PEER REVIEW REPORT ON **PICLORAM** 25 11 2009

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List of all reports from PRAPeR Expert Meetings

Date		Section
21-24 04 2009	PRAPeR expert meeting 66	Physical and Chemical Properties
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REPORT OF PRAPeR EXPERT MEETING 66

PICLORAM

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
April 2009	UK	Picloram addendum 2 Vol 3 B2_B3_B5_B6_B7_B8_B9 (April 2009).doc
2009-04-09	UK	Picloram evaluation table rev1-0 (2009-04-09).doc
April 2009	UK	Picloram addendum3 Vol4 (April 2009).doc
2009-02-12	UK	Picloram reporting table rev 1-1 (2009-02-12).doc
June 2008	UK	Picloram studies relied on v2 June 2008.doc
April 2009	UK	Picloram updated list of endpoints (April 2009).doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** Galera

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: PICLORAM

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Picloram (Hb)

1. Physical and Chemical Properties

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 0.1 RMS to include the correct GAP table in the list of end points. See reporting table 0(1)	The list of end points has been updated accordingly by the RMS.	Open point fulfilled.
	Open point: 0.2 RMS to consider use of picloram rather than the acid equivalent when revising the end points. See reporting table 0(3)	The meeting agreed that the term “acid equivalent” is confusing as picloram is an acid and the active substance content should be expressed as picloram. The list of end points is to be amended accordingly.	Open point still open. RMS to revise the list of end points reflecting that the active substance content should be expressed as picloram rather than acid equivalent.
	Open point: 0.3 RMS to provide a comparison table between the technical specification and the composition of the toxicological batches, including a clear identification of the tested compound and the impurities.	Message to tox and ecotox sections to consider the information on the tox and ecotox batches presented in Addendum 3 to Vol. 4. The study of bacterial mutation (Ames test) should not be considered in the peer review (new study).	Open point fulfilled. Message sent to section 2 (tox) and section 5 (ecotox).

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 0(4)		
1.1	Point of clarification for the applicant: Applicant to provide the manufacturing dates of the batches analysed in the 7 batch study. See reporting table 1(1)	The information on the manufacturing dates of the batches analysed in the 7 batch study was provided by the notifier and summarized in Addendum 3 to Vol. 4	Point of clarification addressed.
	Open point: 1.1 RMS to present in an addendum the justification based on the QC data for the levels in the technical specification. See reporting table 1(2)	The meeting agreed that the QC data are not conflicting with the proposed limits for the impurities in the specification and the “rule of thumb” (mean plus 3 SD) may not be truly applicable for QC data. The meeting agreed that based on the QC data the proposed specification is acceptable.	Open point fulfilled.
	Open point: 1.2 RMS to update the LoEP to mention that the minimum purity of the FAO specification is on dry weight basis. See reporting table 1(13)	The list of endpoints has been updated accordingly by the RMS.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 1.3 RMS to update the end points on vapour pressure. See reporting table 1(15)	The list of endpoints on vapour pressure has been updated by the RMS.	Open point fulfilled.
	Open point: 1.4 RMS to update the end points on temperature for solubility to 20°C. See reporting table 1(16)	The list of end points on temperature for solubility to 20°C has been updated by the RMS.	Open point fulfilled.
	Open point: 1.5 RMS to update the end points on boiling point. See reporting table 1(17)	The list of end points on boiling point has been updated by the RMS.	Open point fulfilled.
	Open point: 1.6 RMS to update the end points on flammability. See reporting table 1(18)	The list of end points on flammability has been updated by the RMS.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
1.2	Point of clarification for the applicant: To address the possibility of a second pKa due to the structural formula of the active substance (an amino acid like) See reporting table 1(25)	The information provided by the notifier has been presented in Addendum 2 to the DAR. The calculation provided does not address the basicity of the amino group. New data gap: method used for determination of pKa is not according to one of the methods in OECD 112 and therefore a new pKa study is required. The information received addresses the pKa of the N in the pyridine moiety, not that of the NH_2 group, which is similar to the amino group of an amino acid.	Point of clarification addressed. New data gap proposed, see below.
	New data gap 1.1 identified at PRAPeR 66 meeting: Determination of the pKa according to OECD 112 method is required.		Data gap open.
	Open point: 1.7 RMS to amend list of tests and studies relied upon concerning pH. See reporting table 1(26)	The list of tests and studies will be updated at the end of the peer review process. The point remains open.	Open point still open.
	Open point: 1.8 RMS to amend list of tests and studies relied upon concerning relative density.	The list of tests and studies will be updated at the end of the peer review process. The point remains open.	Open point still open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 1(27)		
1.3	Point of clarification for the applicant: Applicant to provide justification as to why the determination of relevant impurities after storage is not required. See reporting table 1(29)	The notifier has provided further information as to why they believe that the relevant impurity will not form during storage of the product. This information is presented in Addendum 2 to the DAR. The meeting agreed that HCB is not formed on storage.	Point of clarification addressed.
1.4	Point of clarification for the applicant: Applicant to provide further information on procedures for cleaning application equipment to address the efficacy of cleaning. See reporting table 1(31)	The information on procedures for cleaning application equipment has been provided by the notifier and has been presented in Addendum 2 to the DAR.	Point of clarification addressed.
	Open point: 1.9 RMS to include the information on the method of analysis for the relative impurity in an addendum.	The information is provided in Addendum 2 to the DAR and accepted by the meeting.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 1(32)		
	Open point: 1.10 RMS to amend the LoEP concerning the analytes of the monitoring methods for soil See reporting table 1(36)	The list of endpoints concerning the analytes of the monitoring methods for soil has been amended by the RMS.	Open point fulfilled.
	Open point: 1.11 RMS to amend the LoEP concerning the analytes of the monitoring methods for water See reporting table 1(38)	The list of endpoints concerning the analytes of the monitoring methods for water has been amended by the RMS.	Open point fulfilled.
	Open point: 1.12 The acceptability of the residue methods GRM 00.19, GRM 00.18 and GRM 00.17 taking into account the number of fragment-ions used for quantitation and confirmation to be	The meeting concluded that in all 3 residue methods only one fragment ion had been validated and an additional one for identification that is not in line with GD 825/00. The meeting could not agree that other fragment ions could be used for confirmation in this case.	Open point fulfilled. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	discussed in a meeting of experts See reporting table 1(40)		
	New open point 1.13 EFSA to highlight in the conclusion that the meeting could not agree on the acceptability of the residue methods GRM 00.19, GRM 00.18 and GRM 00.17.		Open point open.
1.5	Point of clarification for the applicant: Applicant to provide information on the characteristics of the water used in the method validations. See reporting table 1(47)	The information on the characteristics of the water used in the method validations is presented in an Addendum to the DAR.	Point of clarification addressed.
	New open point 1.14 RMS to update the list of end points according to PRAPeR 66.	In the box of melting point it should be stated ”decomposition occurs during melting” Box of boiling point: “not applicable” pH dependence of water solubility Minimum purity: 920 g/kg on a dry weight basis, minimum/maximum as wet cake should be included as well Representative uses: concentration should be given in the column “g/hl” Analytical method for residues in food of animal origin: matrices should be specified	Open point open. New data gap: specification for the “wet cake” should be provided New data gap: water solubility

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Body fluids and tissues method: it should be stated that the compound is neither toxic nor very toxic.	should be determined at pH 5, 7 and 9
	New data gap 1.2 identified at PRAPeR 66 meeting: Specification for the "wet cake" should be provided.		Data gap open.
	New data gap 1.3 identified at PRAPeR 66 meeting: Water solubility should be determined at pH 5, 7 and 9.		Data gap open.
	Message to section 2 (mammalian toxicology): Please consider the information on the tox batches presented in Addendum 3 to Vol. 4. The Ames study should not be considered in the peer review (new study).		
	Message to section 5 (ecotoxicology): Please consider the information on the ecotox batches presented in Addendum 3 to Vol. 4.		

Appendix 2: Evaluation table

0. General

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 0 Open points: ***4*** Points for clarification: ***0*** Data gaps: ***0***			Section 0 Open points: ***1*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 0.1 RMS to include the correct GAP table in the list of end points See reporting table 0(1)	DAS: No further comment	RMS: 08.04.09 The endpoints have been updated. Open point addressed.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 0.2 RMS to consider use of picloram rather than the acid equivalent when revising the end points. See reporting table 0(3)	DAS: No further comment	RMS: 08.04.09 Picloram expressed as acid equivalent as formulated and in all the exposure sections, therefore would require substantial changes to the DAR. As long as it's clear how it's being expressed then there is no consequence. Open point addressed.	PRAPeR 66 (21 – 24 April 2009): Open point still open. RMS to revise the list of end points reflecting that the active substance content should be expressed as picloram rather than acid equivalent.
	Open point: 0.3 RMS to provide a comparison table between the technical specification and the composition of the toxicological batches, including a clear identification	DAS: No further comment	RMS: 08.04.09 See Addendum 3 (Confidential information). The proposed technical specification for picloram contains a number of impurities not detected in the batches tested in the toxicity studies, and also a number of	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled. Message sent to section 2 (tox) and section 5 (ecotox).

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	of the tested compound and the impurities. See reporting table 0(4)		impurities present at levels higher than in the tested batches. A study of bacterial mutation (Ames test) using a representative batch of the technical material (as manufactured) in order to address concerns regarding the toxicity of these impurities has been conducted and was found to be negative see Addenda 1. Open point addressed.	
	Open point: 0.4 RMS to provide a summary table of the different toxicological studies performed with the different derivatives of picloram (with doses converted in picloram acid equivalents), in order to compare their toxicity profile. See reporting table 0(5)	DAS: No further comment	RMS: 08.04.09 This is not a useful exercise as most of the package has been conducted with picloram acid, with the exception of the teratology studies which were conducted with either the potassium salt or the triisopropanolamine. Open point addressed.	Open point transferred to section 2 (mammalian toxicology).

