PEER REVIEW REPORT ON **CYFLUFENAMID** 08 02 2008

TABLE OF CONTENTS



List of all reports from EPCO Expert Meetings

| Date | | Section |
|---|---|---|
| 27-30 11 2007 | PRAPeR expert meeting 36 | Physical and Chemical Properties |
| 03-06 12 2007 | PRAPeR expert meeting 37 | Environmental Fate and Behaviour |
| 03-07.12.2007 | PRAPeR expert meeting 38 | Ecotoxicology |
| 10-13 12 .2007 | PRAPeR expert meeting 39 | Mammalian Toxicology |
| 12-13 12 .2007 | PRAPeR expert meeting 40 | Residues |

**REPORT OF PRAPeR EXPERT MEETING 36**

CYFLUFENAMID

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 | Cyflufenamid addendum2 Vol3 (Nov 2007).doc |
| 12.11.2007 | UK | Cyflufenamid evaluation table rev1-0 (2007-11-12) phys-chem.doc |
| 22.06.2007 | UK | Cyflufenamid reporting table rev 1-1 (2007-06-22).doc |
| Nov 2007 | UK | Cyflufenamid revised list of endpoints (Nov 2007).doc |

3. Documents tabled at the meeting:

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

The conclusions of the meeting were as follows:

4. **Data on preparations:** NF-149EW

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

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

7. **Reference list:** Not discussed

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

Appendix 1: Discussion table: CYFLUFENAMID

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Cyflufenamid (Fu)

## 1. Physical and Chemical Properties

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.1<br>RMS should consider using the current harmonised version of the list of end points.<br><br>See reporting table 0(1). | The template has been used and the open point is fulfilled. | Open point fulfilled. |
| 1.1 | Data requirement<br>The applicant should justify the minimum purity of the active substance given that the batch data suggest that 980 g/kg would be reliable.<br><br>It should be noted that the applicant has stated that QC data has been sent to the rapporteur on 6 June 2007.<br><br>See reporting table 1(1). | Data requirement fulfilled.<br><br>New open point<br>The meeting agreed that the 5-batch data supported a minimum purity of 980 g/kg. QC data were not required. RMS should consider including this information in an addendum to the DAR. | Data requirement fulfilled.<br><br>New open point proposed, see open point 1.13 |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New open point 1.13:<br>The meeting agreed that the 5-batch data supported a minimum purity of 980 g/kg. QC data were not required. RMS should consider including this information in an addendum to the DAR. | | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. |
| | Open point 1.2<br>The CIPAC number 759 should appear in the list of end points.<br><br>See reporting table 1(3). | The CIPAC number has been changed open point fulfilled. | Open point fulfilled. |
| | Open point 1.3<br>The method of analysis with regard too the LOQ should be discussed in a meeting of experts.<br><br>The applicant has stated that a report will be available September 2007.<br><br>See reporting table 1(5). | Open point fulfilled.<br>The meeting agreed that the original method addressed the requirement accordingly therefore the new study is not required. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.4<br>Rapporteur to update the list of references relied on to remove the references to solubility and partition co-efficient for the metabolites.<br><br>See reporting table 1(8). | The references have been updated open point fulfilled. | Open point fulfilled. |
| | Open point 1.5<br>UV spectra. The rapporteur to add all the molar coefficients to the list of end points.<br><br>See reporting table 1(9). | The molar coefficients have been added to the list of end points and the open point is fulfilled. | Open point fulfilled. |
| | Open point 1.6<br>Rapporteur to update the references relied on.<br><br>See reporting table 1(17). | The references have been updated and the open point is fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.7<br>A final assessment of the air method is not possible until a residue definition is set.<br><br>See reporting table 1(20). | Open point still open.<br>There is currently no residue definition in air.<br>The meeting agreed that dependent on the residue definition further data may be required.<br>**Message to fate & behaviour**: residue definition for air to be confirmed. | Open point open. |
| | Open point 1.8<br>Rapporteur to amend the list of references relied on to remove the reference to impurity methods that are not required.<br><br>See reporting table 1(21). | The references have been updated and the open point is fulfilled. | Open point fulfilled. |
| | Open point 1.9<br>For the residue methods the analyte should be mentioned in the LOEP.<br><br>See reporting table 1(26). | The list of end points has been amended open point fulfilled. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.10<br>From the comment made by the rapporteur in column 3 of the reporting table it would appear that there was some communication between the primary lab and the lab that conducted the ILV such that initially the method did not work. This is not correct procedure and this issue should be discussed in a meeting of experts.<br><br>The applicant has stated that a justification will be provided. 6 June 2007.<br><br>See reporting table 1(32). | Open point fulfilled.<br>The independent laboratory contacted the primary laboratory due to initial problems with the method. The IL was advised to reduce the batch size and not to store the extracts. The meeting agreed that this is an important clarification.<br>**New data requirement:** An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier. | Open point fulfilled.<br><br>New data requirement:<br><br>An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 1.2 | New data requirement:<br><br>An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier | | Data requirement open. |
| | Open point 1.11<br>The high RSD values for the residues in food method should be discussed in a meeting of experts and in general the level of validation in accordance with SANCO/825/00 should be considered.<br><br>The applicant has stated that a justification will be provided. 6 June 2007.<br><br>See reporting table 1(33). | Open point fulfilled. See open point 1.10. | Open point fulfilled, see open point 1.10 |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 1.12<br>It should be discussed by a meeting of experts if the validation data for the confirmatory drinking water method is acceptable.<br><br>See reporting table 1(37). | Open point fulfilled<br>The meeting agreed that there is a GC-MS confirmatory method that has been evaluated in the DAR which demonstrates specificity although the method was validated at concentrations 100 times higher than the LOQ and is therefore not acceptable as a confirmatory method.<br>There is an LC-MS method submitted in the original dossier to support pre-registration studies for the fate & behaviour section. The method determines residues of cyflufenamid and metabolites in leachate water at levels down to 0.05 µg/L. Although summarised in section 4 of the dossier it has not been included in the DAR. In this exceptional case, these raw data were assessed by the experts and the method was deemed acceptable as a confirmatory method.<br><br>**New open point**: Reference to this study should be included with the correct Annex point. | Open point fulfilled.<br><br>New open point proposed, see open point 1.14 |
| | New open point 1.14:<br><br>Reference to this study should be included with the correct Annex point. | | Open point open. |
| | New open point 1.15:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting. | Clarification of the temperature of decomposition is required. Weight loss was observed at 140ºC and it is likely that partial decomposition began around this temperature. Therefore the boiling point should reflect that partial decomposition had occurred.<br>The concentration tested for surface tension should be included<br>It should be classified as Not highly flammable<br>The LC-MS confirmatory method for the determination of residues in water should be included<br>The amount of active substance per hectare should be confirmed in the table of representative uses | 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: ***1***<br>Open points: ***12*** | | | Section 1<br>Data requirements: ***1***<br>Open points: ***4*** |
| | Open point 1.1<br>RMS should consider using the current harmonised version of the list of end points.<br><br>See reporting table 0(1). | | The Endpoints have been re-formatted updated using the Sept 05 guidance.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| 1.1 | Data requirement<br>The applicant should justify the minimum purity of the active substance given that the batch data suggest that 980 g/kg would be reliable.<br><br>It should be noted that the applicant has stated that QC data has been sent to the rapporteur on 6 June 2007.<br><br>See reporting table 1(1). | Quality control data on technical cyflufenamid produced on an industrial scale manufacturing plant, together with analysis of 5 representative batches of such material, support a minimum purity of 980 g/kg of the active substance in the industrial scale technical product.<br>The Applicant confirms that the data was provided to RMS (UK PSD) on 6 June 2007. | Quality control data support a minimum purity of 980 g/kg, the endpoints have been amended.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Data requirement fulfilled.<br><br>New open point proposed, see open point 1.13 |
| | New open point 1.13:<br>The meeting agreed that the | | | PRAPeR 36 (27. – 30.11.2007): |

