (Parent) = 0.01–1 µg/ml<br>Soil (Parent/M03) = 0.4–75 µg/l<br>Soil (M01/M02) = 0.4–100 µg/l<br>Water (Parent/M01/M02) = 0.2–25 µg/l<br>Air (Parent) = 0.01–1 µg/ml<br>Animal(Parent/M01/M02) = 0.1-10µg/ml<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.17<br>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.<br><br>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.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | New open point 1.19:<br><br>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):<br><br>Open point open.<br><br>PRAPeR 61 (13 – 16 January 2009):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | New open Point 1.20:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 61 meeting. | | | PRAPeR 61 (13 – 16 January 2009):<br><br>Open point open. |

**REPORT OF PRAPeR EXPERT MEETING 62**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**4. Fate and behaviour in the environment**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| December 2008 | UK | Fluopicolide addendum 2 Vol 3 B6-B8-B9 (December 2008).doc |
| December 2008 | UK | Fluopicolide addendum 2 Vol 4 (December 2008) cover page.doc |
| 16-12-2008 | UK | Fluopicolide evaluation table rev1-2 (16-12-2008).doc |
| 2007-04-02 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| November 2008 | UK | Fluopicolide updated list of endpoints (November 2008).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| None | | |

The conclusions of the meeting were as follows:

**4. Data on preparations:** AE F053616 06 WG 71 Al (vines); AE B066752 04 SC 61 Al (potatoes)

**5. Classification and labelling:** candidate for R53

**6. Recommended restrictions/conditions for use:** none identified

**7. Reference list:** not discussed

**Areas of concern:** leaching of a.s. and soil metabolites that require non-relevance assessment.

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 4. Fate and behaviour

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 4.1 | Data requirement<br>Notifier to provide an estimation of soil photolysis half lives at other latitudes (i.e 40 ºN and 45 ºN).<br><br>Applicant indicated to submit a position paper (Report MEF-06/495) by April 2007.<br><br>See reporting table 4(14).<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Data requirement still open.<br><br>Calculation of $DT50_{photolysis}$ for adequate latitudes in Europe. | The experts had no issue with the experimentally determined half life in the study. However the issue of the light energy applied in the experiment and how this equates to natural conditions that will occur in the EU was the basis for this point of clarification.<br><br>In the response to the point of clarification reconfirmed in PRAPeR 37 the applicant has presented a new position paper that has been summarised and assessed by the RMS in the addendum 2 (starting on page 34).<br>The RMS using argumentation provided by the applicant equated the study conditions to a 85 day DT50 representative location Tunis to 355 days representative location London, (June summer sunlight days (day length for the latitude)).<br><br>The basis of the applicants position is that the light energy used in the study was exaggerated compared to the natural light conditions in Scotland. Therefore the applicant proposes to correct the values obtained in the study to estimate the half life that according their position should represent degradation at Scotland latitude.<br><br>In the correction one of the factors relates to the wavelengths interval considered (290 – 800 nm in the study versus 300 – 3000 nm in the applicant recalculations). EFSA noted that the Global radiation spectrum (data from CIE publication No. 20, 1972) are the reference used in these calculations but it is not transparent that the values provided in these global radiation tables are at ground level and how the angle of incidence of the radiation was accounted for. A clarification of these details would be welcomed.<br><br>A different picture of the half life related to Scotland natural summer sunlight conditions is included in the original study report produced by the contract organisation that did the experiment. (Energy in the experiment produced by the apparatus was equated to a measurement in a June 1990 reference day that they equated to a wider period of | Data requirement amended.<br>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).<br>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. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | meteorological June values 1982 to 1989).<br><br>Based on the information available the experts were not able to identify that one approach or the other (That of the applicant or the contract laboratory) for equating to natural light conditions was more reasonable. Clearly, the different approaches give a different picture.<br>The data requirement was amended and reset with the aim of getting a less confused picture of the possible contribution of photolysis to the field dissipation study half lives.<br><br>If the calculations presented above were accepted (85 day DT50 representative location Tunis to 355 days representative location London) after the data requirement set has been addressed, the soil photolysis process would not be expected to be contributing significantly to degradation relative to other processes. In this situation (degradation is primarily biodegradation) normalised field DT50 values would be clearly appropriate for use in leaching modelling (as already discussed and agreed under OP 4.9 during fate and behaviour PRAPeR 37) | |
| | New open point 4.21:<br><br>RMS to include in the LoEP the values from HS fitting presented in the addendum.<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Open point open. | Hockey Stick values as presented in the addendum of November 2007 have been included in the LoEP. | Open point fulfilled. |
| | New open point 4.22:<br>RMS to include the non normalised SFO DT50 values for parent used for their calculation of the accumulated PECsoil | These values have now been incorporated into the List of End Points. The RMS also wishes to state that in Volume 3, Section B.8.1.5(a), the RMS calculated DT50 for fluopicolide of 133 days for the Rodelsee site is <u>incorrect</u> and should read **253 days ($r^2$ = 0.818) for 0-20cm depth** (SFO). The RMS apologises for this mistake. | Open point fulfilled |