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

<table>
<tr><th>No.</th><th>Column A
Conclusions from the Reporting Table</th><th>Column B
Comments from the notifier / applicant</th><th>Column C
Rapporteur Member State comments on the notifier / applicant comments</th><th>Column D
Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure</th></tr>
<tr><td></td><td>Section 1
Open points: 12
Points for clarification: 5
Data gaps: 0</td><td></td><td></td><td>Section 1
Open points: 4
Points for clarification: 0
Data gaps: 3</td></tr>
<tr><td>1.1</td><td>Point of clarification for the applicant:
Applicant to provide the manufacturing dates of the batches analysed in the 7 batch study.

See reporting table 1(1)</td><td>Report 03-218-E:<table><tr><th>Technical Lot</th><th>Commercial Batch Number</th><th>Manufacture Date</th></tr><tr><td>TSN104168</td><td>RB28162951</td><td>28-Feb-2003</td></tr><tr><td>TSN104169</td><td>RB10162952</td><td>10-Feb-2003</td></tr><tr><td>TSN104170</td><td>RB24162901</td><td>24-Feb-2003</td></tr><tr><td>TSN104171</td><td>QK07162951</td><td>07-Nov-2002</td></tr><tr><td>TSN104172</td><td>RB22162902</td><td>22-Feb-2003</td></tr><tr><td>TSN104173</td><td>QJ01162965</td><td>01-Oct-2002</td></tr><tr><td>TSN104174</td><td>QL06162956</td><td>06-Dec-2002</td></tr></table>Report FOR-07-004:<table><tr><th>Technical Lot</th><th>Commercial Batch Number</th><th>Manufacture Date</th></tr><tr><td>TSN106014</td><td>UJ22162952</td><td>22-Oct-2006</td></tr><tr><td>TSN106015</td><td>UH14162953</td><td>14-Aug-2006</td></tr><tr><td>TSN106016</td><td>UI01162901</td><td>01-Sept-2006</td></tr><tr><td>TSN106018</td><td>UI30162955</td><td>30-Sept-2006</td></tr><tr><td>TSN106020</td><td>UI19162952</td><td>19-Sept-2006</td></tr><tr><td>TSN106023</td><td>UJ02162901</td><td>02-Oct-2006</td></tr><tr><td>TSN106248</td><td>VD26162955</td><td>26-Apr-2007</td></tr></table></td><td>RMS: 08.04.09
The information provided by the Notifier indicates that the batches analysed are representative of production. For completeness the information has been presented in Addendum 3 (Confidential information) to the DAR.

The RMS considers that this point is addressed.

The RMS notes that Report FOR 07-004 has not been submitted to the RMS therefore this information is surplus to requirements.</td><td>PRAPeR 66 (21 – 24 April 2009):

Point of clarification addressed.</td></tr>
<tr><td></td><td>Open point: 1.1
RMS to present in an addendum the justification based on the QC data for the levels in the technical</td><td>DAS: the notifier has no further comments. A justification letter was provided to the RMS in July 2007.</td><td>RMS: 08.04.09
The information has been presented in the Addendum 3 (Confidential information) to the DAR.
Open point addressed.</td><td>PRAPeR 66 (21 – 24 April 2009):

Open point fulfilled.</td></tr>
</table>

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	specification. See reporting table 1(2)			
	Open point: 1.2 RMS to update the LoEP to mention that the minimum purity of the FAO specification is on dry weigh basis. See reporting table 1(13)	DAS: No further comment	RMS: 08.04.09 The LoEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 1.3 RMS to update the end points on vapour pressure. See reporting table 1(15)	DAS: No further comment	RMS: 08.04.09 The LoEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 1.4 RMS to update the end points on temperature for solubility to 20°C. See reporting table 1(16)	DAS: No further comment	RMS: 08.04.09 The LoEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 1.5 RMS to update the end points on boiling point.	DAS: No further comment	RMS: 08.04.09 RMS: 08.04.09 The LoEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 1(17)			
	Open point: 1.6 RMS to update the end points on flammability. See reporting table 1(18)	DAS: No further comment	RMS: 08.04.09 The LoEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
1.2	Point of clarification for the applicant: To address the possibility of a second pKa due to the structural formula of the active substance (an amino acid like) See reporting table 1(25)	DAS: A supplementary document NAFST-09-27, provides additional information aimed at increasing the robustness of the assessment to support the request for the possibility of a second pKa due to the structural formula of the active substance. A second pKa was calculated to be -3.85. Since the value is a negative number, no additional experimental studies to confirm the pKa are required or have been performed.	RMS: 08.04.09 The information provided by the Notifier has been presented in Addendum 2 to the DAR. The RMS considers that this point is addressed.	PRAPeR 66 (21 – 24 April 2009): Point of clarification addressed. New data gap proposed, see below.
	New data gap 1.1 identified at PRAPeR 66 meeting: Determination of the pKa according to OECD 112 method is required.			PRAPeR 66 (21 – 24 April 2009): Data gap open.
	Open point: 1.7 RMS to amend list of tests and studies relied upon concerning pH	DAS: No further comment	RMS: 08.04.09 The list of tests and studies will be updated at the end of the peer review process.	PRAPeR 66 (21 – 24 April 2009): Open point still open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 1(26)			
	Open point: 1.8 RMS to amend list of tests and studies relied upon concerning relative density See reporting table 1(27)	DAS: No further comment	RMS: 08.04.09 The list of tests and studies will be updated at the end of the peer review process.	PRAPeR 66 (21 – 24 April 2009): Open point still open.
1.3	Point of clarification for the applicant: Applicant to provide justification as to why the determination of relevant impurities after storage is not required. See reporting table 1(29)	DAS: The notifier highlights that if a starting material used in the manufacturing of the technical picloram does not contain HCB, then HCB is not found in the technical material. No known pathways exist for the formation of HCB in technical picloram after manufacture. Because of this, it is extended to formulations that no known pathways for the formation of HCB exist. Since no known pathways are present for the formation of this impurity in technical picloram, and the impurity has been identified as an impurity in a starting material, it is proposed that the analysis of this impurity in formulated materials is not required before or after storage, since this impurity is monitored in the technical, and is below the limits set for technical picloram at the time of formulation manufacturing. A supplementary document is	RMS: 08.04.09 The Notifier has provided further information as to why they believe that the relevant impurity will not form during storage of the product. This information is presented in Addendum 2 to the DAR. The RMS believes that this justification is acceptable and therefore the determination of relevant impurities in the product after storage is not required. The RMS considers that this point is addressed.	PRAPeR 66 (21 – 24 April 2009): Point of clarification addressed.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		additional justification aimed at increasing the understanding as to why the determination of relevant impurities after storage is not required.		
1.4	Point of clarification for the applicant: Applicant to provide further information on procedures for cleaning application equipment to address the efficacy of cleaning See reporting table 1(31)	DAS: The procedure for tank cleaning after using picloram has to follow the Good Field Agricultural practices. The following procedure should be followed up: Wash out spray equipment thoroughly with water and detergent immediately after use. Spray out, fill with clean water. Spray out again before storing or using another product. Traces of picloram could cause harm to susceptible crops sprayed later.	RMS: 08.04.09 The information provided by the Notifier has been presented in Addendum 2 to the DAR for completeness. No data have been submitted to support the effectiveness of the cleaning procedures.	PRAPeR 66 (21 – 24 April 2009): Point of clarification addressed.
	Open point: 1.9 RMS to include the information on the method of analysis for the relative impurity in an addendum. See reporting table 1(32)	DAS: No further comment	RMS: 08.04.09 The information is presented in Addendum 2 to the DAR. The RMS considers that this point is addressed.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 1.10 RMS to amend the LoEP concerning the analytes of the monitoring methods for soil.	DAS: No further comment	RMS: 08.04.09 The LOEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 1(36)			
	Open point: 1.11 RMS to amend the LoEP concerning the analytes of the monitoring methods for water. See reporting table 1(38)	DAS: No further comment	RMS: 08.04.09 The LOEP have been updated.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	Open point: 1.12 The acceptability of the residue methods GRM 00.19, GRM 00.18 and GRM 00.17 taking into account the number of fragment-ions used for quantitation and confirmation to be discussed in a meeting of experts See reporting table 1(40)	DAS: the notifier believes that sufficient information regarding the fragment ions has been supplied in the tier summaries of the dossier sections submitted and provided in the DAR. The notifier has no additional comments.	RMS: 08.04.09 Methods GRM 00.19, GRM 00.18 and GRM 00.17 all utilise GC/NCI-MS using capillary column HP-5MS for determination of residues of picloram. For method GRM 00.17 Quantitation was conducted using m/z 246, with confirmation at m/z 248 or additional ions m/z = 210,212 and 250. For methods GRM 00.19 & GRM 00.18 quantitation was conducted using m/z 246, and it was stated in the DAR that for confirmation m/z 248 could be used. It was not specifically stated for these two methods that any other ions were available, however, given the measurement systems are identical for all 3 methods the RMS is of the opinion that the m/z ratios suggested for method GRM 00.17 can also apply to methods 00.18 & 00.19 and the methods are acceptable.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled. New open point proposed, see below.

<table>
<tr><th>No.</th><th>Column A
Conclusions from the Reporting Table</th><th>Column B
Comments from the notifier / applicant</th><th>Column C
Rapporteur Member State comments on the notifier / applicant comments</th><th>Column D
Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure</th></tr>
<tr><td></td><td>New open point 1.13
EFSA to highlight in the conclusion that the meeting could not agree on the acceptability of the residue methods GRM 00.19, GRM 00.18 and GRM 00.17.</td><td></td><td></td><td>PRAPeR 66 (21 – 24 April 2009):

Open point open.</td></tr>
<tr><td>1.5</td><td>Point of clarification for the applicant:
Applicant to provide information on the characteristics of the water used in the method validations.

See reporting table 1(47)</td><td>DAS: The waters used in the method were from different locations within the UK and France and also represented different types/sources.