| 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 Meeting |
|---|---|---|---|---|
| | 5-batch data supported a minimum purity of 980 g/kg. QC data were not required. RMS should consider including this information in an addendum to the DAR. | | | Open point open. |
| | Open point 1.2<br>The CIPAC number 759 should appear in the list of end points.<br><br>See reporting table 1(3). | Agreed. The CIPAC number for cyflufenamid is 759. | RMS: Endpoints have been updated<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.3<br>The method of analysis with regard too the LOQ should be discussed in a meeting of experts.<br><br>The applicant has stated that a report will be available September 2007.<br><br>See reporting table 1(5). | A study is being conducted to identify the LOQs in the method of analysis of the impurities in the technical active substance. The Applicant confirms that the report is expected to be available in December 2007 and will be provided to the RMS. | The study referenced in column B was not available to the RMS at the time of writing this comment, but will be evaluated once it is received. | 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>Rapporteur to update the list of references relied on to remove the references to solubility and partition co-efficient for the metabolites.<br><br>See reporting table 1(8). | | The studies have been deleted from the updated references relied on list<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.5<br>UV spectra. The rapporteur to add all the molar coefficients to the list of end points.<br><br>See reporting table 1(9). | | Endpoints have been updated<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.6<br>Rapporteur to update the references relied on.<br><br>See reporting table 1(17). | | The studies have been deleted from the updated references relied on list. | 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 1.7<br>A final assessment of the air method is not possible until a residue definition is set.<br><br>See reporting table 1(20). | The Applicant considers that the residue definition in air is the parent compound alone, cyflufenamid. | The method reported in the DAR is acceptable for the determination of the active substance in air. There is currently no residues definition proposed for air. If a residue definition for air is set as something other than cyflufenamid, then a further method will be required. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point still open. |
| | Open point 1.8<br>Rapporteur to amend the list of references relied on to remove the reference to impurity methods that are not required.<br><br>See reporting table 1(21). | | The study of Unemoto, T, 2000, which makes reference to the analysis of hexane, has been deleted form the list of references relied on. The study of Unemoto, T, 2000a, which makes reference to the determination of toluene and Isopar G has not been removed from the list of references relied on, as this study was relied on to determine the analytical profile of batches used in Tox testing.<br><br>Addressed | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. |
| | Open point 1.9<br>For the residue methods the analyte should be mentioned in the LOEP.<br><br>See reporting table 1(26). | | The list of end points has been amended to include this information.<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 1.10<br>From the comment made by the rapporteur in column 3 of the reporting table it would appear that there was some communication between the primary lab and the lab that conducted the ILV such that initially the method did not work. This is not correct procedure and this issue should be discussed in a meeting of experts.<br><br>The applicant has stated that a justification will be provided. 6 June 2007.<br><br>See reporting table 1(32). | With respect to the ILV of analytical methods for residues in plant, plant products, foodstuff and feedingstuff, the current version of the guidance document on residue analytical methods (SANCO/825/00 rev.7, 17/03/2004), states that "where the chosen laboratory requires communication with developers of the method to carry out the analysis, this must be reported". Therefore, communication between the primary laboratory and that chosen for the ILV, which was documented in the study report, is acceptable.<br>The Applicant confirms that this justification was provided to RMS on 6 June 2007. | As noted by the Notifier, the current guidance on the conduct of ILV studies states only that any communication between the independent laboratory and the developers of the method must be documented. It does not state that such communication is not acceptable. The RMS considers that the communication and subsequent minor modifications to the method do not invalidate the ILV study; however we do accept that it would be helpful for the details regarding batch size and storage of extracts to be incorporated into the analytical procedure as they do appear to be critical to the acceptability of the method. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled.<br><br>New data requirement, see 1.2<br><br>An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier. |
| 1.2 | New data requirement:<br><br>An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier | | | 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 1.11<br>The high RSD values for the residues in food method should be discussed in a meeting of experts and in general the level of validation in accordance with SANCO/825/00 should be considered.<br><br>The applicant has stated that a justification will be provided. 6 June 2007.<br><br>See reporting table 1(33). | The RSD values for the determined residues in food are within the limits specified in the EU guidance document for analytical methods (SANCO/825/00 rev.7, 17/03/2004), i.e. <20% per commodity and level. Furthermore, the mean recovery at each fortification level for each commodity was in the specified range of 70-110%. Although there was some variability in the initial determinations in the ILV study, subsequently modifications gave recovery and RSD values that met the above SANCO document.<br>The Applicant confirms that this justification was provided to RMS (UK PSD) on 6 June 2007. | Communication between the independent laboratory and the developers of the method as described in open point 1.10 above took place after the independent laboratory had analysed three batches and obtained unacceptable results. After incorporating the minor changes proposed by the developers of the method, the two subsequent batches of data were acceptable. The RMS considers that the results of the first three batches can be disregarded. The results of batches 5 and 6 are within the acceptable limits described in SANCO/825/00. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled. See open point 1.10. |
| | Open point 1.12<br>It should be discussed by a meeting of experts if the validation data for the confirmatory drinking water method is acceptable.<br><br>See reporting table 1(37). | | The RMS welcomes a discussion on this point at a meeting of experts. | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point fulfilled.<br><br>New open point proposed, see open point 1.14 |

| 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 Meeting |
|---|---|---|---|---|
| | New open point 1.14:<br><br>Reference to this study should be included with the correct Annex point. | | | PRAPeR 36 (27. – 30.11.2007):<br><br>Open point open. |
| | New open point 1.15:<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**

CYFLUFENAMID

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 | Cyflufenamid addendum2 Vol3 (Nov 2007).doc |
| 12.11.2007 | UK | Cyflufenamid evaluation table rev1-0 (2007-11-12) fate.doc |
| 22.06.2007 | UK | Cyflufenamid reporting table rev 1-1 (2007-06-22).doc |
| Nov 1007 | UK | Cyflufenamid revised list of endpoints (Nov 2007).doc |

3. Documents tabled at the meeting:

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

The conclusions of the meeting were as follows:

**4. Data on preparations:** NF-149 EW

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

8. **Recommended restrictions/conditions for use:** none

9. **Reference list:** not discussed

| |
|---|
| **Areas of concern:** potential leaching for 149-F1 and 149-F6, subject to non-relevance assessment |

Appendix 1: Discussion table: CYFLUFENAMID

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Cyflufenamid (Fu)