<table>
<tr><th>No.</th><th>Subject</th><th>Discussion Expert Meeting</th><th>Conclusions Expert Meeting</th></tr>
<tr><td></td><td>in the/a table in the LoEP.<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Open point open.</td><td></td><td></td></tr>
<tr><td></td><td>New open point 4.23:<br><br>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 field.<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Open point open.</td><td>Following the PRAPeR 37 meeting, RMS clarified in addendum 2 that the maximum observed formation levels of metabolites are:<br><br>Table B.8.2 Maximum observed formation of fluopicolide metabolites M01 and M02 in field dissipation studies<br><br><table><tr><th></th><th>% molar basis (adjusted for molecular weight)</th><th>% wt/wt</th><th>Study location</th></tr><tr><td>M01</td><td>24.1</td><td>11.9</td><td>Senas (1999)</td></tr><tr><td>M02</td><td>16.3</td><td>9.6</td><td>Senas (1999)</td></tr></table><br>Formation % from the Senas 2000 field site shown in Table B.8.145 of the DAR should be excluded from consideration. The RMS PECsoil calculations for M01 in vines have been amended in the List of End Points to reflect the revised observed formation rates. Amendment of PECsoil for M02 is not needed as this has already been conducted with the correct values as shown in Table B.8.2 above.</td><td>Open point fulfilled</td></tr>
<tr><td>4.3</td><td>Data requirement<br>Applicant to provide</td><td>New FOCUS PEARL GW calculations for the potato and the vines GAP have been submitted by the notifier and assessed by the RMS in addendum 2 from page 39 onward.</td><td>Data requirement fulfilled.</td></tr>
</table>

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | 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.**<br><br>For some of the metabolites it may not be confirmed that the 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.<br><br>Applicant indicated to submit new PEC GW calculations with a second model and lower interception rate for vines by May 2007. | The experts were content with the new modelling as evaluated in the addendum which was considered appropriate. However final acceptability will depend on the confirmation that normalised field half lives represent primarily biodegradation (see discussion at data requirement 4.1, where the data requirement is still open) | |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | See reporting table 4(79).<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Data requirement maintained. The applicant is requested to submit a first Tier standard FOCUS PEARL modelling.<br><br>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. | | |
| | Open point 4.18<br>RMS to indicate in the LoEP box “relevant metabolites” in soil the max. amount of M02 | For clarification of the maximum amount of M02 in field studies, please see Open Point 4.23 above; the maximum amount is 16.3% on a molar basis. The List of End Points has been amended. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | (with respect to applied fluopicolide) found in field studies (at this stage this value is 21.3 %).<br><br>See reporting table 4(84).<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Open point still open. | | |
| | New open point 4.24:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting.<br><br><u>PRAPeR 37 (03. – 06.12.2007):</u><br><br>Open point open. | RMS indicated that the amendments required to the List of End Points have been implemented. | Open point fulfilled |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | Section 4<br>Data requirements: ***4***<br>Open points: ***20*** | | | Section 4<br>Data requirements: ***1***<br>Open points: ***0*** |
| | Open point 4.1<br>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.<br>RMS to amend the list of end points accordingly.<br><br>MS experts to discuss if the half lives derived from the study dosed with M02 may however still be used for modelling.<br><br>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.<br><br>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.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.2<br>RMS to clarify normalized laboratory DT50's values for fluopicolide and metabolites. I.e for fluopicolide in LoEP | | RMS: Please see RMS Addendum 1 (Nov 2007), and updated LoEP.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | the range is 194 – 333 d when for 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.<br><br>See reporting table 4(10). | | | |
| | Open point 4.3<br>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.<br><br>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.<br>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.<br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| 4.1 | Data requirement<br>Notifier to provide an estimation of soil photolysis half lives at other latitudes | 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 | 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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement still open. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | (i.e 40 ºN and 45 ºN).<br><br>Applicant indicated to submit a position paper (Report MEF-06/495) by April 2007.<br><br>See reporting table 4(14). | degradation studies and contains in the appendix a calculation of soil photolysis half lives at other latitudes. The report will be submitted with the updated dossier.<br>**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. | updated LoEP.<br>RMS concludes that soil photolysis at 40ºN and 45ºN is unlikely to significantly influence the degradation of fluopicolide in soil.<br>Addressed.<br><br>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). | Calculation of $DT50_{photolysis}$ for adequate latitudes in Europe.<br><br>PRAPeR 62 (13 -17 10.2008):<br><br>Data requirement amended.<br>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).<br>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. |
| | Open point 4.4<br>MS experts to discuss the formation fractions derived from laboratory studies for | | RMS has no further comment to make in relation to this open point. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | modelling purposes. This discussion should also include the effect of temperature and moisture normalization procedures.<br><br>See reporting table 4(17). | | Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.5<br>MS experts to discuss potential influence of the different extraction method employed on the respective results of the laboratory and field studies.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion.<br><br>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.<br><br>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.<br>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. | PRAPeR 37 (03. – 06.12.2007):<br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | 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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.6<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.7<br>MS experts to discuss the conceptual model used to derive the kinetic parameters used for modelling. In particular paying attention to:<br>– the absence of a flow from the parent to the sink | | RMS: RMS agrees with Applicant comment to this point. RMS believes that formation constants have been normalised by the process.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | compartment and<br>– the effect of normalization of degradation constants without the corresponding normalization of the formation constants.<br><br>Applicant provided an explanatory note in the "Comments to the reporting table". To be considered by MSs experts in their discussion.<br><br>See reporting table 4(34). | | | |
| | Open point 4.8<br>MS experts to discuss in an experts meeting the kinetic evaluation of field dissipation studies.<br><br>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 submitted upon request. | 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 possible, a discussion of this open point is still possible.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.21 |
| | New open point 4.21:<br><br>RMS to include in the LoEP the values from HS fitting | | RMS December 2008: The LOEP have been amended as requested. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | presented in the addendum. | | | PRAPeR 62 (13 -17 10.2008):<br><br>Open point fulfilled. |
| 4.2 | Data requirement<br>Applicant to present the position paper with their evaluation of the accumulation studies.<br><br>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.<br><br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement fulfilled. |
| | Open point 4.9<br>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).<br><br>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.<br><br>To assess the influence of photo-degradation in overall degradation of fluopicolide in soil under field conditions, the Applicant ran | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | 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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.10<br>MS experts to discuss whether the lysimeter study represents a worst case with respect to the formation of metabolites.<br><br>See reporting table 4(54). | | 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 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. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | Open Point: to be discussed at Expert Meeting. | |
| | Open point 4.11<br>RMS to update GAP table with 5d minimum application interval for potatoes.<br><br>See reporting table 4(59). | | RMS: The GAP table in the LOEPs has been amended.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.12<br>MS experts to discuss if the use of the 90$^{th}$ percentile is appropriate for PEC soil calculations.<br><br>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 90$^{th}$ percentile DT50 values in PECsoil calculations is one of the subjects discussed in the DE paper.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.22: |
| | New open point 4.22:<br>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.<br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open.<br><br>PRAPeR 62 (13 -17 10.2008):<br><br>Open point fulfilled. |
| | Open point 4.13<br>MS experts to discuss if FOCUS GW scenarios with normalized $DT_{50}$ 's are appropriate for PEC soil | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |

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| | calculation.<br><br>See reporting table 4(61). | | | |
| | Open point 4.14<br>MS to discuss whether the M01 half lives may be considered appropriate degradation half lives for modelling PEC soil.<br><br>See reporting table 4(62). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.15<br>MS experts to discuss which maximum amount formed of M01 should be considered for PEC soil calculations.<br><br>40.2 % comes form laboratory studies. It is doubtful that field studies are capable to identify the maximum formation of a metabolite.<br><br>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 | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br>New open point proposed, see open point 4.23. |

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| | | | lab studies.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | New open point 4.23:<br><br>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 field. | **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.<br>Maximum formation values of the 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). | RMS December 2008: The LOEPs have been amended as appropriate to reflect the discussions at the Expert Meeting in December 2007.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open.<br><br>PRAPeR 62 (13 -17 10.2008):<br><br>Open point fulfilled. |
| | Open point 4.16<br>MS experts to discuss the different approaches taken for the PEC soil calculation.<br><br>See reporting table 4(69). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point closed. |
| 4.3 | Data requirement<br>Applicant to provide results with a second FOCUS model following the recommendations given in | 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.<br>Report MEF-07/165 refers to point 4 | 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. | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement maintained. The applicant is requested to submit a first Tier standard FOCUS PEARL modelling. |

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|---|---|---|---|---|
| | 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.**<br><br>For some of the metabolites it may not be confirmed that the 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.<br><br>Applicant indicated to submit new PEC GW calculations with a second model and lower interception rate for vines by May 2007.<br><br>See reporting table 4(79). | (81) in the reporting tables which was mentioned as a data requirement but is not explicitly mentioned in the evaluation table.<br>**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 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).<br>The outcome of these modelling assessments is essentially the same as previous assessments. All metabolites remain within the current trigger values. | 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).<br><br>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.<br><br>Based on the new $PEC_{GW}$, the following metabolites are predicted to exceed<br>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.<br><br>For both the models, $PEC_{GW}$ of M-01 following use on vines were between | 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.<br><br>PRAPeR 62 (13 -17 10.2008):<br><br>Data requirement fulfilled. |

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| | | | >0.75 µg/l and <10 µg/l. $PEC_{GW}$ of the other metabolites simulated were all <0.75 µg/l.<br><br>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 >0.75 µg/l and <10 µg/l at Jokioinen (PELMO, application every year).<br><br>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..<br><br>Open Point: to be discussed at Expert Meeting.<br><br>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 | |

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| | | | December 2008. The RMS considers that the calculations are acceptable.<br>Addressed. | |
| 4.4 | Data requirement<br>Applicant to repeat the FOCUS GW calculations following the GAP as reported in the Representative uses table.<br><br>Applicant indicated to submit repeated PEC GW calculations with a lower interception rate for vines by May 2007.<br><br>See reporting table 4(80). | See comment under data requirement 4.3 above. | RMS: Please see comment under data requirement 4.3 above.<br><br>Open Point: to be discussed at Expert Meeting.<br><br>RMS December 2008: Please see above for Data Requirement 4.3. | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement fulfilled for PELMO. For PEARL: see data requirement 4.3. |
| | Open point 4.17<br>MS experts to discuss the approach taken by the RMS to calculate the amount of M02 formed in field<br><br>See reporting table 4(84). | | RMS: RMS has no further comment to make in relation to this open point.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point closed. |
| | Open point 4.18<br>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 %). | | RMS: RMS proposes that this open point be dealt with after discussion proposed at open point 4.17.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point still open.<br><br>PRAPeR 62 (13 -17 10.2008):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | See reporting table 4(84). | | RMS December 2008: The LOEPs have been amended as appropriate.<br>Addressed. | |
| | Open point 4.19<br>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).<br><br>See reporting table 4(88). | | RMS: LoEP has been amended in relation to input parameters used in modelling.<br><br>Addressed. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | Open point 4.20<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled. |
| | New open point 4.24:<br><br>RMS to amend the list of end | | RMS December 2008: The LOEPs have now been amended as appropriate. | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |

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|---|---|---|---|---|
| | points according to the discussions during the PRAPeR 37 meeting. | | Addressed. | PRAPeR 62 (13 -17 10.2008):<br><br>Open point fulfilled. |

**REPORT OF PRAPeR EXPERT MEETING 63**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**5. Ecotoxicology**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| December 2008 | UK | Fluopicolide addendum 2 Vol 3 B6-B8-B9 (December 2008).doc |
| December 2008 | UK | Fluopicolide addendum 2 Vol 4 (December 2008) cover page.doc |
| 16-12-2008 | UK | Fluopicolide evaluation table rev1-2 (16-12-2008).doc |
| 2007-04-02 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| November 2008 | UK | Fluopicolide updated list of endpoints (November 2008).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** see report of PRAPeR 38

5. **Classification and labelling:** see report of PRAPeR 38

6. **Recommended restrictions/conditions for use:** see report of PRAPeR 38

7. **Reference list:** see report of PRAPeR 38

**Areas of concern:** see report of PRAPeR 38

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 5. Ecotoxicology

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New open point 5.13:<br>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).<br><br><u>PRAPeR 38 (03 – 07 12.2007):</u><br><br>Open point open. | In the revised risk assessment an interception of 60-80% was assumed by the RMS. This cover the BBCH >57 (interception >70%). Since fluopicolide is applied to BBCH 53-81, earlier stages are not covered. The experts agreed with the RMS to reduce the number of application or to increase spray drift interval to addresse the risk for earlier stage use. | Open point open:<br><br>RMS to update the LoE according to the current standard format. |
| | New open point 5.14:<br>RMS to revise LoEP with correct short-term bird endpoint.<br><br><u>PRAPeR 38 (03 – 07 12.2007):</u> | It has been done | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point open. | | |
| | Open point 5.5<br>RMS to include the information and argumentation regarding the ecotoxicological relevance of GW metabolites presented in column 3 in an addendum for the sake of completeness.<br><br>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".<br><br>No discussion in an | RMS presented in the addendum 2 revised risk assessment from groundwater metabolites using revised PECgw. The meeting agreed to request the 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 open.<br><br>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. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | experts meeting is required.<br><br>See reporting table 5(27).<br><br><u>PRAPeR 38 (03 – 07 12.2007):</u><br><br>Open point still open. | | |
| | Open point 5.6<br>RMS to correct the list of endpoint with exact %-age effect on fecundity instead of <50%. Note that highest conc. with effects <50% for *A. rhopalosiphi* was 2 L/ha<br><br>See reporting table 5(38).<br><br><u>PRAPeR 38 (03 – 07 12.2007):</u><br><br>Open point still open: RMS to revise LoEP | It hs been done | Open point fulfilled. |
| | Open point 5.7<br>RMS to update the list of endpoints for earthworms. It is still not clear if the values | It has been done.<br>The applicant proposed that it is more appropriate to express the endpoint for the formulation contening more than one a.s in g /ha and to compare this with the application rate for the estimation of the risk. The meeting agreed to leave the endpoint in mg a.s /kg soil and to update the LoE. A clarification on the endpoint for earthworm reported in the | Open point open:<br><br>RMS to update the LoE with the endpoint for earthworm in |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | for the formulation are based on a.s. or formulation concentrations. Furthermore, values should be given as mg/kg DS.<br><br>Corrected calculations should be included in a corrigendum.<br><br>See also the comment from the applicant on the reporting table to be discussed in an experts meeting.<br><br>See reporting table 5(39).<br><br><u>PRAPeR 38 (03 – 07 12.2007):</u><br><br>Open point still open. | LoE is also nessessary. | mg a.s./kg soil. A clarification on the endpoint for earthworm reported in the LoE is also nessessary. |
| 5.1 | Data requirement identified at PRAPeR 38:<br><br>Notifier to address the ecotoxicological relevance of toluene in the technical material. | The applicant provide a statement which was evaluated by RMS. Overall the toluene derived from fluopiconide technical use in PPPs will not cause concern from an ecotoxicological perspective. The experts agreed.<br>A summary of the applicant report should be included in an addendum. | Data requirement fulfilled.<br><br>New open point proposed, see below. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | PRAPeR 38 (03 – 07 12.2007):<br><br>Data gap open. | | |
| | New open point 5.15:<br><br>RMS to include in an addendum a summary of the applicant. | | Open point open. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | Section 5<br>Data requirements: **-**<br>Open points: ***12*** | | | Section 5<br>Data requirements: **-**<br>Open points: ***4*** |
| | Open point 5.1<br>RMS to clarify in an addendum how the MAF for different vegetation was calculated and used in the assessment of risk to birds.<br><br>Note: This open point was set after a comment on the reporting table during the written procedure.<br><br>See reporting table 5(9). | | RMS: See Addendum 1 (Nov 2007).<br>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.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.2<br>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.<br><br>See reporting table 5(15). | | RMS: See Addendum 1 (Nov 2007)<br>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.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled.<br><br>Two new open point proposed, see open point 5.13 and 5.14 |
| | New open point 5.13:<br>RMS to include a note in the | | RMS (December 2008): See revised LOEPs. | PRAPeR 38 (03 – 07 12.2007): |