<table><tr><th>Sample no</th><th>Type</th><th>Source</th></tr><tr><td>R00-999-019</td><td>River Water</td><td>River Odet, Quimper, Brittany, France</td></tr><tr><td>R00-999-018</td><td>Lake Water</td><td>Letcombe Lake, Letcombe Regis, Oxfordshire, UK</td></tr><tr><td>R96-000-596</td><td>Ground Water</td><td>Wantage, Oxfordshire, UK</td></tr><tr><td>R96-999-020</td><td>Ground Water</td><td>Bossington, Somerset, UK</td></tr><tr><td>R00-999-020</td><td>Drinking Water</td><td>Letcombe Laboratories, Letcombe Regis, Oxfordshire, UK</td></tr></table>
Although no characterisation work was carried out at the time of the validation, the notifier believes the variability’s in the water sources offer sufficient robustness for the method to be acceptable and used in determining</td><td>RMS: 08.04.09
The information provided by the Notifier has been presented in Addendum 2 to the DAR for completeness. The RMS believes that this point is addressed.</td><td>PRAPeR 66 (21 – 24 April 2009):

Point of clarification addressed.</td></tr>
</table>

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		picloram concentrations in water.		
	New open point 1.14 RMS to update the list of end points according to PRAPeR 66: In the box of melting point it should be stated ”decomposition occurs during melting” Box of boiling point: “not applicable” pH dependence of water solubility Minimum purity: 920 g/kg on a dry weight basis, minimum/maximum as wet cake should be included as well Representative uses: concentration should be given in the column “g/hl” Analytical method for residues in food of animal origin: matrices should be specified Body fluids and tissues method: it should be stated that the compound is neither toxic nor very toxic.			PRAPeR 66 (21 – 24 April 2009): Open point open. New data gaps 1.2 and 1.3 proposed, see below.
	New data gap 1.2 identified at PRAPeR 66 meeting:			PRAPeR 66 (21 – 24 April 2009):

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Specification for the “wet cake” should be provided.			Data gap open.
	New data gap 1.3 identified at PRAPeR 66 meeting: Water solubility should be determined at pH 5, 7 and 9.			PRAPeR 66 (21 – 24 April 2009): Data gap open.
	Message to section 2 (mammalian toxicology): Please consider the information on the tox batches presented in Addendum 3 to Vol. 4. The Ames study should not be considered in the peer review (new study).			
	Message to section 5 (ecotoxicology): Please consider the information on the ecotox batches presented in Addendum 3 to Vol. 4.			

REPORT OF PRAPeR EXPERT MEETING 67

PICLORAM

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
April 2009	UK	Picloram addendum 2 Vol 3 B2_B3_B5_B6_B7_B8_B9 (April 2009).doc
2009-04-09	UK	Picloram evaluation table rev1-0 (2009-04-09).doc
April 2009	UK	Picloram addendum3 Vol4 (April 2009) cover page.doc
2009-02-12	UK	Picloram reporting table rev 1-1 (2009-02-12).doc
June 2008	UK	Picloram studies relied on v2 June 2008.doc
April 2009	UK	Picloram updated list of endpoints (April 2009).doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
None		

The conclusions of the meeting were as follows:

4. Data on preparations: GALERA (GF-224)

5. Classification and labelling: candidate for R53

8. **Recommended restrictions/conditions for use:** only spring application once in three years has been assessed

9. Reference list: Not discussed

Areas of concern: Risk assessors should be aware that the agreed DT_{50} end points for picloram are considered to only be valid for assessing use rates of products equivalent to

a picloram dose that results in a soil concentration up to 0.07 mg picloram /kg dw soil.

There is a data gap for a soil photolysis study. Therefore there is no environmental assessment of any potential soil photolysis transformation products if these are formed. Information from aqueous photolysis experiments indicates photolysis may be a pertinent process.

Appendix 1: Discussion table: PICLORAM

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Picloram (Hb)