## 4. Fate and behaviour

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 4.1 | Data requirement<br>Applicant to provide further details on the monitoring study on phenyl acetic acid (PAA) in soil performed in Japan, to support the reported natural background concentrations in soil.<br><br>In the comments received on the reporting table, the applicant stated that the study has been submitted to RMS on 6 June 2007.<br><br>See reporting table 4(3). | In the DAR the applicant submitted a reasoned case to argue against the need for additional studies with radiolabelling in the non-fluorinated phenyl ring and provided brief details of a monitoring study in Japan indicating the naturally occurring soil concentrations.<br>A study report was presented and evaluated in the addendum (p. 22), indicating that the substance PAA was naturally occurring, at levels above the worst case soil PEC calculated in the DAR. However, only one soil type (from Japan) was monitored and in the opinion of the RMS the study provided evidence of limited quality only on the determination of PAA in soil. Therefore it is hard to state this is the natural background. However, PAA can be formed through metabolism of different substances, and therefore it is considered plausible that PAA is a naturally occurring compound. The experts agreed that the concern was sufficiently addressed. | Data requirement fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 4.1<br>RMS to add in the LoEP the mean/median value for parent DT50lab and for metabolites (as they were used for PECsoil calculations) and to specify that the reported mean values for metabolites (normalised for FOCUS modelling) refer to arithmetic mean.<br><br>See reporting table 4(4). | The LoEP was amended. PECsoil for metabolites appears to have been calculated based on the arithmetic mean non-normalised DT50 values. PECaccumulation was calculated for 149-F1 and 149-F6 because these two are persistent.<br>DT50 values were derived from decline from maximum observed %, not from a kinetic approach. Therefore they are not degradation rates but dissipation rates. RMS is asked to clarify this in the LoEP.<br>Following the FOCUS recommendations, it would have been expected that the max DT50 was used for PECaccumulation calculations. RMS suggests that values could be recalculated, experts also feel that normal evaluation practice should be followed for consistency.<br>Note: It cannot be seen from the updated LoEP which information was removed from the previous version. | Open point fulfilled.<br><br>New open point: proposed, see open point 4.7 |
| | New open point 4.7:<br>RMS to recalculate PECaccumulation for 149-F1 and 149-F6 using max DT50 lab values, and to provide clarification on DT50 calculation (decline from maximum observed) in the LoEP. | | Open point open. |
| 4.2 | Data requirement<br>Applicant to provide further information to support the choice of field trial sites, | In laboratory studies a supposed OM dependency for degradation was found (high OM, slow degradation). In the field studies only soils with low OM% were studied. It was questioned in the comments on the DAR if the field studies are sufficiently worst-case with regard to degradation.<br>No further studies were performed but applicant re-assessed the field studies and | Data requirement fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | specifically with regard %OC content, to cover the wide range of European conditions.<br><br>In the comments received on the reporting table, the applicant stated that the study has been submitted to RMS on 6 June 2007.<br><br>See reporting table 4(5). | concluded that in the field studies no trend of OM% with degradation was observed, and that the OM % range was sufficient to cover EU agricultural field conditions (also presented in addendum p 24). Further, applicant stated that cereals are often grown on OM-poor soils (at least in UK). RMS used the worst-case lab DT50 for groundwater modelling to demonstrate that then there still is a safe use with regard to leaching. The experts can agree on the approach followed by RMS and considered the data requirement fulfilled. | |
| 4.3 | Data requirement<br>Applicant to provide the original study on PEC groundwater calculations.<br><br>In the comments received on the reporting table, the applicant stated that the information on the calculation of PECgw has been submitted to RMS on 6 June 2007.<br><br>See reporting table 4(12). | No separate study was submitted in the dossier. A PECgw calculation was only performed for the Tier II dossier (risk assessment notifier). RMS does not consider this to be a problem (and recalculated PECgw anyway). EFSA thinks that all input files should be available for recalculation purposes. RMS did validate the outcome of the notifier's calculations and could reproduce the results. EFSA considers that this often happens with other substances (RMS recalculates but original notifier input files not reported), and often this would lead to an open point. All experts agreed that the necessary information is present in the addendum.<br>It is considered that the input files do not really have to be presented in the DAR (or addendum) but they should be included in the dossier so that RMS can check. This message should be transferred to notifiers: sufficient detail on input values should be provided in the dossier to enable recalculation by RMS and other MS's.<br><br>Data requirement not fulfilled formally. But, since values were validated by RMS in PECgw recalculations, it is accepted that DR remains open in this case. RMS could provide their input values in more detail; however, this was already done in the addendum. | Data requirement not fulfilled formally.<br>However, since values were validated by RMS, it is agreed that the data requirement is not essential to finalise the assessment. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | | |
| | Open point 4.2<br>MS to discuss the suitability of the approach used to model the metabolites for groundwater contamination in a meeting of experts.<br><br>EFSA note: the direct application of metabolites instead of using sequential degradation in the model would result in a best case as the amount of the leaching of metabolite during its formation from the parent is excluded in the modelling. Therefore this approach is not recommended.<br><br>See reporting table 4(14). | This point was discussed in the addendum (p. 27). Since the metabolic pathway was very complicated the kinetic approach (which is now recommended) was not followed. Metabolites were added as parent on the second date of application of the parent. No actual formation fractions are known.<br><br>In the addendum, two approaches were presented. For both the approaches, the PELMO model was run using a linear metabolism scheme (no sinks). Some of the experts feel this pathway is unlikely in part and it seems that a compartment sink should have been present at some stage.<br><br>One approach is based on arithmetic mean DT50 values for all substances (parent and metabolites, assuming a formation fraction of 100 % for metabolites for each stage of the metabolic pathway). This approach can be considered worst-case for the metabolites.<br>The other approach is that RMS recalculated using the longest lab DT50 for parent and arithmetic mean DT50 for metabolites used formation fractions of 1 for metabolites from their precursor metabolites (or parent), resulting in the same application rate for metabolites as for parent. The use of the longest DT50 for parent (which could lead to not worst-case assessment of metabolites) may have been counterbalanced by putting the metabolite formation to 100 % of precursor. This approach can be considered worst-case for the parent compound.<br><br>Experts agreed on these two approaches to be reasonably worst-case. However, it is noted that in risk assessment none of the two approaches were used, since they do not appear in the LoEP. This was justified by RMS in the LoEP by stating that both metabolites have already undergone a relevance assessment, at the stage of the original DAR.<br>The experts are of the opinion that the first approach in the addendum seems the most appropriate and should be included in the LoEP (and omit the original DAR approach from the LoEP)<br><br>The approaches in the addendum are considered to be worst-case for the parent. For all metabolites (and especially for F6 as it is estimated to leach above 0.75 µg/L) some | Open point fulfilled.<br><br>New open point proposed, see open points 4.8 and 4.9 |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | doubts remain concerning the timing of formation and leaching process simulated in the model, since it depends highly on DT50 and formation fraction input values. The experts consider this to be a general problem in modelling.<br>Open point closed.<br><br>'Intermediate leaching potential' was described for one of the metabolites: it seems that it was not the leaching potential that was intermediate, but this could also concern the application date. This information was also presented in the LoEP but this is considered to be confusing. New open point: RMS to clarify what intermediate means. | |
| | New open point 4.8:<br>RMS to update the LoEP to include the first approach for PECgw calculations presented in addendum (arithmetic mean DT50 for a.s. and metabolites) and delete the original DAR approach from the LoEP. | | Open point open. |
| | New open point 4.9:<br>RMS to clarify what '149-F was an intermediate leacher' means or delete this information from the LoEP. | | Open point open. |
| | Open point 4.3<br>MS to discuss the appropriate DT50 value to be used in FOCUSgw modelling in a meeting of | In the DAR the DT50 value used in the modelling was derived from a mean rate constant.<br>The experts discussed whether is appropriate the use of the arithmetic mean instead of the geomean as indicated by FOCUS recommendations.<br>However, in the LoEP this issue was already clarified by a statement concerning the difference between the two values. In the addendum also a table was provided comparing | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | experts.<br><br>See reporting table 4(17). | the arithmetic and geometric means (p. 32). The experts agreed that the geometric mean is the correct value, however, in this case the arithmetic mean is accepted because the longer DT50 values would not have significantly affected the conclusions of the groundwater assessement.<br>Furthermore, the DAR is prepared before FOCUS Kinetics was implemented.<br>Open point closed. | |
| | Open point 4.4<br>RMS to provide explanations on the inconsistency between the timing of application as indicated in the GAP table and the actual dates of application used in the assessment.<br><br>EFSA note:<br>it is noted that in all field trials cyflufenamid was applied in late May or middle June. In addition, in FOCUS GW the crop interception factors were calculated based on applications to cereals at GS 20-39 and GS 40-89 (it was not possible to check the actual dates of application used in the modelling because the | Discussed in the addendum on page 33. The time of application has now been stated more precisely in the addendum and included in the updated LoEP. Open point closed. | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | original report on FOCUS PECgw is not available).<br><br>See reporting table 4(18). | | |
| | Open point 4.5<br>RMS to update the list of references relied on with respect the reference Brewin (2002).<br><br>See reporting table 4(20). | Open point remains open. | Open point remains open. |
| | Open point 4.6<br>RMS to update the list of references relied on with a cross reference between the phys-chem and the fate section for the studies by Yamasaki (1999), Aikens (2001) and Aikens & Millais (2002)<br><br>See reporting table 4(21). | Open point remains open. | Open point remains open. |
| | Message from other meetings | phys-chemistry: Residue definition for air to be confirmed. Fate meeting confirms that residue definition for air is parent only. | |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Residue definition for RA | Soil: cyflufenamid, 149-F, 149-F1, 149-F6, 149-F11<br>Surface Water: cyflufenamid, 149-F11 (via drift of the parent) plus cyflufenamid, 149-F, 149-F1, 149-F6, 149-F11 (via runoff/drainage from soil)<br>Sediment: cyflufenamid, (via drift) plus cyflufenamid, 149-F, 149-F1, 149-F6, 149-F11 (via runoff/drainage soil)<br>Groundwater: cyflufenamid, 149-F, 149-F1, 149-F6, 149-F11<br>Air: cyflufenamid | |
| | New open point 4.10:<br><br>RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting. | Box Water-sediment study: was only labelled at fluorinated phenyl position. This means that any PAA formed in water/sediment was not detected. It is unknown to the fate meeting if this compound could be potentially toxic to aquatic organisms. Probably it would also occur in natural water-sediment systems but this question was not raised to the notifier (only for soil, also based on the non-labelling of the ring from which PAA was derived). But in the present dossier no information is present. EFSA to consider in their conclusion. | 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 4<br>Data requirements: ***3***<br>Open points: ***6*** | | | Section 4<br>Data requirements: ***0***<br>Open points: ***6*** |
| 4.1 | Data requirement<br>Applicant to provide further details on the monitoring study on phenyl acetic acid (PAA) in soil performed in Japan, to support the reported natural background concentrations in soil.<br><br>In the comments received on the reporting table, the applicant stated that the study has been submitted to RMS on 6 June 2007.<br><br>See reporting table 4(3). | A report (number RD-01179) on the determination of the levels of phenylacetic acid (PAA) in Japanese soil shows that the PAA content was 0.076 mg/kg of soil which is 1.6 times higher than the maximum theoretical residue that could be formed from cyflufenamid (NF-149).<br>The Applicant confirms that the report of this study was submitted to RMS on 6 June 2007. | The report has been briefly evaluated in Addendum 2 (Yamasaki, 2001, report number RD-01179).<br><br>In the opinion of the RMS the study provided evidence of limited quality only on the determination of PAA in soil.<br><br>However, despite the shortcomings of the study the RMS considers it highly plausible that PAA is a naturally occurring compound and that the potential formation of such a substance from applied cyflufenamid would have an insignificant effect on the naturally occurring levels of this substance derived from alternative sources.<br><br>The RMS considers the data requirement fulfilled. | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement fulfilled. |
| | Open point 4.1<br>RMS to add in the LoEP the mean/median value for parent DT50lab and for | | The LoEP has been updated.<br><br>Actual and TWA values for the individual metabolites over time have | 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 |
|---|---|---|---|---|
| | metabolites (as they were used for PECsoil calculations) and to specify that the reported mean values for metabolites (normalised for FOCUS modelling) refer to arithmetic mean.<br><br>See reporting table 4(4). | | been removed from the LoEP. This is because the RMS does not consider it valid to calculate these based on a degradation DT50 (a dissipation DT50 should really be used). | New open point proposed, see open point 4.7 |
| | New open point 4.7:<br>RMS to recalculate PECaccumulation for 149-F1 and 149-F6 using max DT50 lab values, and to provide clarification on DT50 calculation (decline from maximum observed) in the LoEP. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |
| 4.2 | Data requirement<br>Applicant to provide further information to support the choice of field trial sites, specifically with regard %OC content, to cover the wide range of European conditions.<br><br>In the comments received on the reporting table, the applicant stated that the study has been submitted to | The trial sites and soils used in the field dissipation study were selected in accordance with the recommendations of SETAC-1995 procedures for assessing the environmental fate and ecotoxicity of pesticides. The soil types chosen were specifically located in areas of N. and S. Europe with soil types representative of crop production areas of the intended uses of NF-149 EW. Furthermore, information from field trials experts is that organic matter in typical cereal growing areas in the | The Applicant has provided further clarification regarding the selection of sites for the field dissipation study and this information is assessed in Addendum 2.<br><br>Given the very wide range of $DT_{50}$ values observed in the laboratory soils, and the potential relationship between $DT_{50}$ and soil OM%, the RMS considers it would have been useful to have tested soils with a wider range of OM% under field conditions. However | PRAPeR 37 (03. – 06.12.2007):<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 group |
|---|---|---|---|---|
| | RMS on 6 June 2007.<br><br>See reporting table 4(5). | EU has a **maximum** of 3-5% organic matter.<br>Although in laboratory studies there was a tendency for a long $DT_{50}$ to be associated with high organic matter content, this was not seen in the field dissipation study. In the field study, the shortest $DT_{50}$ value (10.2 days) was associated with an intermediate level of organic matter content (1.89%) and the longest $DT_{50}$ value corresponded with the lowest content (1.38%).<br>The Applicant confirms that the justification that the maximum organic matter content in typical cereal growing areas in the EU (3-5%) was provided to the RMS on 6 June 2007. | the RMS considers that the submitted field dissipation data meets the data requirements and does not consider it necessary to request any further information.<br><br>For further reassurance the RMS has simply re-run the groundwater exposure assessment using a simple worst case laboratory DT50 of 412 d in place of the original value of 19.4 d used in the DAR. All other input parameters were as per the modelling in the DAR. Even with this conservative value the cyflufenamid PECgw was still 0.000µg/l according to FOCUS PELMO simulations, indicating no risk to groundwater even using the most conservative degradation input parameter.<br><br>Therefore the RMS considers that no further information is required. | |
| 4.3 | Data requirement<br>Applicant to provide the original study on PEC groundwater calculations.<br><br>In the comments received on the reporting table, the applicant stated that the information on the calculation | A separate study report on PECgw calculations is not available. This is not unusual as separate reports are not normally produced for other risk assessments (e.g. for assessing risks to avian, aquatic and other terrestrial vertebrates) as they are derived from information contained in the dossier.<br>Calculations were carried out in | The RMS can confirm that the calculation of PECgroundwater provided by the Applicant was presented in their MIII summary document only, and therefore no specific reference to a separate study is included in the DAR. The RMS can also confirm that the values presented in the DAR were independently | PRAPeR 37 (03. – 06.12.2007):<br><br>Data requirement not fulfilled formally.<br>However, since values were validated by RMS, it is agreed that the data requirement is not essential to finalise the assessment. |