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| | 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). | | 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.<br><br>Open point fulfilled. | Open point open.<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Open point open.<br><br>RMS to update the list of end points according to the current standard format. |
| | New open point 5.14:<br>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.<br><br>Open point fulfilled. | PRAPeR 38 (03 – 07 12.2007):<br>Open point open.<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Open point fulfilled. |
| | Open point 5.3<br>RMS to include the information on Log Pow values for the metabolites in an addendum (only data for M02 and M03 are available in | | RMS: See Addendum1<br>Further consideration and discussion with respect to log Pow and low bioconcentration potential of fluopicolide metabolites presented (B.9.2). | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |

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|---|---|---|---|---|
| | Vol.B.2.1 of the DAR. No discussion in an experts meeting is required.<br><br>See reporting table 5(21). | | Point addressed. | |
| | Open point 5.4<br>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.<br><br>See reporting table 5(25). | | RMS: See Addendum1<br><br>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.<br>(LOEPs also corrected).<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.5<br>RMS to include the information and argumentation regarding the ecotoxicological relevance of GW metabolites presented in column 3 in an addendum for the sake of completeness.<br><br>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 | | RMS: See Addendum1<br>Aquatic risk of groundwater metabolites presented (Tables 9.2.2 and 9.2.3).<br>Low aquatic risk indicated.<br>Ecotoxicological relevance of GW metabolites discussed.<br>GW metabolites considered ecotoxicologically not relevant<br><br>Point addressed.<br>(also addresses Open pt. 5.12) | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open.<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Open point open.<br><br>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. |

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|---|---|---|---|---|
| | 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".<br><br>No discussion in an experts meeting is required.<br><br>See reporting table 5(27). | | 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.<br><br>Open point fulfilled. | |
| | Open point 5.6<br>RMS to correct the list of endpoint with exact %-age effect on fecundity instead of <50%. Note that highest conc. with effects <50% for *A. rhopalosiphi* was 2 L/ha<br><br>See reporting table 5(38). | | RMS: See Addendum1<br>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 proposed uses.<br><br>Point addressed.<br><br>RMS (December 2008): The LOEPs has been revised to include<br>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. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open: RMS to revise LoEP<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Open point fulfilled. |

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| | | | Open point fulfilled. | |
| | Open point 5.7<br>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.<br><br>Corrected calculations should be included in a corrigendum.<br><br>See also the comment from the applicant on the reporting table to be discussed in an experts meeting.<br><br>See reporting table 5(39). | | RMS: See Addendum1<br>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.<br><br>Point addressed<br><br>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 have been also been amended (see Open pt. 5.8). No change in low risk conclusion.<br><br>Open point fulfilled. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point still open.<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Open point open:<br><br>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. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the evaluation group |
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| | Open point 5.8<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting.<br><br>RMS (December 2008): See Open pt. 5.8 | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.9<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.10<br>RMS to include the argumentation for why no 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.<br><br>See reporting table 5(48). | | RMS: See Addendum1<br>Further discussion presented (B.9.8) concluding likely insignificant effects of M03 on soil microbial activity in the absence of data.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |

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| | Open point 5.11<br>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.<br><br>See reporting table 5(49). | | RMS: See Addendum1<br>Further discussion presented (B.9.9) concluding insignificant effects of M01 on off-field non-target plants.<br><br>Point addressed. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.12<br>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.<br><br>See reporting table 5(53). | | RMS: Ecotoxicological relevance of GW metabolites discussed in Addendum 1 (Nov 2007). RMS considers the GW metabolites to be ecotoxicologically not relevant.<br>(see also Open pt. 5.5)<br>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 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. | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point closed; see open point 5.5 |

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| | | | Point addressed.<br><br>Open Point: to be discussed at Expert Meeting. | |
| 5.1 | Data requirement identified at PRAPeR 38:<br><br>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<br>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%.<br>A review of the literature shows that the 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. | 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 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 | PRAPeR 38 (03 – 07 12.2007):<br>Data requirement open.<br><br>PRAPeR 63 (12. – 16.01.2009)<br><br>Data requirement fulfilled.<br><br>New open point proposed, see below. |

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| | | 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.<br>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. | 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.<br><br>Data gap closed. Point addressed. | |
| | New open point 5.15:<br><br>RMS to include in an addendum a summary of the applicant. | | | PRAPeR 63 (12. – 16.01.2009)<br><br>Open point open. |

**Report of PRAPeR Expert MEETING 64**

FLUOPICOLDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

**2. Mammalian Toxicology**

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| December 2008 | UK | Fluopicolide addendum 2 Vol 3 B6-B8-B9 (December 2008).doc |
| December 2008 | UK | Fluopicolide addendum 2 Vol 4 (December 2008) cover page.doc |
| 16-12-2008 | UK | Fluopicolide evaluation table rev1-2 (16-12-2008).doc |
| 2007-04-02 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| November 2008 | UK | Fluopicolide updated list of endpoints (November 2008).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** SC: “EXP 11120A”; WG: “EXP 11074B”