4. Fate and behaviour

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 4.1 RMS to clarify the soil classification of the soil from Douglas County, KS in a corrigendum and correct the soil classification of this soil in the LoEP if this was wrong. If this is correct, than the normalization should be corrected. Remark: The normalisation procedure used by the RMS is correct. However, the normalisation of the soil from Douglas County, KS could be regarded to be correct only if it was silty clay as indicated in Table B.8.16 of the DAR. If it was silty loam as indicated in Table B.8.23 and in the LoEP	The RMS has clarified that the soil from Douglas County, KS is a silty clay soil; therefore the normalized DT_{50} of this soil as well as the geomean of 5.2 d is correct. The corrections regarding the soil classification have been done appropriately in Addendum 2 and for the LoEP. Open point fulfilled.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	than the normalisation still seems to be wrong See reporting table 4(2)		
	Open point: 4.2 MSs experts to discuss in a meeting the need for further identification of the compound called as 'Largest Unknown' in the study by Knowles, S., Swales, S.A., 2002, and/or the explanation (to be included in an addendum by RMS with the anomalies of the unknowns) which supports that this unknown fraction is an artefact. See reporting table 4(3)	The RMS's clarification on the unknown compounds including the Largest Unknown from the study by Knowles, S., Swales, S.A., 2002, is included in the Addendum 2 (from page 33). The meeting discussed the information provided and concluded that it was probable that the category 'largest unknown' is an artefact of the analytical procedure and any unknown compound would be < 5 % AR. Open point fulfilled.	Open point fulfilled.
	Open point: 4.3 MSs experts to discuss in a meeting that whether the degradation of picloram is dose related and whether it is supported that DT_{50}	A potential dose-dependence has been indicated by the RMS (higher dose, higher DT50). The lowest dose was about twice as high as the intended use rate. Therefore the DT50 values at the lowest dose are representative for the intended use. The calculation of the parent rate in g a.s./ha was incorrect in the original DAR (wrong units lb/acre). Clarification provided in the reporting table is presented below (1.5 g/cm^3 bulk density and equal mixing in 5 cm depth soil). The resulting g/ha doses are as follows:	Open point fulfilled. New open points 4.19 and 4.20 proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	values from the lowest dose, which are always the shortest ones, are used in the estimation of the exposure from the study by Cook, W.L., Buehrer, J.T., 1999. MSs experts to discuss the exclusion or inclusion of DT_{50} values from the study by McCall, P.J., Jeffries, T.K., 1978, as well. See reporting table 4(5)	**0.07 µg/g – 52.5 g/ha used for extracting DT50 end points for use in exposure assessment** 0.11 µg/g – 82.5 g/ha 0.25 µg/g – 187.5 g/ha 0.38 µg/g – 285 g/ha 0.52 µg/g – 390 g/ha The highly exaggerated rates in the McCall study are not within recommendations in the current guidelines. Therefore it is considered that this study should not be used for deriving DT50 values for use in exposure assessment. The RMS confirmed that the McCall results are NOT in the LoEP rate of aerobic laboratory degradation box. RMS to include in the LoEP in a separate column (X) the dose rates associated with each endpoint. RMS to ensure that McCall et al 1978 is not present in the List of studies relied on. The experts agreed that the DT50 endpoints from the lowest dose rate from the Cook/Buehrer 1999 study are appropriate to use in this case (the intended use assessed). It is noted that based on the proposed dose-dependency of degradation the risk assessment is covered and represents around once to twice the intended use rate. Open point fulfilled.	
	New open point: 4.19 RMS to include in the LoEP in a separate column (X) the dose rates associated with each endpoint.		Open point open.
	New open point: 4.20		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	RMS to ensure that the study by McCall et al 1978 is not present in the List of studies relied on.		
4.1	Point of clarification for the applicant: Applicant to provide information/argumentation which supports the discussion on the possible dose-related degradation of picloram observed in the study Cook, W.L., Buehrer, J.T., 1999 (e.g by provision better quality images of the graphs in the study report of the mentioned study). See reporting table 4(5)	See discussion above at open point 4.3. No visual assessment was provided by the applicant but it was synthesized during the meeting and indicated a dose dependency (without mechanistic explanation). Point of clarification addressed.	Point of clarification addressed.
	Open point: 4.4 MSs experts to discuss in a meeting whether it is agreed that the degradation endpoints derived from the study by Knowles, S., Swales, S.A., 2002 is excluded. If not, what	This concerns a lab incubation of the lysimeter soil kept in the dark used as rate study. The study was conducted at 20 degrees and at unknown soil moisture therefore normalisation may be or may not be necessary. SFO and FOMC fits and evaluation of the fits together with argumentation supporting the exclusion of these DT_{50} values from the subsequent modelling are presented in Addendum 2 from page 51. The RMS indicated that for SFO visual fits are poor although chi2 was acceptable. FOMC	Open point fulfilled. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	DT_{50} value should be used. To support the discussion RMS to provide the kinetic fit (e.g SFO and FOMC) of the upper layer of HAN soil in an addendum. See reporting table 4(6)	gave good visual fit and chi2, however DT90 was extrapolated beyond the study duration (10 % AR was not reached during the study). So DFOP or HS fits would appear appropriate and the Hockey Stick is available in the DAR Table B8.15 page 218. HS fit provided by the notifier gave the best fit with a DT50 slow phase of 252.6 days (chi2 2.8, not reported in the DAR but checked in the meeting). The experts discussed whether the study is acceptable. There seems to be no reason to exclude the study. The experts concluded that the HS slow phase DT50 value needs to be added to the data set and an appropriate moisture correction should be performed. The number of DT50 endpoints was 8 and would become 9 so a median value could be calculated. The median would be 83 days. The geomean would go from 48 to approximately 58 days. The experts agreed that the median should be used for exposure assessment. Open point fulfilled. New open point: RMS to include in the LoEP and in the calculation the median of the HS DT50 value derived for the top soil of the lysimeter, and to check the normalisation for moisture (however no impact on median since the DT50 concerned is not the median value).	
	New open point: 4.21 RMS to include in the LoEP and in the calculation the median of the HS DT50 value derived for the top soil of the lysimeter, and to check the normalisation for moisture (however no impact on median since the DT50		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	concerned is not the median value).		
	Open point: 4.5 MSs experts to discuss in a meeting the requirement of a new soil photolysis study. See reporting table 4(7)	A soil photolysis study is available in the DAR. This used a Mercury arc lamp and therefore was not accepted by the RMS. The RMS is of the opinion that soil photolysis should be addressed at MS level if the applied for uses in the MS are considered likely to involve greater potential for soil photolysis. However soil photolysis is an Annex II requirement (unless the deposition of the active substance at the soil surface is unlikely to occur). Photodegradation in soil is not an issue for the exposure assessment for the parent in this case, since modelling is based on laboratory studies. However, it should be considered whether formation of soil photolysis metabolites is probable. Just as an indication: In aqueous photolysis there is fast photolytic degradation of the parent and there is some information on metabolites formed, but these are considered to be of no concern according to guidance (non-relevance in groundwater and aquatic ecotoxicology) (short-chain aliphatic compounds). Open point fulfilled. New open points: EFSA to indicate a data gap in the EFSA conclusion (lack of valid soil photolysis study). RMS to remove all current entries in the box soil photolysis and replace with ‘data gap’.	Open point fulfilled. New open points 4.22 and 4.23 are proposed, see below.
	New open point: 4.22 EFSA to indicate a data gap in the EFSA conclusion (lack of valid soil photolysis study).		Open point open.
	New open point: 4.23 RMS to remove all current entries in the		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	box soil photolysis and replace with 'data gap'.		
4.2	Point of clarification for the applicant: Applicant to clarify the column names and what the values in the table exactly mean in the study by Knowles, S., Schnöder, F., 2003a (the table of concern is referenced in the DAR as Table B.8.33). It should be noted that pending on the information submitted by the applicant new DT_{50} and PECsoil calculation might be needed. See reporting table 4(12)	The notifier has not clarified what the column names mean. The data from this table (Table B.8.33 in the DAR) were not used for DT50 calculation. Instead, the combined total extractable radioactivity in the 0 – 20 cm layer was used resulting in DT50/DT90 values of 49.2d/163.3d. This is regarded as conservative. Although the column names were not clarified by the notifier, the point of clarification can be regarded as addressed as no further action is required.	Point of clarification regarded as addressed as no further action is required.
	Open point: 4.6 MSs experts to discuss in a meeting to cancel the DT_{50} of 14 days derived from the study by Knowles, S., Unsworth, C., 2003 from the LoEP.	The field DT_{50} values available in the DAR and included in the LoEP are: 14d, 39d, 20d and 49d. For PECsoil calculation DT_{50} of 49d was used. The statement by the RMS that it was worst-case is not correct (this was the lowest DT50). The DT50 endpoint was derived from only 4 data points which is not acceptable. There is no impact on the risk assessment since PECsoil is based on highest field DT50 of 49 days and groundwater/surface water exposure modelling is based on laboratory data.	Open point fulfilled. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 4(14)	Open point fulfilled. New open point: RMS to remove the 14 d value from the LoEP and delete the geomean field DT50 value (not pertinent to this exposure assessment).	
	New open point: 4.24 RMS to remove the 14 d value from the LoEP and delete the geomean field DT50 value (not pertinent to this exposure assessment).		Open point open.
	Open point: 4.7 MSs experts to discuss in a meeting to include the Koc values (or any of them) from the study Knowles, S., Swales, SA., 2002 in the LoEP. See reporting table 4(17)	Beside the 8 values, 3 other Kd values are available from a second study using 3 soil layers of a lysimeter. The incorporation of these 3 Koc values into the dataset would lead to the change of the arithmetic mean from 35 L/kg (n=8) to 37 ml/g (n=11). For FOCUS modelling 35 L/kg was used. Reasons to (have) exclude(d) the values would be that heat treatment > 100 degrees C of the soils prior to use in batch sorption studies may have caused changes in sorption properties. According to the guidelines this invalidates the study. The meeting concluded that the values should be left out (as is already the case). No changes needed. Open point fulfilled.	Open point fulfilled.
	Open point: 4.8 MSs experts to discuss in a meeting to include in the LoEP and use in the PEC calculations 1 as 1/n instead of 0.9.	In Column C of the evaluation table some considerations are made by the RMS. Only Kd values were available for picloram. As Kd sorption assumes linear adsorption, a 1/n of 1 is appropriate. A default value of 1 has already been agreed in several peer reviews during (at least) stage 3 of the peer review program. NB for Kf, the default value would be 0.9 as stated in the guidance. However, no guidance is given on default 1/n values for Kd values.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 4(18)	The experts agreed that a value for 1/n of 1 is appropriate. This implies that new groundwater modelling is necessary (see below, open point 4.9). Open point fulfilled.	
	Open point: 4.9 MSs experts to discuss the need of new PECgw and PECsw calculations for picloram. If they are regarded as needed, the proper input parameters to be used should be discussed. See reporting table 4(18)	New modelling for groundwater and surface water/sediment for picloram is needed based on changes in DT50 and 1/n values. Agreed values: DT50 soil 82.8 days (median lab value) K(d)oc 35 L/kg 1/n 1 DT50water 1000 d (default) DT50sediment 196 d (geomean of 2 whole system DT50) For groundwater modelling two models should be used. Open point fulfilled.	Open point fulfilled. New open point proposed, see below.
	New open point: 4.25 RMS to provide new PECgw, $PEC_{SW,}$ PEC_{SED} calculations. For PEC gw two models should be used. For the new input parameters refer to open point 4.9.		Open point open.
	Open point: 4.10 RMS to include information and results on the series of test	After further examination of the study report, the RMS clarified that there was no toxic control (which contained both picloram and sodium benzoate) applied in the test. This fact has been confirmed in Addendum 2 (page 66).	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	solution containing both picloram and sodium benzoate in an addendum. Remark: Based on the study description there were test vessels, which contained both items together. This information can be valuable to decide whether picloram is toxic to microorganisms (note that soil DT_{50} values with high doses were originally excluded without information on biomass of the soils). See reporting table 4(20)	Open point fulfilled.	
	Open point: 4.11 MSs experts to discuss in a meeting the proper DT_{50} values (for water and sediment) to be used in the PECsw calculations for picloram. See reporting table	The original evaluation used 300 d in water phase and geomean DT50 the whole system was used in the sediment phase for picloram. According to FOCUS kinetics this default value should be 1000 d (in this case for the water phase, based on the assumption that degradation indeed takes place in the sediment). The 300 d was used as a conservative default value which was common at the time of dossier submission. This difference will not have a large impact on the initial water PEC at the intended use	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	4(23)	(single application). For future calculations 1000 d is recommended to be in line with current guidance. Recalculation is requested at open point 4.9. Open point fulfilled.	
	Open point: 4.12 MSs experts to discuss in a meeting the proper formation fraction (or 'application rate') to be used in the PECsw calculations for the metabolites. See reporting table 4(24)	The metabolites concerned are Aminopyralid (which is 3,6-dichloro analogue/metabolite) and 5,6-dichloro-analogue/metabolite. The maximum observed of 10.55% (3,6-analogue, alkaline system) and 18.95% (5,6-analogue, acidic system) was used in the PECsw calculations (FOCUS step 1&2). In both cases the maximum observed was at the end of the study. It is noted that about 60% (acidic) and 75% (alkaline) AR was present as parent in the W/S systems at the study end (102 d). The experts discussed whether the use of maximum observed is defendable in this case, since potentially a higher amount of metabolite could have been formed. Obviously formation fractions of 1 would be worst-case for both metabolites. This could theoretically be divided between the two analogues, however this seems not plausible since the metabolites are not formed to the same extent in the two water-sediment systems. From a risk assessment perspective, formation fractions of 1 are considered appropriate conservative exposure estimates for both metabolites. Open point fulfilled. See new open point at open point 4.14.	Open point fulfilled. See new open point 4.26
	Open point: 4.13 RMS to include an assessment of the	The RMS has included all the information regarding the degradation and adsorption in soil of aminopyralid (=3,6-dichloro analogue) in Addendum 2 from the DAR of aminopyralid (new a.s.).	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	degradation and adsorption in soil of aminopyralid (=3,6-dichloro analogue) in an addendum. See reporting table 4(27)	The used endpoints from the aminopyralid dossier, as summarized in Addendum 2, are DT50soil (field normalised geomean DT50 12.1 days which has been commented on) and Koc (mean of studies at pH > 5 is 4.07 L/kg which is considered as a worst-case estimate). As aminopyralid is not a soil metabolite of picloram, the DT50soil is not required for PECsurface water calculations in the picloram dossier. The experts considered that the Koc value of 4.07 L/kg was sufficiently conservative. Open point fulfilled.	
	Open point: 4.14 MSs experts to discuss in a meeting whether the input parameters for the metabolites used in the PECsw calculations are agreed. See reporting table 4(27)	See discussion at open point 4.13 for aminopyralid (3,6-analogue). DT50soil for the metabolites appears to be irrelevant as the metabolites are not formed in soil (formation in water/sediment will be simulated via drift entry at STEP 1-2). It was not clear how the original modelling was performed. The experts agreed that the Koc of aminopyralid seems to be conservative enough to be used also for the 5,6-analogue. An estimate for the soil DT50 of the 5,6-analogue is not needed (as is also the case for aminopyralid in view of the fact that the metabolites are not formed in soil). For water-sediment DT50 a whole system value of 1001 days was used in the original calculations. Following guidance a value of 300 days could be used if TWA PEC values are needed. Open point fulfilled. New open point: RMS to recalculate PECsw/sed STEP 1 and 2 for the two metabolites (aminopyralid and 5,6-analogue), taking into account that formation in soil should be set to a low value (e.g., 0.001, currently not clear from the DAR or addendum) and a Koc value of 4.07 L/kg for both metabolites, and a formation fraction of 1 for water system as indicated in open point 4.12.	Open point fulfilled. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	New open point: 4.26 RMS to recalculate PECsw/sed STEP 1 and 2 for the two metabolites (aminopyralid and 5,6-analogue), taking into account that formation in soil should be set to a low value (e.g., 0.001, currently not clear from the DAR or addendum) and a Koc value of 4.07 L/kg for both metabolites, and a formation fraction of 1 for water system as indicated in open point 4.12.		Open point open.
	Open point: 4.15 EFSA to include in EFSA conclusion a recommendation for restriction of timing of application to spring. See reporting table 4(29)	The EFSA should include in the EFSA conclusion a recommendation for restriction of timing of application to spring (as simulated in Step 3 PECsw calculations), and not more frequently than once every 3 years as annual applications have not been simulated for groundwater. Therefore the open point has been amended.	Open point open. EFSA to include in EFSA conclusion a recommendation for restriction of timing of application to spring and not more frequently than once every 3 years.
4.3	Point of clarification for the applicant: Applicant to submit the information on	The applicant made a comment which resulted in this point of clarification, because they were not content with that 2 DT50 values were not accepted by the RMS. Therefore they wanted to submit more information (recalculation of DT50 values). However, no information was provided. It's not possible to provide anything else at this	Point of clarification addressed.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	recalculation of field kinetics for picloram to the RMS. See reporting table 4(30)	stage. Point of clarification addressed.	
	Open point: 4.16 If RMS accepts this information on recalculation of field kinetics for Picloram from the applicant, RMS to evaluate in an addendum. See reporting table 4(30)	This open point became redundant, see point of clarification 4.3.	Open point closed.
	Open point: 4.17 RMS to revise LOEP in light of EFSA comments. See reporting table 4(32)	The LoEP has been updated as requested. Additional points: • STEP 3 for parent is missing from the LoEP, please add. • As the origin of the quantum yield data is still questionable, quantum yield value to be replaced by the correct value agreed in the phys-chem section of the assessment, if it is confirmed that the study report is in the dossier. Open point open.	Open point open. RMS to update the LoEP as indicated in Column 3 of the discussion table.
	Open point: 4.18 RMS to amend list of tests and studies relied upon in light of EFSA	The list of tests and studies relied is to will be updated at the end of the peer review process. Open point is open.	Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	comments. See reporting table 4(33)		
	New open point : 4.27 RMS to amend the residue definition for further assessment.	Agreed by experts: Soil: picloram Ground water: picloram Surface Water: picloram, aminopyralid and 5,6-dichloro analogue of picloram Sediment: picloram, aminopyralid and 5,6-dichloro analogue of picloram Air: picloram	Open point open.
	Message from section 1 (phys-chem) to section 4: A new water solubility study is required, it is expected that water solubility will be (even) higher than the value established now.	Noted.	Answer: Noted.