| 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 |
|---|---|---|---|---|
| | of PECgw has been submitted to RMS on 6 June 2007.<br><br>See reporting table 4(12). | accordance with recommendations of the FOCUS ground water scenarios group (FOCUS, 2000). FOCUS scenarios were implemented into 4 models. PELMO (version 2.2.2) was used to investigate the potential for contamination of groundwater by cyflufenamid and its 4 metabolites/degradates. Information on the calculation was presented in the EU dossier (Section 5, Point 9.2.1). Further information produced by the RMS (UK PSD) can be found in the watermarked Draft Assessment Report issued by EFSA.<br>The Applicant confirms that this information was provided to RMS on 6 June 2007. | validated by the RMS by repeating the modelling using identical input parameters.<br><br>The LoEP has been updated to ensure all information needed to re-run the FOCUS groundwater simulations has been included. | |
| | Open point 4.2<br>MS to discuss the suitability of the approach used to model the metabolites for groundwater contamination in a meeting of experts.<br><br>EFSA note: the direct application of metabolites instead of using sequential degradation in the model would result in a best case as the amount of the leaching of metabolite during its formation from the parent is | The Applicant agrees with the opinion of the RMS (UK PSD) who states that "inputs to soil have been calculated assuming instantaneous input of the parent compound and considering the maximum accumulation of each metabolite in the laboratory degradation studies and the ratio of molecular weights of the parent and metabolites". This was an appropriate approach as it was not possible to produce a kinetic analysis of the formation fractions of metabolites in parent degradation studies.<br>Importantly, a higher tier leaching | This issue is addressed in Addendum 2.<br><br>The RMS accepts that the simplistic approach used in the original DAR ignores the potential for metabolite leaching to occur during the individual formation phases that would be simulated if a formation fraction approach had been used. For simplicity, the RMS has repeated the FOCUS groundwater assessment assuming a formation fraction of 100% for each stage of the metabolic pathway (i.e. parent → 149-F11 → | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point fulfilled.<br><br>New open points proposed, see open points 4.8 and 4.9 |

| 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 |
|---|---|---|---|---|
| | excluded in the modelling. Therefore this approach is not recommended.<br><br>See reporting table 4(14). | study was conducted which showed that in spite of multiple worst case conditions (above average rainfall plus irrigation), there was no leaching of parent cyflufenamid down to 40 cm or any of the metabolites (149-F, 149-F1 or 149-F6) below 80 cm. Additionally, no quantifiable residues of the parent were detected in any soil water sample collected at depths of 40, 80 or 120 cm. Therefore it was considered that the potential of cyflufenamid and its metabolites to leach to groundwater at concentrations of 0.1 μg/ml of higher was negligible.<br>The Applicant confirms that the above was provided to RMS on 6 June 2007. | 149-F → 149-F1 → 149-F6). This assumption is cleary worst case and the calculations are presented for illustrative purposes only. Results indicate that the method has no significant impact on parent or metabolites 149-F11 or 149-F. Higher concentrations of metabolites 149-F1 and 149-F6 are generated, however both these metabolites were subject to a relevance assessment in the original DAR.<br>Revised results are presented in Addendum 2 for information.<br><br>Overall the RMS considers that no further information is required. | |
| | New open point 4.8:<br>RMS to update the LoEP to include the first approach for PECgw calculations presented in addendum (arithmetic mean DT50 for a.s. and metabolites) and delete the original DAR approach from the LoEP. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |
| | New open point 4.9:<br>RMS to clarify what '149-F was an intermediate leacher' means or delete this information from the LoEP. | | | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point open. |
| | Open point 4.3<br>MS to discuss the | | This point is discussed further in Addendum 2. | PRAPeR 37 (03. – 06.12.2007): |

| 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 |
|---|---|---|---|---|
| | appropriate DT50 value to be used in FOCUSgw modelling in a meeting of experts.<br><br>See reporting table 4(17). | | The selection of alternative DT50 values is not considered by the RMS to affect the conclusions of the existing FOCUSgw modelling.<br><br>Overall the RMS considers that no further information is required. | Open point fulfilled. |
| | Open point 4.4<br>RMS to provide explanations on the inconsistency between the timing of application as indicated in the GAP table and the actual dates of application used in the assessment.<br><br>EFSA note:<br>it is noted that in all field trials cyflufenamid was applied in late May or middle June. In addition, in FOCUS GW the crop interception factors were calculated based on applications to cereals at GS 20-39 and GS 40-89 (it was not possible to check the actual dates of application used in the modelling because the original report on FOCUS PECgw is not available).<br><br>See reporting table 4(18). | | This point is discussed further in Addendum 2.<br>Information on application dates has been included in the Addendum and LoEP to demonstrate that there is in fact no significant inconsistency between the GAP and the application dates used in the exposure assessment.<br><br>Overall the RMS considers that no further information is required. | 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 4.5<br>RMS to update the list of references relied on with respect the reference Brewin (2002).<br><br>See reporting table 4(20). | | The references relied on list has been updated.<br><br>Addressed | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point still open. |
| | Open point 4.6<br>RMS to update the list of references relied on with a cross reference between the phys-chem and the fate section for the studies by Yamasaki (1999), Aikens (2001) and Aikens & Millais (2002)<br><br>See reporting table 4(21). | | The references relied on list has been updated.<br><br>Addressed | PRAPeR 37 (03. – 06.12.2007):<br><br>Open point still open. |
| | New open point 4.10:<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**