5. **Classification and labelling:** none proposed

6. **Recommended restrictions/conditions for use:** none proposed

7. **Reference List:** not discussed

| **Areas of concern:** none |
|---|

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 2. Mammalian toxicology

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 2.3 | Data gap identified at PRAPeR 39:<br>Notifier to provide further information on M01 if deemed necessary.<br><br><u>PRAPeR 39 (10– 13 12.2007):</u><br><br>Data gap open. | The additional information on M01 was presented by RMS in the Addendum 2:<br>2-years dog study, multigeneration rat study, developmental study in rabbit, 90-days dog. Detailed risk assessment for BAM as groundwater metabolite was additionally performed.<br>Genotoxicity: *in vitro* and *in vivo* studies indicate no genotoxic potential<br>Based on the available data set, BAM does not seem to have any effects on reproduction, development, there were no indication of carcinogenic effects.<br>RMS proposed to use the ADI from the parent, but there are also enough studies on BAM to set an ADI for BAM itself (only the long-term mouse study and the developmental rat study are not available). The effect levels of BAM and fluopicolide are very similar. Due to the fact that BAM is a metabolite of several active ingredients (e.g. dichlobenil), it was decided by the experts to set the trigger values on BAM studies and not to use the ADI from fluopicolide.<br>The experts proposed the ADI for BAM of 0.05 mg/kg bw/d, based on the a) long-term rat study (NOAEL = 5.7 mg/kg bw/d) and b) the 2-years dog study (NOAEL = 4.5 mg/kg bw/d), both performed with BAM itself.<br>Taking into account the whole tox profile of fluopicolide and BAM (even if the studies on BAM are partially old and might have some limitations), it was agreed that there is no need to increase the SF for BAM.<br><br>The experts noted that ARfD for fluopicolide was set at 0.18 mg/kg bw, based on liver and kidney findings and impaired growth in the 28-days rat study (even if these are not really acute effects/concerns).<br>ARfD for BAM could be set at 0.3 mg/kg bw, based on maternal body weight loss in the developmental tox study in rabbits (NOAEL = 30 mg/kg bw/d) and a SF of 100. | Data gap obsolete.<br>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 metabolite. |
| | Message from Section 1 on Physical and chemical | In the Addendum 2 the tox batch analysis and the technical specification are presented. The experts agreed that M01 as an impurity is not of relevance. | Answer from section 2 to section 1: |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | properties:<br>Please confirm the relevance of 2,6-dichlorobenzamide (BAM or M01) and confirm the maximum level | | BAM is not relevant as impurity in the technical specification of fluopicolide. |
| | Message from Section 5 on residues:<br>Please confirm the new ADI for M-01 (0.045 mg/kg bw/day?)<br>Can we still use the ARfD set for fluopicolide also for M-01? | See 2.3 | Answer from section 2 to section 5:<br><br>The ADI for BAM (M-01) is 0.05 mg/kg bw/day and the ARfD for BAM is 0.3 mg/kg bw. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
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| | Section 2<br>Data requirements: ***2***<br>Open points: ***11*** | | | Section 2<br>Data requirements: ***0***<br>Data gaps: ***0***<br>Open points:***0*** |
| | Open point 2.1<br>The relevance of the liver weight increase in the 90 day study in dog to be agreed on in an experts' meeting<br><br>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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br>The NOAEL of 70 mg/kg bw/d in the 90-day dog study was confirmed. |
| | Open point 2.2<br>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<br><br>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.<br>An additional expert opinion has recently been provided by Dr. C. | 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.<br><br>Carcinogenic Potential of Fluopicolide:<br>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 ppm a dose level at which the | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br>Neither for fluopicolide nor for metabolite M01 was a classification for carcinogenicity proposed. |

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| | | Gopinath who was responsible for the 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. | 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.<br><br>The Notifier provided a position paper (Virginie Payraudeau 2/11/2006 – See | |

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| | | | 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.<br><br><u>Carcinogenic Potential of M-01 (BAM)</u><br>The key elements of the RMS assessment the following:<br><br>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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| | | | ii. There was no indication of progression from adenomas to carcinomas.<br><br>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.<br><br>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 carcinogen. | |

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| | | | 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.<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 2.3<br>The amount of bioavailable fluopicolide after oral administration to be agreed on in an experts' meeting<br><br>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.<br><br>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 correction factor of 0.62 was allowed to account for the extent of oral | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. Value of 62% for oral absorption was confirmed. |

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| | | | 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."<br><br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 2.4<br>The need for setting an ARfD, and the most relevant study to be considered, to be discussed in an experts' meeting<br><br>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.<br><br>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.<br>Open Point: to be discussed at Expert | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br><br>ARfD: 0.18 mg/kg bw |

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| | | | Meeting. | |
| 2.1 | Data requirement<br>Applicant to provide a GLP revision of the acute dermal study (Krotlinger 2003)<br><br>The applicant announced in the written procedure that the report M-220872-02-1 (Krotlinger 2003) is available and can be submitted immediately.<br><br>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.<br><br>Addressed. | PRAPeR 39 (10– 13 12.2007):<br><br>Data requirement fulfilled. |
| | Open point 2.5<br>RMS to provide further details on the results of the *in vivo* dermal absorption study (see comment by NL) in an addendum<br><br>See reporting table 2(18). | | RMS: Further details are presented in Addendum 1 (Nov 2007). See Section B.6.12.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| | Open point 2.6<br>Dermal absorption to be discussed in a meeting of experts<br><br>See reporting table 2(19). | | See Open Point 2.2 above.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| | Open point 2.7<br>The experts to consider | | RMS: It is the RMSs view that although the maximum proposed application | PRAPeR 39 (10– 13 12.2007): |