Appendix 2: Evaluation table

4. Environmental fate and behaviour

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 4 Open points: ***18*** Points for clarification: ***3*** Data gaps: ***0***			Section 4 Open points: ***12*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 4.1 RMS to clarify the soil classification of the soil from Douglas County, KS in a corrigendum and correct the soil classification of this soil in the LoEP if this was wrong. If this is correct, than the normalization should be corrected. Remark: The normalisation procedure used by the RMS is correct. However, the normalisation of the soil from Douglas County, KS could be regarded to be correct only if it was silty clay as indicated in Table B.8.16 of the DAR. If it was silty loam as indicated in Table B.8.23 and in the LoEP than the normalisation	DAS: It does appear a Silt Loam field capacity value (26%) was chosen rather than the Silty clay value (40%) for the Kansas soil in the normalization procedure. However, choosing the correct value will reduce the normalized half-life. The resulting geometric mean is 46.5 day versus the 48.3 day value used in the PECgw assessment. Thus, the existing assessment may be considered conservative.	RMS: 08.04.09 By the RMS calculation the corrected DT50 value of 5.2 days is correct for a silty clay and a field capacity of 40 % moisture. The tables B.8.23 and B.8.35 should therefore read 'silty clay' in the soil texture and soil type column for Tables B.8.23 and B.8.35 respectively. The Focus default moisture should read 40 not 26 in both Tables. However as the final corrected DT50 value is correct at 5.2 days, then no re-calculation of the geometric mean DT50 value is required. Corrected versions of the relevant tables have been included in Addendum 2 where they are now referred to as B.8.23b and B.8.35b. The Appropriate changes have been	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	still seems to be wrong See reporting table 4(2)		made to the LoEP. The RMS considers that the open point is closed.	
	Open point: 4.2 MSs experts to discuss in a meeting the need for further identification of the compound called as 'Largest Unknown' in the study by Knowles, S., Swales, S.A., 2002, and/or the explanation (to be included in an addendum by RMS with the anomalies of the unknowns) which supports that this unknown fraction is an artefact. See reporting table 4(3)	DAS: No further comment	RMS: 08.04.09 The RMS has included the Notifiers original argumentation in full in Addendum 2. The Notifier also submitted a total of 33 chromatograms to assist in the illustration of this argument. The RMS has not reproduced all of these chromatograms in the addendum, but has reproduced chromatograms to which the Notifier specifically refers along with a small number of others. As indicated in the DAR, the RMS considers that the peak unidentified radioactivity at study end of 5.7% AR is likely to be due to an analytical artefact rather than a specific metabolite from picloram.	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.
	Open point: 4.3 MSs experts to discuss in a meeting that whether the degradation of picloram is dose related and whether it is supported that DT_{50} values from the lowest dose, which are always the shortest ones, are used in the estimation of the exposure from the study	DAS: See notifier's comments in point 4.1 below.	RMS: 08.04.09 The RMS previous comments in Reporting Table are reproduced below for ease of reference. Also see comments in Point of clarification 4.1 below. [RMS 04.02.09: Additional information on mineralisation of another substance, 3,4-dichlorobenzoic acid, in	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open points 4.19 and 4.20 proposed see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	by Cook, W.L., Buehrer, J.T., 1999. MSs experts to discuss the exclusion or inclusion of DT_{50} values from the study by McCall, P.J., Jeffries, T.K., 1978, as well. See reporting table 4(5)		each soil was provided in the study report, but there were no additional measurements of microbial activity of the soil apart from indirectly via rate of degradation and mineralisation. The study report provides graphical presentation of degradation of picloram at each dose in each soil and the effect of dose on half-life for each soil. The graphs in the CADDY version of the study report are relatively indistinct, and it would be useful to request the Notifier to provide better quality images to include in an addendum.]	
	New open point: 4.19 RMS to include in the LoEP in a separate column (X) the dose rates associated with each endpoint.			PRAPeR 67 (20 – 24 April 2009): Open point open.
	New open point: 4.20 RMS to ensure that the study by McCall et al 1978 is not present in the List of studies relied on.			PRAPeR 67 (20 – 24 April 2009): Open point open.
4.1	Point of clarification for the applicant: Applicant to provide information/argumentation which supports the discussion on the possible dose-related degradation of picloram observed in the	DAS: Based on simple examination, the rate effect is clear in the Cook & Buehrer study. It is important to highlight that the lowest rate in the Cook & Buehrer study is actually higher than the GAP rate being supported at Annex 1, therefore the existing assessment may be	RMS: 08.04.09 In addition to the Notifiers argumentation the RMS would draw the attention to Table B.8.22. For two soils DT50 increases with increasing application rate. For the remaining two soils the general trend is the same, though it could be said that the effect is	PRAPeR 67 (20 – 24 April 2009): Point of clarification addressed.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	study Cook, W.L., Buehrer, J.T., 1999 (e.g by provision better quality images of the graphs in the study report of the mentioned study). See reporting table 4(5)	considered conservative. If the concept of the application rate effect is accepted as true, the exclusion of the McCall & Jeffries data is justified because that study employed an application rate of >30 times the GAP being supported at Annex I. Additionally, newly collected field dissipation kinetics which support the findings of the soil dissipation submitted in the Annex I dossier will be used for end-use product submissions for Annex III.	no longer observed at the highest two application rates. However, these highest two application rates are ≥ 33x the proposed application rate. The proposed application rate for the Annex I listing use is 23.5 g as/ ha, and the lowest application rate used in the relevant study is equivalent study is 134 g/ ha. Therefore the RMS considers the Notifier is correct in stating that the DT50 values used are conservative.	
	Open point: 4.4 MSs experts to discuss in a meeting whether it is agreed that the degradation endpoints derived from the study by Knowles, S., Swales, S.A., 2002 is excluded. If not, what DT_{50} value should be used. To support the discussion RMS to provide the kinetic fit (e.g SFO and FOMC) of the upper layer of HAN soil in an addendum. See reporting table 4(6)	DAS: No further comment.	RMS: 08.04.09 Based upon the graphical fit and residual plots presented in the addendum it is considered by the RMS that SFO kinetics is not appropriate for use in modelling. It is noted that the increase of the geometric mean to 51.6 days which would occur compares to the geomean of 48.3 days reported in the DAR. The RMS therefore considers that the use of the revised value in subsequent modelling would have an insignificant impact on PEC values. FOMC kinetics describes the degradation well. Giving a DT90 of 67155 d and a calculated DT50 for use in FOCUS modelling of 20227 d.	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open point proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			However, the RMS considers that there is significant uncertainty around these values due to their extrapolation beyond the study duration, and that they are clear anomalies when compared to the rest of the acceptable data set. The RMS therefore considers that the end-points derived from this study should be excluded from the geometric mean DT50 calculation. Full details of the fitting and the RMS considerations are presented in Addendum 2.	
	New open point: 4.21 RMS to include in the LoEP and in the calculation the median of the HS DT50 value derived for the top soil of the lysimeter, and to check the normalisation for moisture (however no impact on median since the DT50 concerned is not the median value).			PRAPeR 67 (20 – 24 April 2009): Open point open.
	Open point: 4.5 MSs experts to discuss in a meeting the requirement of a new soil photolysis study. See reporting table 4(7)	DAS: It is clear that soil photolysis is not a major route of degradation and therefore support the opinion of the RMS regarding the importance of soil photolysis *"that it is not considered important"* for the representative use. The notifier highlights that a new soil	RMS: 08.04.09 Previous comments made by the RMS in the Reporting Table are reproduced below for ease of reference. [RMS 04.02.09: Our opinion regarding the importance of soil photolysis for the	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open points 4.22 and 4.23 are proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		photolysis study is in preparation for Annex III/MS en-use product submissions.	representative use is clear, i.e. we do not consider it important. However, the issue as to whether this should subsequently be considered a data gap could be considered by an expert meeting.]	
	New open point: 4.22 EFSA to indicate a data gap in the EFSA conclusion (lack of valid soil photolysis study).			PRAPeR 67 (20 – 24 April 2009): Open point open.
	New open point: 4.23 RMS to remove all current entries in the box soil photolysis and replace with 'data gap'.			PRAPeR 67 (20 – 24 April 2009): Open point open.
4.2	Point of clarification for the applicant: Applicant to clarify the column names and that what the values in the table exactly mean in the study by Knowles, S., Schnöder, F., 2003a (the table of concern is referenced in the DAR as Table B.8.33). It should be noted that pending on the information submitted by the applicant new DT_{50} and PECsoil calculation might be needed.	DAS: the notifier highlights that the data in this table shows some intermediate extraction results and shows some of the difficultly in successfully extracting residues at the low levels observed in the study. As the data represents the 0 – 10 cm layer and the DT50 from this study was taken from the combined total radioactivity in the 0 – 20 cm layer (conservative worst case) the actual values in table B8.33 have not been used in the kinetic analysis (DT50 calculation). Subsequently a conservative DT50	RMS: 08.04.09 The RMS considers that the Notifier has not clarified what the column names mean. The RMS did supply some clarification in the reporting table 4(12) on this point but the Notifier was asked to confirm/ clarify. However, the Notifier is correct in stating that the DT50 was based upon total extractable radioactivity in the 0 – 20 cm layer, and is therefore conservative.	PRAPeR 67 (20 – 24 April 2009): Point of clarification regarded as addressed.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 4(12)	value has been used in the PECsoil calculation. New field dissipation data to be considered at Member State level will show that the DT50 value of 49 days is an over estimation of the field dissipation for picloram.		
	Open point: 4.6 MSs experts to discuss in a meeting to cancel the DT_{50} of 14 days derived from the study by Knowles, S., Unsworth, C., 2003 from the LoEP. See reporting table 4(14)	DAS: The notifier agrees with the conservative approach taken by the RMS in using this value to represent the worst case field DT50 value. New field dissipation data can be considered at Member State level. Updated soil dissipation kinetics will therefore be used for MS Annex III submissions.	RMS: 08.04.09 Previous comments made by the RMS in the Reporting Table are reproduced below for ease of reference. [RMS 04.02.09: We included this value in the endpoints principally because, whilst the basis of the calculation is not ideal, it leads to the longest field dissipation DT50 value and thus it's use in PECsoil calculation arguably represents a more precautionary approach.]	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open point proposed, see below.
	New open point: 4.24 RMS to remove the 14 d value from the LoEP and delete the geomean field DT50 value (not pertinent to this exposure assessment).			PRAPeR 67 (20 – 24 April 2009): Open point open.
	Open point: 4.7 MSs experts to discuss in a meeting to include the Koc values (or any of them) from	DAS: The notifier believes the mean Koc from the guideline study Knowles, S. 2000 which includes 8 representative EU soils provides a	RMS: 08.04.09 The mean value calculated from the 8 soils and used as input values for FOCUS modelling was 35 mL/ g which	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	the study Knowles, S., Swales, SA., 2002 in the LoEP. See reporting table 4(17)	representative Koc value for picloram. The additional 3 values in the study Knowles, S., Swales, S.A. 2002 would not significantly impact the overall value.	compares to a mean Koc of 37 mL/ g had the additional 3 soils been used. Previous comments made by the RMS in the Reporting Table are reproduced below for ease of reference. [RMS 04.02.09: We are not sure why the Koc values from the Knowles and Swales 2002 study were excluded as they appear to have been appropriately derived. Adding the three additional Koc values raises the average Koc to 37. Thus there would be no practical impact on the risk assessment.]	