CYFLUFENAMID

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 |
|---|---|---|
| 12.11.2007 | UK | Cyflufenamid evaluation table rev1-0 (2007-11-12) ecotox.doc |
| 22.06.2007 | UK | Cyflufenamid reporting table rev 1-1 (2007-06-22).doc |
| Nov 2007 | UK | Cyflufenamid revised list of endpoints (Nov 2007).doc |

3. Documents tabled at the meeting:

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

The conclusions of the meeting were as follows:

**4. Data on preparations:** NF-149 EW

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

**10. Recommended restrictions/conditions for use:** none

**11. Reference list:** xxx

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

Appendix 1: Discussion table: CYFLUFENAMID

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Cyflufenamid (Fu)

## 5. Ecotoxicology

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.1<br>The toxicity endpoint for the long-term risk assessment for mammals to be discussed in an experts' meeting.<br><br>See reporting table 5(5). | RMS used a NOEC of 75 mg/kg bw/d from the **rat** multi-generation study for the long-term risk assessment of mammals.<br>This was questioned by EFSA: should the effects on litter resortion in the **rabbit** developmental study be considered? In that case, the NOEC should be set at 60 mg/kg bw/d.<br><br>RMS: All litter and offspring effects seen in the rabbit developmental study were seen at doses of maternal toxicity and are not considered dose-related.<br><br>Should developmental studies be considered at all or not? In these studies, gavage is used (daily gavage dosing for three weeks), which is a worst case exposure; but the exposure is shorter than in the multi-generation study which could be more realistic.<br>Both could be considered for the long-term risk assessment but the worst case exposure of the gavage dosing should be kept in mind.<br><br>The difference will not change the outcome of the risk assessment. Both values (75 and 60) will be reported in the LoEP pending on the mamtox-meeting; mamtox should decide whether the abortions were dose-related or not.<br>In the rabbit developmental study, the developmental NOEAL was 10 mg/kg bw/d (based on enlarged fontanels and retardation of ossification at 60 mg/kg bw/d; also a reduction in female foetal weight was seen). At 300 mg/kg bw/d, a clear reduction in foetal weight was seen (both sexes). The effects on foetal weight could have been caused by maternal toxicity, which in turn could have been caused by the type of dosing (gavage).<br><br>Question to mamtox: are the effects on foetal weight, ossification and litter resorption seen in the developmental study with rabbits likely to have been caused by the gavage dosing? | Question to mamtox: are the effects on foetal weight, ossification and litter resorption seen in the developmental study with rabbits likely to have been caused by the gavage dosing?<br><br>Open point still open pending mamtox meeting. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | Meeting votes to use 60 mg/kg bw/d as the relevant long-term endpoint. Open point still open pending mamtox meeting. | |
| | Open point 5.2<br>RMS to clarify whether the $LC_{50}$ for earthworms reported as 25 mg a.s./kg based on 'NF-149 EW' has been corrected for organic content in soil.<br><br>The Notifier has indicated that a clarification will be provided by 6 June.<br><br>See reporting table 5(11). | This has been done. Open point fulfilled. | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| 5.1 | Data requirement:<br>Applicant to address the risk to soil micro-organisms from the metabolites.<br>The statement in column 3 does not address the concern for 149-F. The $DT_{50}$ of 9.1 days might be correct but it takes 44 days for the peak to be reached.<br><br>The Notifier will provide further justification to RMS (UK PSD) on 6 June 2007.<br><br>See reporting table 5(15). | The notifier has provided further justification and RMS agrees that a low risk is expected (see evaluation table). Meeting agrees. Data requirement fulfilled. | Data requirement fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 5.3<br>The reproduction test with Collembola to be discussed in an experts' meeting.<br><br>There seems to be no formal data requirement for a Collembola study. However, since the study is available the validity and results should be discussed.<br><br>See reporting table 5(17). | In the reproduction test with Collembola with the formulation, no clear dose relationship was found and so, the reliability of the NOEC was questioned. RMS does consider the study valid (see page 400 in the DAR).<br><br>Further data on Collembola are not considered necessary by the RMS since low toxicity is suggested by data on NTAs and earthworms.<br><br>Meeting agrees. Open point fulfilled. | Open point fulfilled. |
| | Open point 5.4<br>RMS to give the reference to the studies on which the statement "Cyflufenamid and its metabolites showed no fungicidal activity to non-crop plants as this was specific to cereals and powdery mildew. In addition, neither the parent or its metabolites showed any herbicidal or insecticidal activity" as given in B.9.11was | This was done. Open point fulfilled. | Open point fulfilled. |

| | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | based on.<br><br>See reporting table 5(19). | | |
| | Open point 5.5<br>RMS to delete the two position papers by Kawai (2002a and b) from the reference list.<br><br>See reporting table 5(22). | This was done. Open point fulfilled. | Open point fulfilled. |
| | New open point 5.6:<br><br>RMS to include the secondary poisoning and drinking water risk assessment for birds and mammals in the LoEP. | It was noted that the secondary poisoning r.a. to birds and mammals was not included in the LoEP.<br>A drinking water risk assessment was not done at all. EFSA has calculated that no risk is expected. | 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: ***1***<br>Open points: ***5*** | | | Section 5<br>Data requirements: ***0***<br>Open points: ***2*** |
| | Open point 5.1<br>The toxicity endpoint for the long-term risk assessment for mammals to be discussed in an experts' meeting.<br><br>See reporting table 5(5). | | RMS - 22 Aug 2007<br>As previously stated the total litter resorption was considered to be a spontaneous treatment-unrelated incident. Abortions at the highest dose level (300 mg a.s./kg bw/d) were a consequence of severe maternal toxicity at unlikely environmental exposure levels. The NOEC selected was considered the most appropriate endpoint reflecting reproductive effects.<br><br>Point to be discussed further at Expert meeting. | PRAPeR 38 (03 – 07 12.2007):<br><br>Question to mamtox: are the effects on foetal weight, ossification and litter resorption seen in the developmental study with rabbits likely to have been caused by the gavage dosing?<br><br>Open point still open pending mamtox meeting. |
| | Open point 5.2<br>RMS to clarify whether the $LC_{50}$ for earthworms reported as 25 mg a.s./kg based on 'NF-149 EW' has been corrected for organic content in soil.<br><br>The Notifier has indicated that a clarification will be | The $LC_{50}$ value of NF-149 EW to earthworms presented in the study report and in the EU dossier was not corrected for the organic content of the soil because at the time the study was conducted there was not requirement for this in the prevailing testing guideline (OECD 2007, adopted 4 April 1984).<br>In accordance with the current guidance, because the log Kow for | RMS - 22 Aug 2007.<br>Relevant earthworm endpoints have been corrected in the revised LOEPs & TERs amended where appropriate. Low risk indicated for earthworms.<br><br>Addressed. | PRAPeR 32 (15. – 19.10.2007):<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 |
|---|---|---|---|---|
| | provided by 6 June.<br><br>See reporting table 5(11). | cyflufenamid ranges from 4.55 to 4.71, the $LC_{50}$ in the acute toxicity study to earthworms (>1000 ppm) has been corrected using a factor of 2 for organic matter content (10%) in the artificial soil used in the study. The corrected $LC_{50}$ value is >500 ppm.<br>The Applicant confirms that the above reason and the corrected $LC_{50}$ value were provided to RMS on 6 June 2007. | | |
| 5.1 | Data requirement:<br>Applicant to address the risk to soil micro-organisms from the metabolites.<br>The statement in column 3 does not address the concern for 149-F. The $DT_{50}$ of 9.1 days might be correct but it takes 44 days for the peak to be reached.<br><br>The Notifier will provide further justification to RMS (UK PSD) on 6 June 2007.<br><br>See reporting table 5(15). | The worst case maximum PECsoil for the metabolites (6.6 μg/kg) is more than 40-fold below the applied rate of 294 μg/kg of soil of cyflufenamid which had no effect on carbon and nitrogen transformations. As cyflufenamid and the metabolites 149-F1 and 149-F6 had no effect on soil micro-organisms, no risk to soil micro-organisms is expected from other metabolites (149-F and 149-F11). This is supported by their acute toxicity to soil macro-organisms e.g. earthworms. 149-F was only 4 times more toxic to earthworms than cyflufenamid ($LC_{50}$ 149-F = 279 ppm; cyflufenamid $LC_{50}$ >1000 ppm); 149-F1, 149-F6 and 149-F11 were of similarly low toxicity to earthworms as cyflufenamid.<br>The Applicant confirms that the justification was provided to RMS (UK PSD) on 6 June 2007. | RMS - 22 Aug 2007<br>An approximate 19% decline in cyflufenamid over 28d is predicted from PECsoil values. In the soil microbial studies at the highest dose this represents approximately 0.056 mg cyflufenamid degradation. Assuming degradation follows the proposed soil pathway this represents formation of 0.045mg 149-F11, which with a DT50 of 2.5d, will have rapidly degraded to149-F. Thus it is likely that significant exposure to 149-F is probable in this study (max PECsoil 149-F= 0.0066 mg/kg) without effect on microbial activity. Furthermore, both 149-F and 149-F11 were considered not to significantly accumulate in soil (DAR B.8.3).<br>Low risk to earthworms was indicated from 149-F11 and 149-F and its soil metabolite derivatives 149-F1 and 149-F6, the latter also without effect on soil | PRAPeR 38 (03 – 07 12.2007):<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 group |
|---|---|---|---|---|
| | | | microbial activity. Thus, overall, the RMS considered that the weight of evidence, based on likely absence of toxicity and limited transient exposure, indicates that 149-F will be of low risk to soil organisms and processes.<br><br>Point addressed | |
| | Open point 5.3<br>The reproduction test with Collembola to be discussed in an experts' meeting.<br><br>There seems to be no formal data requirement for a Collembola study. However, since the study is available the validity and results should be discussed.<br><br>See reporting table 5(17). | The cyflufenamid study with Collembola (*Folsomia candida*) was conducted in accordance with the draft version of the EU guidance document on terrestrial ecotoxicology (SANCO/10329) prevailing at the time the dossier was compiled and also in accordance with ESCORT 2.<br>Because the $DT_{90f}$ in the field dissipation study with cyflufenamid ranged up to 350 days, this triggered an assessment of effects on soil macro-organisms according to the prevailing draft SANCO/10329 document. (For the same reason tests with 4 species of non-target arthropods were conducted; hazard quotients were not required in the prevailing draft of SANCO/10329). | RMS - 22 Aug 2007<br>According to SANCO/10329, for cyflufenamid (soil DT90 100-365d) the absence of risk to earthworm, NTAs and soil microbial activity is sufficient establish low risk to soil organisms and processes.<br>Nevertheless, a Folsomia study was submitted using NF-149EW formulation. However, although considered acceptable by the RMS, due to absence of a clear dose vs. effect relationship between 0.00355 - 3.55 mg a.s./kg, a reliable NOEC cannot be determined and other evidence on NTAs and earthworms would suggest likely low toxicity.<br><br>Point addressed | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | Open point 5.4<br>RMS to give the reference to the studies on which the statement "Cyflufenamid and its metabolites showed no fungicidal activity to non-crop | | RMS - 22 Aug 2007<br>This information was given in the Biological Assessment Dossier.<br><br>Prince, K.J. & Pickering, J.W (2002). | 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 |
|---|---|---|---|---|
| | plants as this was specific to cereals and powdery mildew. In addition, neither the parent or its metabolites showed any herbicidal or insecticidal activity" as given in B.9.11was based on.<br><br>See reporting table 5(19). | | Biological assessment dossier on the fungicidal product cyflufenamid to be used for the control of Powdery mildew in cereal crops.<br>Agrisearch UK. Ltd for Nippon Soda<br><br>The study referenced has been added to the references relied on list.<br>Point addressed. | |
| | Open point 5.5<br>RMS to delete the two position papers by Kawai (2002a and b) from the reference list.<br><br>See reporting table 5(22). | | RMS - 22 Aug 2007<br>These two papers were not relied in the ecotox section and have been removed for the references relied on list.<br><br>Point addressed | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point fulfilled. |
| | New open point 5.6:<br><br>RMS to include the secondary poisoning and drinking water risk assessment for birds and mammals in the LoEP. | | | PRAPeR 38 (03 – 07 12.2007):<br><br>Open point open. |

**Report of PRAPeR Expert MEETING 39**

CYFLUFENAMID

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 |
|---|---|---|
| March 2007 | UK | Cyflufenamid addendum1 Vol3 B6 exposure (March 2007).doc |
| Nov 2007 | UK | Cyflufenamid addendum2 Vol3 (Nov 2007).doc |
| 12.11.2007 | UK | Cyflufenamid evaluation table rev1-0 (2007-11-12) tox.doc |
| 22.06.2007 | UK | Cyflufenamid reporting table rev 1-1 (2007-06-22).doc |
| Nov 2007 | UK | Cyflufenamid revised list of endpoints (Nov 2007).doc |

3. Documents tabled at the meeting:

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

The conclusions of the meeting were as follows:

4. **Data on preparations:** NF-149 5% EW

5. **Classification and labelling:** None

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

7. **Reference List:** xxx

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

Appendix 1: Discussion table: CYFLUFENAMID

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Cyflufenamid (Fu)

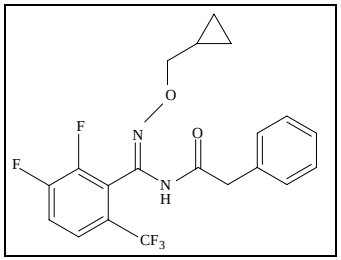
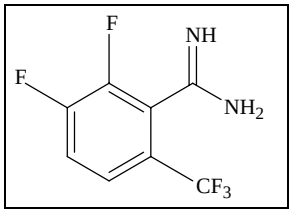
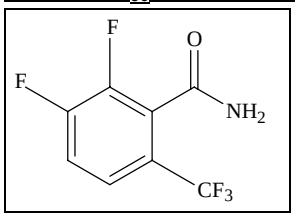
## 2. Mammalian toxicology