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| | 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.<br><br>See reporting table 2(21). | | 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).<br>Open Point: to be discussed at Expert Meeting. | Open point fulfilled. |
| | Open point 2.8<br>The experts to agree on the operator exposure assessment for fluopicolide.<br><br>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.<br><br>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 75$^{th}$ 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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| 2.2 | New data requirement<br>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 | 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.<br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Data requirement fulfilled. |

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| | specification<br><br>See reporting table 2(24). | | | |
| | New open point 2.9<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>see data requirement 2.2 |
| | Open point 2.10<br>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.<br><br>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.<br><br>Open Point: to be discussed at Expert | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled.<br><br>New data gap identified, see 2.3 |

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|---|---|---|---|---|
| | | | Meeting. | |
| 2.3 | Data gap identified at PRAPeR 39:<br>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<br><br>a) data already submitted with the fluopicolide dossier<br>b) tox data on BAM submitted in the US for dichlobenil which were not submitted in Europe for neither fluopicolide nor dichlobenil but were included into the negative reference list of the dichlobenil dossier.<br>The position paper can be made available upon request<br><br>The following conclusions can be drawn from the available data:<br><br>**Pesticidal /biological assessment** – M01 has been shown to have no fungicidal or herbicidal activity.<br><br>**Toxicological assessment** - M01 has been shown:<br><br>- not to be genotoxic in an Ames, HPRT and UDS tests *in-vitro*, and in | 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).<br>These data include further information on longer term toxicity in dogs, reproductive toxicity in rats, and 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.<br>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 | PRAPeR 39 (10– 13 12.2007):<br><br>Data gap open.<br><br>PRAPeR 64 (19 -23 01.2009):<br><br>Data gap obsolete.<br>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 metabolite. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | | micronucleus test *in-vivo*.<br><br>- 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.<br><br>- to have a $LD_{50}$ is in the range between 500 and 2330 mg/kg and therefore not toxic (T) or very toxic (T+).<br><br>- not to be carcinogenic<br><br>- not to be a reproductive toxicant<br><br>therefore to be non-toxicologically relevant<br><br>**Total Dietary Risk Assessment** considering all sources of the diet:<br>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.<br><br>**Ecotoxicological assessment** – M01 (AE C653711) has been shown not to | of the relevance/non-relevance is provided in the Addendum 2 (dated December 2008).<br>Addressed. | |

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| | | be toxic to any of the tested aquatic organisms. Therefore it can be considered as not ecotoxicologically relevant in aquatic systems.<br><br>**M01 (AE C653711) has been shown clearly and comprehensively to be non-relevant.** | | |
| | Open point 2.11<br>Some metabolites are found in rotational crops. Their toxicity should be discussed compared to the toxicological properties of the parent.<br><br>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.<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |
| | Message from section 1 to section 2:<br>Please confirm the relevance of 2,6-dichlorobenzamide (BAM or M01) and confirm the maximum level | | | Answer from section 2 to section 1:<br><br>BAM is not relevant as impurity in the technical specification of fluopicolide. |
| | Message from section 5 to section 2:<br>Please confirm the new ADI for M-01 (0.045 mg/kg bw/day?)<br>Can we still use the ARfD set for fluopicolide also for M-01? | | | Answer from section 2 to section 5:<br><br>The ADI for BAM (M-01) is 0.05 mg/kg bw/day and the ARfD for BAM is 0.3 mg/kg bw. |

**REPORT OF PRAPeR EXPERT MEETING 65**

FLUOPICOLIDE

Rapporteur Member State: UK

Specific comments on the active substance in the section

## 3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

2. Documents submitted for meeting:

| Date | Supplier | File Name |
|---|---|---|
| December 2008 | UK | Fluopicolide addendum 2 Vol 4 (December 2008) cover page.doc |
| 16-12-2008 | UK | Fluopicolide evaluation table rev1-2 (16-12-2008).doc |
| 2007-04-02 | UK | Fluopicolide reporting table rev 1-1 (2007-04-02).doc |
| November 2008 | UK | Fluopicolide updated list of endpoints (November 2008).doc |

3. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| none | | |

The conclusions of the meeting were as follows:

4. **Data on preparations:** EXP 1107 4B

5. **Classification and labelling:** Not relevant.

6. **Recommended restrictions/conditions for use:** refer to PRAPeR 40

7. **Reference List:** Not discussed.

| **Areas of concern:** refer to PRAPeR 40 |
|---|

Appendix 1: Discussion table: FLUOPICOLIDE

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Fluopicolide (Fu)