	Open point: 4.8 MSs experts to discuss in a meeting to include in the LoEP and use in the PEC calculations 1 as 1/n instead of 0.9. See reporting table 4(18)	DAS: The approach taken at the time of the original submission utilised the FOCUS default value for 1/n of 0.9 and has been assessed with laboratory DT50 values for the PECgw calculations. This assessment utilising the laboratory DT50 values represents a conservative approach. Using fully compliant field dissipation data from studies included in the original submission along with additional studies clearly demonstrates no issue for the ground water assessment. The new compliant field dissipation studies and associated ground water risk assessments will be used for end-use product Annex III/MS submissions.	RMS: 08.04.09 At the time of the original evaluation the evaluating officer considered that a 1/n value of 1.0 may be more scientifically appropriate, but guidance indicated that a value of 0.9 should be used. However the RMS considers it inappropriate to retrospectively apply new guidance, and considers it even more inappropriate to retrospectively apply relatively new scientific opinion which contradicts previous guidance. The RMS notes that the Applicant has submitted a new study (Ref: GHE-P-11865), detailing revised DT50 calculations from field studies. However, this study has not been	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		(Study ref: GHE-P-11865).	assessed in detail by the RMS, as in accordance with Regulation (EC) No 1095/2007, these data cannot be taken into consideration in the peer review. The RMS notes that two of the studies from which DT50 values have been calculated have not been assessed by the RMS. Previous comments made by the RMS in the Reporting Table are reproduced below for ease of reference. [RMS 04.02.09: At the time of the assessment, we considered that we should comply with the FOCUS Groundwater guidance in respect of the default 1/n, i.e. 0.9. Use of a 1/n of 1 is considered to be more appropriate by many experts in such circumstances, but is not official guidance, thus it was difficult to argue against the official guidance.]	
	Open point: 4.9 MSs experts to discuss the need of new PECgw and PECsw calculations for picloram. If they are regarded as needed, the proper input parameters to be used should be discussed.	DAS: The notifier agrees with the comment made by the RMS that at the time of the assessment, to comply with the FOCUS Groundwater guidance, the default 1/n value was 0.9. Also see notifier's comments under open point 4.8 with respect to lab and field DT50 values. With respect to PEC Surface Water a change in 1/n from 0.9 to 1 has	RMS: 08.04.09 Whether or not new modelling is required is dependant upon the outcome of open points 4.1, 4.3 (& point of clarification 4.1), 4.4, 4.8 and 4.11 in this evaluation table. However, the RMS is of the opinion that either no change to input parameters is justified or that any	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open point proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 4(18)	minimal impact.	changes to input values are likely to have little impact on any PEC values which would subsequently be calculated. Therefore the RMS considers that new modelling is not required for annex I listing purposes.	
	New open point: 4.25 RMS to provide new PECgw, $PEC_{SW,}$ PEC_{SED} calculations. For PEC gw two models should be used. For the new input parameters refer to Discussion table at open point 4.9.			PRAPeR 67 (20 – 24 April 2009): Open point open.
	Open point: 4.10 RMS to include information and results on the series of test solution containing both picloram and sodium benzoate in an addendum. Remark: Based on the study description there were test vessels, which contained both items together. This information can be valuable to decide whether picloram is toxic to microorganisms (note that soil DT_{50} values with high doses were originally excluded without information on biomass of the soils).	DAS: The notifier agrees with the position of the RMS in the reporting table and has no further comments.	RMS: 08.04.09 From further examination of the study report, tests performed with vessels containing both picloram and sodium benzoate were not performed in this study. The confusion appears to have arisen because a study protocol is attached as an appendix to the report which indicates that a toxicity control could be performed. However, this protocol also indicates that it is an optional requirement. There is no mention of a toxicity control in the core study report and no results are reported for it. A statement to this effect has been added to Addendum 2.	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 4(20)		The RMS apologises for any confusion caused.	
	Open point: 4.11 MSs experts to discuss in a meeting the proper DT_{50} values (for water and sediment) to be used in the PECsw calculations for picloram. See reporting table 4(23)	DAS: The notifier supports the comments of the RMS in the reporting table and has nothing further to add.	RMS: 08.04.09 Previous comments made by the RMS in the reporting table are reproduced below for ease of reference. [RMS 04.02.09: The DT50 in water of 135 days is a dissipation DT50, i.e. overall rate of disappearance from the water phase, not a degradation-only DT50. For FOCUSsw modelling, at the time (pre-FOCUS Kinetics guidance) it was considered better to use a conservative DT50 of 300 days for the water degradation (as there was significant partitioning to sediment) and the geomean whole system DT50 to represent the sediment degradation. It is considered that this is an appropriate approach for an evaluation conducted pre-FOCUS Kinetics.]	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point: 4.12 MSs experts to discuss in a meeting the proper formation fraction (or 'application rate') to be used in the PECsw calculations for the metabolites. See reporting table 4(24)	DAS: see notifiers commnets under previous point (open point 4.11)	RMS: 08.04.09 Previous comments made by the RMS in the reporting table are reproduced below for ease of reference. [RMS 04.02.09: We accept the observation made. However, there was no guidance available at the time of the evaluation (and none now) as to how to treat such instances. It is considered that the approach taken in the DAR is reasonable in the light of available guidance. In addition, given the dynamic water bodies considered at FOCUSsw Step 3, and the relatively slow formation of the metabolites in the water sediment systems, it is considered that in reality, even if higher formations were to be considered as input parameters, the flow dynamics would prevent significant formation in the simulation if TOXSWA were able to simulate formation of the metabolites.]	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. See new open point 4.26
	Open point: 4.13 RMS to include an assessment of the degradation and adsorption in soil of aminopyralid (=3,6-dichloro analogue) in an addendum. See reporting table 4(27)	DAS: No further comment.	RMS: 08.04.09 The requested information from the aminopyralid DAR has been added to Addendum 2 for picloram as requested. However, information for the adsorb/ desorb studies is complicated because additional information was received by the RMS after both the DARs for picloram and aminopyralid were completed. This	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			information resulted in a change to the Kfoc and 1/n input parameters for aminopyralid. This information was summarised in an addendum to the aminopyralid DAR, and is also added to Addendum 2 for picloram for ease of reference. However, the RMS considers that this additional information does not significantly affect the PECsw values calculated for aminopyralid as a result of the proposed use of picloram. The RMS considers all other input parameters used for aminopyralid in surface water modelling reported in the DAR for picloram to be appropriate. The RMS considers the open point closed.	
	Open point: 4.14 MSs experts to discuss in a meeting whether the input parameters for the metabolites used in the PECsw calculations are agreed. See reporting table 4(27)	DAS: No further comment.	RMS: 08.04.09 Previous comments made by the RMS in the reporting table are reproduced below for ease of reference. Also See comments in open point 4.13 above. [RMS 04.02.09: The evaluation of the aminopyralid adsorption study can be included in an addendum. Alternatively, EFSA and MS can consult the aminopyralid DAR on CIRCA.]	PRAPeR 67 (20 – 24 April 2009): Open point fulfilled. New open point proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	New open point: 4.26 RMS to recalculate PECsw/sed STEP 1 and 2 for the two metabolites (aminopyralid and 5,6-analogue), taking into account that formation in soil should be set to a low value (e.g., 0.001, currently not clear from the DAR or addendum) and a Koc value of 4.07 L/kg for both metabolites, and a formation fraction of 1 for water system as indicated in open point 4.12.			PRAPeR 67 (20 – 24 April 2009): Open point open.
	Open point: 4.15 EFSA to include in EFSA conclusion a recommendation for restriction of timing of application to spring. See reporting table 4(29)	DAS: the notifier highlights that the Spring use is supported by the lab DT50 values and subsequent PEC Groundwater calculation. However, a less restrictive practice (ie: autumn uses) will be likely using the previously submitted and additional field DT50 values and re-calculated PEC Groundwater assessment for end-use product Annex III/MS submissions.	RMS: 08.04.09 The open point relates to an action for EFSA and the RMS therefore has no further comments.	PRAPeR 67 (20 – 24 April 2009): Open point open. EFSA to include in EFSA conclusion a recommendation for restriction of timing of application to spring and not more frequently than once every 3 years.
4.3	Point of clarification for the applicant: Applicant to submit the information on recalculation	DAS: As indicated by the RMS in the reporting table, field kinetics have been submitted as part of the original PEC Groundwater assessment. This initial	RMS: 08.04.09 Previous comments made by the RMS in the reporting table are reproduced	PRAPeR 67 (20 – 24 April 2009): Point of clarification addressed.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	of field kinetics for picloram to the RMS. See reporting table 4(30)	assessment utilised the data from 4 field dissipation studies. During the evaluation of the dossier, the RMS was not confident of using data from 2 of the 4 field dissipation studies and therefore all subsequent Groundwater kinetic analysis was based on lab data. Recalculation of the already submitted field kinetics but utilising only the 2 field dissipation studies the RMS is confident with would not represent the most conservative assessment. The notifier believes the initial PEC Groundwater assessment can be taken to support the field kinetics in this submission. Using fully compliant field dissipation data from the 2 studies the RMS is confident of using along with additional studies clearly demonstrates no issue for the PEC ground water assessment.	below for ease of reference. [RMS 04.02.09: This issue is addressed in the DAR and discussed with the Notifier prior to finalisation of the DAR. The RMS was not confident of using the data from these two sites even following discussion, hence the outcome described in the DAR.]	
	Open point: 4.16 If RMS accepts this information on recalculation of field kinetics for picloram from the applicant, RMS to evaluate in an addendum. See reporting table 4(30)	DAS: see notifiers comments under previous point (point 4.2)	RMS: 08.04.09 See previous comments made in reporting table 4(30) and Notifiers comments in point of clarification 4.2 in this evaluation table.	PRAPeR 67 (20 – 24 April 2009): Open point closed.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point: 4.17 RMS to revise LOEP in light of EFSA comments. See reporting table 4(32)	DAS: No further comment.	RMS: 08.04.09 The LoEP has been updated as requested in the reporting table. The RMS notes that the comment made re: the PECsw box actually relates to degradation in water/ sediment. Re: the comment on quantum yield, the RMS cannot identify where this value has originated from. Notifier to clarify or RMS to amend to make consistent with the value reported in the Phys/ chem. props section.	PRAPeR 67 (20 – 24 April 2009): Open point open. RMS to update the LoEP as indicated in Column 3 of the discussion table.
	Open point: 4.18 RMS to amend list of tests and studies relied upon in light of EFSA comments. See reporting table 4(33)	DAS: No further comment.	RMS: 08.04.09 The list of tests and studies relied is to will be updated as appropriate at the end of the peer review process.	PRAPeR 67 (20 – 24 April 2009): Open point open.
	New open point : 4.27 RMS to amend the residue definition for further assessment in line with the conclusions of PRAPeR 67 meeting. (refer to Discussion table)			PRAPeR 67 (20 – 24 April 2009): Open point open.
	Message from section 1 (phys-chem) to section 4:			PRAPeR 67 (20 – 24 April 2009):