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 2.1<br>MSs to discuss the relevance of metabolites 149-F1 and 149-F6.<br><br>See reporting table 2(33). | These metabolites exceed the threshold of 0.1 ug/L, as apparent from the section on fate and behavior.<br>The metabolites were found in rats as well, where they are excreted rapidly and in significant amounts, indicating that they probably have contributed to the toxicological profile of cyflufenamid.<br>The genotoxicity studies available show negative results.<br>The oral toxicity is higher than for the parent compound.<br>The meeting agreed to the RMS's argumentation presented on p 182 in the DAR, that these metabolites are not relevant for the ground water assessment. | Open point fulfilled. |
| | Open point 2.2<br>Reference values to be discussed in an experts' meeting, taking into account relevant effects (in particular the occurrence of brain vacuolation)<br><br>See reporting table 2(40). | ADI:<br>see open point 2.3<br>AOEL:<br>The meeting discussed whether to base the AOEL on the NOAEL of 6.5 mg/kg bw/day for the liver effects from the 90 d dog study with a safety factor of 100 and a correction for the oral absorption.<br>For consistency reasons the meeting agreed to base the AOEL on the 1y dog study (NOAEL 4.1 mg/kg bw/day) with a correction for oral absorption of 70% and a SF of 100, resulting in an AOEL of 0.03 mg/kg bw (rounded).<br>The bioavailability was discussed and the RMS's proposal in the addendum 2, p.16 was considered acceptable when using liver effects as the critical end-point.<br><br>ARfD:<br>No information is available on the first occurrence of brain vacuolation. The NOAEL derived from the 28 d dog study is 93 mg/kg bw/day with regard to neurotoxic effects (see p. 11 of the addendum). Vacuolation was observed at the highest dose level. | Open point fulfilled |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | | The NOAEL for maternal toxicity from the developmental rabbit studies is an overall value of 5 mg/kg bw/day, based on the decreased bw gain in the 1st days. With a SF of 100 the resulting ARfD will be 0.05 mg/kg bw.<br>A sufficiently high margin of safety is provided with regard to the brain effects observed in the 28 d and 90 d dog studies. | |
| | Open point 2.3<br>The relevance of brain vacuolation to be discussed in a meeting of experts.<br><br>See reporting table 2(45). | The finding was observed in the dog (28d and 90d study), not in mice and rats. Information is presented in addendum 2, resulting in a relevant NOAEL of 6.5 mg/kg bw/day from the 90 day study. Brain vacuolation was not observed in the 1 y dog study, because the doses tested were lower.<br>No information is available on the first occurrence of brain vacuolation.<br>The finding has to be considered of relevance for human risk assessment, in the absence of mechanistic studies. The effect is treatment related and duration and dose dependant. Because of the severity of the effects the RMS proposed a higher safety factor (1000) for setting the ADI.<br>The 2 year study in rat was also available: the NOAEL was 4.4 mg/kg bw/day based on liver and kidneys changes. Applying a SF of 100, this would result in an ADI of 0.04 mg/kg bw/day. The margin of safety would be 575 with respect to the NOAEL for the brain vacuolation (23 mg/kg bw/day) and 1350 with respect to the LOAEL (76 mg/kg bw/day). | Open point fulfilled |
| | Open point 2.4<br>MSs to agree on the representativeness of batches used in tox studies to the proposed specification.<br><br>See reporting table 2(53). | The RMS introduced a table with the relevant information that was provided by the Phys Chem Group and the experts concluded that the technical specification was covered by the batches used in the toxicity studies. | 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 Meeting |
|---|---|---|---|---|
| | Section 2<br>Data requirements: **-**<br>Open points: ***4*** | | | Section 2<br>Data requirements: **-**<br>Open points: ***4*** |
| | Open point 2.1<br>MSs to discuss the relevance of metabolites 149-F1 and 149-F6.<br><br>See reporting table 2(33). | | The relative toxicity of these two metabolites is considered in the DAR in Section B.6.8.2.3. It is suggested that the increased acute toxicity will only be relevant to high dose levels (evidence being the nervous system effects seen at high dose levels only). 149-F1 and 149-F6 are both rat metabolites, and 149-F1 in particular is excreted in significant amounts (14% in urine), with 149-F6 up to 3% in urine. The significant *in situ* generation of these metabolites means that the toxicity of these metabolites should have been taken into account in the long-term studies with cyflufenamid. If it was necessary to perform a risk assessment for these metabolites then the ADI and ARfD for cyflufenamid should be appropriate since these metabolites will have contributed to the toxicity driving these reference values.<br>Since residues are expected to be at low levels for the supported uses (e.g. up to 0.02 mg/kg in wheat, 0.07 mg/kg in barley, <0.01 mg/kg for animal products) it may not be necessary to | PRAPeR 39 (10– 13 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 Meeting |
|---|---|---|---|---|
| | | | include these metabolites in residue definitions.<br>Cyflufenamid $LD_{50}$ >5000 mg/kg bw<br>  <br>149-F1 $LD_{50}$ 434 ♂, 349 ♀<br>  <br>149-F6 $LD_{50}$ 686 ♂, 686 ♀<br>  <br>For discussion at Expert meeting | |
| | Open point 2.2<br>Reference values to be discussed in an experts' | With respect to the brain vacuolation, an international panel of expert neurotoxicologists and | The expert report for neurotoxicity was addressed at Point 2(54) in the Reporting Table, and has been | PRAPeR 39 (10– 13 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 Meeting |
|---|---|---|---|---|
| | meeting, taking into account relevant effects (in particular the occurrence of brain vacuolation)<br><br>See reporting table 2(40). | neuropathologists independently reviewed all the neurotoxicological information on cyflufenamid, including original study reports and the histopathological slides. They concluded that a clear NOELneurotoxicity for the brain lesion in the dog was 97 and 93 mg/kg bw/day (2000 ppm) based on the 28-day dog toxicity study in the dog. See Open point 2.3 for further information. | reproduced in Addendum 2.<br>For the ADI it is necessary to clarify what safety margin is appropriate over the NOAEL for brain vacuolation, and following from that which NOAEL and safety factor should be used for the ADI. This is discussed in Point 2(41) in the Reporting Table, at Section B.6.10.1 in the DAR and summarised in Addendum 2.<br>For the ARfD it is necessary to resolve the conflicting findings in the two rabbit developmental studies. A dose of 10 mg/kg bw/d was the LOAEL in one study, but an NOAEL in the other study (same lab, same test material a short time apart, almost identical methods, same strain but different source of animals). The RMS proposal is to take the conservative approach in view of the uncertainty (clear NOAEL of 5 mg/kg bw/d, leading to ARfD=0.05). The alternative value would be 0.1. The brain vacuolation effect is not relevant to setting the ARfD since an ARfD based on the NOAEL for this effect in the shortest study would be similar to or higher than an ARfD based on the developmental studies.<br>For the AOEL it is necessary to clarify what safety margin is appropriate over the NOAEL for brain vacuolation – as is the case for the ADI. Following this the appropriate NOAEL and safety | 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 |
|---|---|---|---|---|
| | | | factor can be decided. It is then necessary to determine the appropriate oral absorption value, which in turn will be dependent on which NOAEL is selected to derive the AOEL (i.e. whether based on liver effects or not). This issue is discussed in detail at Point 2(44) in the Reporting Table with alternative proposals for oral absorption ranging from 18% up to 70%.<br>The issues around the setting of the reference values (and also the revised dermal penetration values) are summarised in Addendum 2.<br><br>For discussion at Expert meeting | |
| | Open point 2.3<br>The relevance of brain vacuolation to be discussed in a meeting of experts.<br><br>See reporting table 2(45). | An international panel of expert neurotoxicologists and neuropathologists independently reviewed all the neurotoxicological information on cyflufenamid, including original study reports and the histopathological slides. They concluded that high dose levels produced a unique pattern of toxic damage to oligodendrocytes and oedema of myelin in the white matter in certain areas of the brain of dogs. The effect was dose-related and resolved slowly after cessation of dosing. There was a clear NOELneurotoxicity for the lesion which was 97 and 93 mg/kg | The expert report for neurotoxicity was addressed at Point 2(54) in the Reporting Table, and has been reproduced in Addendum 2.<br>It is necessary to clarify what safety margin is appropriate over the NOAEL for brain vacuolation, since this impacts on the setting of both the ADI and the AOEL..<br>The issues surrounding the significance of this effect are covered at Section B.6.10.1 in the DAR and at Point 2(41) in the Reporting Table.<br><br>For discussion at Expert meeting | PRAPeR 39 (10– 13 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 Meeting |
|---|---|---|---|---|
| | | bw/day (2000 ppm) in the 28-day dietary toxicity study. The cause of the brain lesion in the dog was not known. The rat and mouse were not affected.<br>The Applicant confirms that this independent expert report was submitted to the RMS (UK PSD). | | |
| | Open point 2.4<br>MSs to agree on the representativeness of batches used in tox studies to the proposed specification.<br><br>See reporting table 2(53). | | The batch of cyflufenamid used in most of the toxicology studies was of lower purity than the proposed minimum specification, and hence may represent the 'worst-case' with respect to impurities. For the impurity present in the technical specification at 1% a case can be made for structural similarity (isomerisation) and there are data available ($LD_{50}$ >5000 mg/kg bw, negative Ames test, tentative identification in the rat metabolism study) to address any concerns with this impurity.<br>For the impurity present at 0.3% in the technical specification there is evidence that it is a rat metabolite of cyflufenamid, that it is naturally occurring in rats and there are data available in the open literature (e.g. $LD_{50}$ >2000 mg/kg bw). The RMS considers that there are no concerns regarding this impurity at 0.3% (see Appendix 4A in the DAR).<br><br>For discussion at Expert meeting. | PRAPeR 39 (10– 13 12.2007):<br><br>Open point fulfilled. |

**REPORT OF PRAPeR EXPERT MEETING 40**

CYFLUFENAMID

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 |
|---|---|---|
| 12.11.2007 | UK | Cyflufenamid evaluation table rev1-0 (2007-11-12) residues.doc |
| 22.06.2007 | UK | Cyflufenamid reporting table rev 1-1 (2007-06-22).doc |
| Nov 2007 | UK | Cyflufenamid revised list of endpoints (Nov 2007).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: CYFLUFENAMID