## 3. Residues

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New open point 3.6:<br>RMS to amend the list of end points according to the discussions during the PRAPeR 40 meeting.<br><br><u>PRAPeR 40 (12 – 13 December 2007):</u><br><br>Open point open. | | Open point fulfilled.<br><br>The list of end points was up-dated according the discussion during the PRAPeR 40 meeting in the version of November 2008. |
| | PRAPeR meeting 64 has set an ADI and ARfD for metabolite M-01. Therefore, it was necessary to readdress the residue definitions for risk assessment for plant and animal matrices, the risk assessment for the consumer and the dietary burden calculations for livestock. | PRAPeR 40: Metabolite M-01 (BAM) was included in the DOR for RA for plant and animal matrices under the assumption that the toxicological endpoints of parent should be applied also for M-01.<br>ADI parent: 0.08 mg/kg bw and ARfD for parent (0.18 mg/kg bw).<br><br>RMS suggested new ADI for this metabolite: 0.045 mg/kg bw in Addendum 2 to Vol 3 (December 2008).<br><br>PRAPeR 64 set the following toxicological endpoints for M-01 (BAM):<br>**<u>ADI for M-01: 0.05 mg/kg bw</u>**. The **<u>ARfD for M-01 is 0.3 mg/kg bw</u>**.<br><br>In the previous evaluation, the DOR for RA was the sum of the parent + metabolite M01.<br>The general question raised by the meeting was whether the metabolite should be expressed as the parent or to consider the parent and this metabolite separately based on the respective end points tox for the parent and metabolite M01 (BAM).<br>The available analytical methods determined the parent and metabolite M01 separately. | New open point 3.7. proposed |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | The best approach is to perform the RA for the parent and the metabolite M01 respectively. **DOR for RA : Fluopicolide and metabolite M-01 seperately**.<br>Based on the metabolism studies on grapes and potatoes, M01 was recovered at negligible levels. Therefore no new residue trials analysing for the metabolite were triggered.<br>During processing, the residue picture in the processed commodities remained unchanged (the parent was stable).<br><br>On the basis of these new toxicological end points, the consumer risk assessment should be performed again.<br>The outcome of the consumer risk assessment for the intended uses will not change significantly.<br>In rotated cabbage and straw only, M01 was recovered at a level of 0.02-0.03 mg/kg.<br>No M01 residues are expected in plant parts. | |
| | In Addendum 1 (November 2007) and Addendum 2 (December 2008) the RMS provided an assessment of relevance of ground water metabolites. The toxicologists referred the discussion of the risk assessment through drinking water to the PRAPeR 65 meeting. | UK has provided a calculation for M01 and other metabolites showing that the exposure should be below 10 % of the ADI (0.45 mg/kg for M-01 and the ADI of parent ( 0.08 mg/kg bw) for the other metabolites) according to the WHO guideline.<br><br>Dichlobenil was not included in Annex I because of this metabolite. The concentration in groundwater (FOCUS) was predicted in concentrations of up to 364 µg/L (worst case scenario). The meeting noted that in the case of Dichlobenil, the active substance was metabolised to M-01 to a high extent.<br>RMS (NL) for Dichlobenil to look to the general discussion within the EU review process for clarification and to be consistent with the decisions taken for dichlobenil with regard to the toxicological reference values for M-01.<br>UK will be required to provide a risk assessment. | New open point 3.7. proposed |
| | New Open point 3.7:<br>RMS to amend the list of end points according to the discussions during the PRAPeR 65 meeting. | LoEPs to be amended according to the following: -DOR for RA in plant commodities, livestock dietary burden calculation, consumer risk assessment including drinking water risk assessment. | Open point open. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New Open point 3.8:<br>for NL (RMS for Dichlobenil):<br>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. | RMS (NL) for Dichlobenil 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. | Open point open. |

# Appendix 2: Evaluation table

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Section 3<br>Data requirements: **-**<br>Open points: ***6*** | | | Section 3<br>Data requirements: **-**<br>Open points: ***1*** |
| | Open point 3.1<br>Residue definition for risk assessment in rotational crops to be discussed in an expert meeting<br><br>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.<br>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.<br>Therefore for the above reasons, M01 should not be included in the residues definition for monitoring.<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled.<br><br>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<br>MS to consider whether rotational crop studies are sufficient for drawing final conclusions and whether restrictions are needed in an expert meeting.<br><br>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).<br><br>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).<br><br>To conclude, a sufficient variety of crops have been looked at with | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | | | sufficient residues data (8 trials on each rotational crop) to conclude that residues in rotational crops will not be significant and restrictions are not needed.<br>Open Point: to be discussed at Expert Meeting. | |
| | Open point 3.3<br>MRL proposal on grapes to be discussed in an expert meeting (validity of the trials with 4 applications, considering the persistency of the compound)<br>RMS to provide the meeting with statistical analysis of the results.<br><br>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).<br><br>Open Point: to be discussed at Expert Meeting. | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | Open point 3.4<br>MS to discuss the approach for risk assessment depending on final decision on residue definition for risk assessment in rotational crops<br><br>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).<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |
| | Open point 3.5<br>RMS to check if balance data allow %ages of transference to be calculated<br><br>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.<br><br>Addressed | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |
| | Open point 3.6<br>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: 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. | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point fulfilled. |

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
|---|---|---|---|---|
| | See reporting table 3(40). | | Open Point: to be discussed at Expert Meeting. | |
| | New open point 3.6:<br>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<br>No conversion factor required for MO1 for grapes and potatoes (insignificant levels present in the crops) may be required for other crops.<br>Addressed. | PRAPeR 40 (12 – 13 December 2007):<br>Open point open.<br>PRAPeR 65 (19 -23 01.2009): |
| | New Open point 3.7:<br>RMS to amend the list of end points according to the discussions during the PRAPeR 65 meeting. | | | PRAPeR 65 (19 -23 01.2009):<br>Open point open. |
| | New Open point 3.8:<br>for NL (RMS for Dichlobenil):<br>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. | | | PRAPeR 65 (19 -23 01.2009):<br>Open point open. |