Appendix 2: Evaluation table

# Appendix 1: Discussion Table, Cyflufenamid (Fu)

## 3. Residues

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | Open point 3.1<br>RMS to elaborate further on whether isomerisation into the Z-isomer has taken place and if so, to clarify the impact on the risk assessment in an addendum<br><br>See reporting table 3(3). | There was a typo in the open point in the evaluation table since the Z-isomer is the parent compound. Therefore the isomerisation to the E-isomer was actually meant.<br><br>The levels of E-isomer in the technical material are negligible (<1%) and in the plant metabolism study the presence of the E-isomer was identified in low amounts (4%TRR, up to approx. 10% of parent residues) which indicate a slight isomerisation of the Z-isomer in the E-isomer. The isomerisation is probably due to photo-isomerisation and residue levels of the E-isomer are 10 fold lower than the levels of the parent isomer. The intention is to include this isomer in the residue definition, because the analytical method in the residue trials is expected to measure both the E and the Z isomer. In addition, there also seems to be a conversion of isomers in solution and if high temperatures are used in the chromatographic system of the analytical method the isomers are expected to flip to one another. Also for routine monitoring methods it probably won't be possible to make a distinction between both isomers. It is therefore decided to include the E-isomer in the residue definitions for enforcement and for risk assessment. This has no implications for the proposed MRLs and for the risk assessment since both isomers were probably measured in the residue trials. However, this should be confirmed by the applicant.<br><br>In conclusion it is decided to include both isomers in the residue definitions, but the applicant should submit some confirmatory information concerning the analytical method(s) used in the residues trials and the methods proposed for monitoring with regard to whether the methods are able to separate the isomers or not. | Open point fulfilled |
| | Open point 3.2<br>To be discussed in an experts' meeting whether a, and if so what, residue definition for risk assessment and monitoring for food of animal origin should | According to the dietary burden calculation the need for a livestock metabolism study is triggered. Therefore a residue definition should be proposed for animal commodities and the need to include the E-isomer and the two metabolites (149-F1 and 149-F6) in that residue definition should be considered.<br><br>According to the mammalian toxicology section, the two metabolites can be considered be equally toxic to the parent compound. Since metabolite 149-F1 is present at significant | Open point fulfilled. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | be proposed<br>The meeting consider aspects such as fat solubility of parent compound, toxicological relevance of metabolites 149-F1, 149-F6 (higher acutely toxic)<br><br>See reporting table 3(5). | percentages of the TRR in milk, liver and kidneys, it is decided to include this metabolite in the residue definition for risk assessment.<br>Based on this residue definition for risk assessment and the available metabolism study it is clear that residues in milk, muscles and kidneys will be below 0.01 mg/kg, but the fat and liver samples are a borderline case. In addition, the residue seems to be fat soluble and the residue might therefore accumulate over time. Nevertheless, according to the residue levels in milk it seems that a plateau is reached very quickly (after two days) and there seems to be a good turn-over of the compound. Based on the metabolism study it is finally decided not to request a livestock feeding study and to consider the residue levels for risk assessment below the LOQ in animal products.<br><br>For enforcement, the intention of the meeting is to also set the residue definition as the sum of the parent compound and metabolite 149-F1 since parent compound was not identified in the liver and in the kidney. It is acknowledged that the metabolite has a simple structure and that there are concerns about the possibility of the metabolite to be generated by other pesticides too. Nevertheless, no other pesticide producing this metabolite could be identified during the meeting and as for plant commodities, it is decided to also include the E-isomer in both enforcement and risk assessment residue definitions.<br><br>Therefore, it is finally decided to set the residue definition for enforcement and risk assessment as the sum of the parent compound, the E-isomer and metabolite 149-F1. MRLs for animal commodities are set at the LOQ (still to be defined).<br><br>Since no enforcement analytical method is available for the animal commodities and MRLs are proposed for animal commodities, a data requirement for the enforcement analytical method will be transferred to the phys-chem section. | |
| 3.1 | New data gap<br><br>A clarification concerning the analytical methods used in the residue trials to be submitted. | A clarification concerning the analytical methods used in the residue trials should be submitted with regard to whether the methods are able to separate the isomers or not. (see open point 3.1) | Data gap open. |

| No. | Subject | Discussion Expert Meeting | Conclusions Expert Meeting |
|---|---|---|---|
| | New data requirement to be transferred to the phys-chem section. | Analytical method for animal commodities is required for the following residue definition: sum of cyflufenamid, the E isomer and metabolite 149-F1. | New data requirement to be transferred to the phys-chem section.<br><br>Analytical method for animal commodities is required for the following residue definition: sum of cyflufenamid, the E isomer and metabolite 149-F1. |
| | New open point 3.3:<br>RMS to amend the list opf end point according to the discussions during the PRAPeR 40. | LOEP to be updated considering above discussions. | New 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: ***2*** | | | Section 3<br>Data requirements: ***0***<br>Data gaps***: 2***<br>Open points: ***1*** |
| | Open point 3.1<br>RMS to elaborate further on whether isomerisation into the Z-isomer has taken place and if so, to clarify the impact on the risk assessment in an addendum<br><br>See reporting table 3(3). | | It seems that it is isomerisation from parent (z isomer) to the E isomer during plant metabolism studies that is in question.<br>The applicant has not addressed any implications of isomerisation on risk assessment in their submission.<br>The reports on plant metabolism do not provide further significant clarification on whether isomerisation has occurred. The applicant does include the E isomer of cyflufenamid in their proposed metabolic pathway (Figure B.7.1).<br>It can only be assumed so as the peak for radiochemical purity determination was named 'NF-149' which is the z-isomer. Therefore it is possible that a limited amount of isomerisation has occurred in the plant metabolism to account for the amounts of 149-(E)-FB reported as found in the plant metabolism studies. | 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 |
|---|---|---|---|---|
| | | | It is not considered that the findings of 149-(E)-FB reported (expected to be on the basis of isomerisation) need to be considered from a risk assessment perspective on the basis that the amounts formed ranged in straw from 0.5% to 4% TRR only, and that the highest mg/kg amount of E isomer of cyflufenamid (149-(E)-FB ) reported in the 1N rates of study was 0.013 mg/kg in straw, only a small amount above 0.01 mg/kg and insignificant compared to amounts of parent (z isomer). Mg/kg amounts of 149-(E)-FB were generally only slightly higher (compared to straw) in forage (up to 0.21 mg/kg) and in the range of 2-3% TRR.<br><br>Addressed (suggest point is discussed in residues Expert meeting) | |
| | Open point 3.2<br>To be discussed in an experts' meeting whether a, and if so what, residue definition for risk assessment and monitoring for food of animal origin should be proposed<br>The meeting consider | | With regard to the DE comment and the RMS response to point 3(5) in the reporting table, there seems to be agreement that animal product residues are not expected as a result of the currently proposed use. On this basis a residue definition is not currently proposed by the RMS.<br>However if the Residues Expert | 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 |
|---|---|---|---|---|
| | aspects such as fat solubility of parent compound, toxicological relevance of metabolites 149-F1, 149-F6 (higher acutely toxic)<br><br>See reporting table 3(5). | | meeting considers that a residue definition is required, then a rationale for a residue definition proposal for animal products for cyflufenamid and metabolite 149-F1 for monitoring purposes and risk assessment is provided by the RMS in column 3 of the reporting table point 3(5).<br>All columns of Reporting table points 3(5), 3(6), 3(7), 3(8), 3(9), 3(10), 3(11) provide relevant considerations (e.g. on fat solubility). UK RMS toxicologist advice is that metabolite 149-F1 is of relevance toxicologically compared to parent, at least on an acute basis, and metabolite 149-F1 is of higher acute toxicity than metabolite 149-F6. However, the EFSA comment seems to state that 149-F6 has a higher acute toxicity, so this is an aspect that needs to be resolved in discussion.<br>Addressed (suggest point is discussed in toxicology and residues Expert meetings). | |
| 3.1 | New data gap<br><br>A clarification concerning the analytical methods used in the residue trials to be submitted. | | | PRAPeR 40 (12 – 13 December 2007):<br><br>Data gap 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 |
|---|---|---|---|---|
| 3.2 | New data gap to be transferred to the phys-chem section.<br><br>Analytical method for animal commodities is required for the following residue definition: sum of cyflufenamid, the E isomer and metabolite 149-F1. | | | PRAPeR 40 (12 – 13 December 2007):<br><br>Data gap open (see phys-chem) |
| | New open point 3.3:<br>RMS to amend the list opf end point according to the discussions during the PRAPeR 40. | | | PRAPeR 40 (12 – 13 December 2007):<br><br>Open point open. |