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	A new water solubility study is required, it is expected that water solubility will be (even) higher than the value established now.			Answer: Noted.

REPORT OF PRAPeR EXPERT MEETING 68

PICLORAM

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
April 2009	UK	Picloram addendum 2 Vol 3 B2_B3_B5_B6_B7_B8_B9 (April 2009).doc
2009-04-09	UK	Picloram evaluation table rev1-0 (2009-04-09).doc
April 2009	UK	Picloram addendum3 Vol4 (April 2009) cover page.doc
2009-02-12	UK	Picloram reporting table rev 1-1 (2009-02-12).doc
June 2008	UK	Picloram studies relied on v2 June 2008.doc
April 2009	UK	Picloram updated list of endpoints (April 2009).doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. Data on preparations: Galera.

5. Classification and labelling: N, R51/53

10. Recommended restrictions/conditions for use: none for ecotox (for fate: only spring application and only once per 3 years)

11. Reference list: Not discussed

Areas of concern: none

Appendix 1: Discussion table: PICLORAM

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Picloram (Hb)

5. Ecotoxicology

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 5.1 RMS to address in an addendum explanation of conversion factor use to convert the acute endpoint from mallard duck study (Beavers 1986a) from picloram potassium salt (2250 mg picloram potassium salt/kg bw) to picloram acid equivalent (1994 mg ae/kg bw). See reporting table 5(1)	An explanation of the conversion factor was presented in the addendum 2. Note: in the ecotox-addendum it is stated that the phys-chem addendum further addresses this issue, but due to an error this was not done.	Open point fulfilled.
	Open point. 5.2 RMS to address in an addendum explanation of conversion factor of 0.864 use to convert the short-term endpoint from bobwhite quail study (Beavers 1986b) from picloram potassium	The issue was addressed in the addendum 2. A conversion factor of 0.864 was used. Open point fulfilled. However, in the LoEP the daily dose end point is now expressed in ae (acid equivalent) and the ppm end point is expressed in salt. New open point: RMS to clarify the LoEP (report the short-term endpoints both for ae and salt and add the conversion factor in a footnote).	Open point fulfilled. New open point proposed, see below.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	salt to picloram acid equivalent. RMS to also report in an addendum the raw data (i.e. mean body weight and food consumption table included in the reporting table). See reporting table 5(3)		
	New open point: 5.7 RMS to clarify the LoEP (report the short-term endpoints both for ae and salt and add the conversion factor in a footnote).		Open point open.
	Open point: 5.3 More details on acute and long-term endpoints for mammals used for risk assessment in the German national authorisation would be needed to decide if they are relevant for picloram peer review. Could, please, Germany provide this	Germany (DE) informed the meeting that they have more rabbit studies available at national level than presented in the DAR. However, these studies were not sent to the RMS by DE. Therefore the RMS believes that the standard set of studies should be used. It seems that the studies that DE refers to are already available in the mammalian toxicology section of the DAR. The lowest endpoint is the NOAEL for rabbit of 40 mg/kg bw/d (developmental study). The NOAEL of 40 mg/kg bw /d was based on an effect on weight gain, which was only seen at day 6-8 but not later in the study. Switzerland considered the 40 mg/kg bw/d not ecotoxicologically relevant at national level. The meeting agreed that this is not ecotoxicologically relevant. The mammalian toxicology developmental endpoint is 400 mg/kg bw/d (highest tested dose) according to the LoEP. At this dose there is a tendency for effect (increasing litter resorption and litter size). Switzerland used this endpoint for national registration. NB the DAR mentions a developmental NOAEL of 200 mg/kg bw/d from this study, it has to be	Open point still open. RMS to crosscheck the endpoints with the mammalian toxicology section and update LoEP if necessary.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	information? See reporting table 5(4)	checked whether the LoEP is correct. Some MSs always take the lowest endpoint from the mammalian toxicology LoEP as first tier. The long-term ecotoxicology endpoint is currently 1000 mg/kg bw/d (2-generation study rat). Has this endpoint been revised by the mammalian toxicology section also? The RMS will check. With 400 mg/kg bw/d there would not be a risk to mammals. However, the developmental study has generally not be taken into account so far. The risk assessment for mammals has to be recalculated based on the NOAEL of 200 or 400 mg/kg bw/d. Both for 200 and 400 mg/kg bw/d the TERlt is >1000. Message to mamtox: what is the developmental NOAEL from the rabbit developmental study with potassium salt (page 115 of the DAR)? Answer: The mammalian toxicology meeting has decided that the relevant developmental endpoint for picloram is 300 mg/kg bw/d, however this is based on another study with the TIPA salt. From the rabbit developmental study with the K-salt they set the endpoint at ≥400 mg/kg bw/d (this was mistakenly reported as 200 in the original DAR). The RMS will check with mammalian toxicology whether the TIPA-endpoint would be appropriate to use for ecotox. The final conclusions on this will be provided in the LoEP by the RMS. Open point still open.	
	Open point: 5.4 MSs to discuss in a PRAPeR expert meeting the endpoint to be used for risk assessment to mammals, if necessary. See reporting table 5(4)	See discussion under open point 5.3.	Open point closed.
	Open point: 5.5 RMS to include in an	This information was included in the addendum 2. Open point fulfilled. This herbicide is not toxic to algae nor to *Lemna*. The question was raised whether	Open point fulfilled.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	addendum full data on cell count, biomass and growth rate from Desjardins 2001 study, as it was done for metabolite studies on algae in tables B.9.12 to B.9.18 of the DAR. See reporting table 5(5)	another aquatic plant species should be tested, maybe *Meriophyllum*? Picloram is a systemic herbicide which is absorbed into plant leaves and roots. It works mainly on dicotyledonous species, which could explain why *Lemna* is not sensitive. At low concentrations it has a positive effect, and only at high concentrations it has a negative effect. The lead formulation (also containing another a.s.) was tested on algae and *Lemna*. Again low toxicity was found. The lack of effect could be caused by the low concentrations tested or by the low sensitivity of *Lemna.* The a.s. occurred in max. 43% in the sediment in the water/sediment study. This could be a reason to test a rooted plant species. The meeting considered that testing of a second higher aquatic plant species might be triggered. However, this should be considered at MS level (depending on formulation, with maybe other a.s.). The meeting agreed that it is not necessary to identify an Annex II data gap.	
	Open point: 5.6 RMS to address in an addendum explanation of conversion factor use to convert the endpoint from se*lenastrum capricornutum* study (Hughes, 1990) from picloram potassium salt to picloram acid equivalent. See reporting table 5(6)	The issue was addressed in addedndum 2. See also open point 5.1 and 5.2. Open point fulfilled.	Open point fulfilled.
	Message to section 2		Answer:

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	(mammalian toxicology): What is the developmental NOAEL from the rabbit developmental study with potassium salt (page 115 of the DAR)?		The mammalian toxicology meeting has decided that the relevant developmental endpoint for picloram is 300 mg/kg bw/d, however this is based on another study with the TIPA salt. From the rabbit developmental study with the K-salt they set the endpoint at ≥400 mg/kg bw/d (this was mistakenly reported as 200 in the original DAR).
	Message from section 1 (phys-chem): Please consider the information on the tox and ecotox batches presented in Addendum 3 to Vol. 4.		Answer: There seem to be some inconsistency: information on purity of batches differs between the ecotox DAR/addendum and the addendum 3 to Vol.4. This should be checked by the RMS. New open point proposed, see below. The meeting considered that the impurity sulphuric acid (occurring in batch AGR274601 (1989), tested on Daphnia (chronic) and earthworm) is sufficiently addressed.
	New open point: 5.8 RMS to check the purity of all batches;		Open point open.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	there are differences between Table C.1.6 in addendum 3 of Vol.4 and DAR B.9. To be addressed in a revised DAR.		
	Message from section 4 (fate and behaviour): PECsw have changed.		Answer: The risk assessment to aquatic organisms has to be revised based on the new PECsw for metabolites (however, no risk is expected since the TER-values are >10000 based on the old PECs).
	Message from section 4 (fate and behaviour): A restriction for use has been set for groundwater: picloram can only be applied in spring and only once per three years.		Answer: No action required for ecotox.

Appendix 2: Evaluation table

5. Ecotoxicology

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 5 Open points: ***6*** Points for clarification: ***0*** Data gaps: ***0***			Section 5 Open points: ***3*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 5.1 RMS to address in an addendum explanation of conversion factor use to convert the acute endpoint from mallard duck study (Beavers 1986a) from picloram potassium salt (2250 mg picloram potassium salt/kg bw) to picloram acid equivalent (1994 mg ae/kg bw). See reporting table 5(1)	DAS: In the study, all doses were adjusted to 100% active ingredient, picloram potassium salt. In order to convert to acid equivalents, the conversion factor of 0.864 was applied to the values quoted in the report (M.W. of picloram 241.5 / M.W. of picloram K salt 279.6).	RMS: 08.04.09 An explanation of the conversion factor is provided by the Notifier and is discussed further in DAR Addendum 2. Open point addressed.	PRAPeR 68 (4 – 8 May 2009): Open point fulfilled.
	Open point. 5.2 RMS to address in an addendum explanation of conversion factor of 0.864 use to convert the short-term endpoint from bobwhite quail study (Beavers 1986b) from	DAS: As 5 (1).	RMS: 08.04.09 As 5.1 in relation to conversion factor. The body weight and food consumption data mentioned have been added to Addendum 2 to the DAR.	PRAPeR 68 (4 – 8 May 2009): Open point fulfilled. New open point proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	picloram potassium salt to picloram acid equivalent. RMS to also report in an addendum the raw data (i.e. mean body weight and food consumption table included in the reporting table). See reporting table 5(3)		Open point addressed.	
	New open point: 5.7 RMS to clarify the LoEP (report the short-term endpoints both for ae and salt and add the conversion factor in a footnote).			PRAPeR 68 (4 – 8 May 2009): Open point open.
	Open point: 5.3 More details on acute and long-term endpoints for mammals used for risk assessment in the German national authorisation would be needed to decide if they are relevant for picloram peer review. Could, please, Germany provide this information? See reporting table 5(4)	DAS: Endpoints align with those given in the Toxicology section	RMS: 08.04.09 This is also a point for the German authority. Currently the mammalian endpoints align with those given in the Mammalian Toxicology section. If these should change as a result of discussions in that area, then further consideration of their relevance to wild mammal risk assessment will be undertaken (see 5.4). No change to these endpoints is proposed at present.	PRAPeR 68 (4 – 8 May 2009): Open point still open. RMS to crosscheck the endpoints with the mammalian toxicology section and update LoEP if necessary.
	Open point: 5.4	DAS: No further comments	RMS: 08.04.09	PRAPeR 68 (4 – 8 May 2009):

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	MSs to discuss in a PRAPeR expert meeting the endpoint to be used for risk assessment to mammals, if necessary. See reporting table 5(4)		This is reliant upon point 5.3 above. If necessary, then there could be further consideration at PRAPeR of the endpoints most relevant to wild mammal risk assessment. No change to these endpoints is proposed at present.	Open point closed. See open point 5.3
	Open point: 5.5 RMS to include in an addendum full data on cell count, biomass and growth rate from Desjardins 2001 study, as it was done for metabolite studies on algae in tables B.9.12 to B.9.18 of the DAR. See reporting table 5(5)	DAS: The notifier agrees with the comment.	RMS: 08.04.09 This information has been added to Addendum 2 to the DAR. Open point addressed.	PRAPeR 68 (4 – 8 May 2009): Open point fulfilled.
	Open point: 5.6 RMS to address in an addendum explanation of conversion factor use to convert the endpoint from se*lenastrum capricornutum* study (Hughes, 1990) from picloram potassium salt to picloram acid equivalent. See reporting table 5(6)	DAS: In the study, all exposure levels were expressed in terms of measured picloram potassium salt. In order to convert to acid equivalents, the conversion factor of 0.864 was applied to the values quoted in the report (M.W. of picloram 241.5 / M.W. of picloram K salt 279.6).	RMS: 08.04.09 As 5.1.	PRAPeR 68 (4 – 8 May 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Message to section 2 (mammalian toxicology): What is the developmental NOAEL from the rabbit developmental study with potassium salt (page 115 of the DAR)?			Answer from section 2: The mammalian toxicology meeting has decided that the relevant developmental endpoint for picloram is 300 mg/kg bw/d, however this is based on another study with the TIPA salt. From the rabbit developmental study with the K-salt they set the endpoint at ≥400 mg/kg bw/d (this was mistakenly reported as 200 in the original DAR).
	Message from section 1 (phys-chem): Please consider the information on the tox and ecotox batches presented in Addendum 3 to Vol. 4.			PRAPeR 68 (4 – 8 May 2009): Answer: There seem to be some inconsistency: information on purity of batches differs between the ecotox DAR/addendum and the addendum 3 to Vol.4. This should be checked by the RMS. New open point proposed, see below. The meeting considered that the impurity sulphuric acid (occurring in batch AGR274601 (1989), tested on Daphnia (chronic) and earthworm) is sufficiently addressed.
	New open point: 5.8 RMS to check the purity of all batches; there are differences between Table C.1.6 in addendum 3 of Vol.4 and DAR B.9. To be			PRAPeR 68 (4 – 8 May 2009): Open point open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	addressed in a revised DAR.			
	Message from section 4 (fate and behaviour): PECsw have changed.			PRAPeR 68 (4 – 8 May 2009): Answer: The risk assessment to aquatic organisms has to be revised based on the new PECsw for metabolites (however, no risk is expected since the TER-values are >10000 based on the old PECs).
	Message from section 4 (fate and behaviour): A restriction for use has been set for groundwater: picloram can only be applied in spring and only once per three years.			PRAPeR 68 (4 – 8 May 2009): Answer: No action required for ecotox.

Report of PRAPeR Expert MEETING 69

PICLORAM

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
28/04/2009	UK	J.Toxicol Environ Health, 1981, 7(2), 207-22
April 2009	UK	Picloram addendum 2 Vol 3 B2 B3 B5 B6 B7 B8 B9 (April 2009)
09/04/2009	UK	Picloram evaluation table rev1-0 (2009-04-09)
July 2007	UK	Picloram addendum1 Vol3 B6 (July 2007)
April 2009	UK	Picloram addendum3 Vol4 (April 2009)
12/02/2009	UK	Picloram reporting table rev 1-1 (2009-02-12)
June 2008	UK	Picloram studies relied on v2 June 2008
April 2009	UK	Picloram updated list of endpoints (April 2009)

3. Documents tabled at the meeting:

Date	Supplier	File Name
04/05/2009	UK	Picloram: revised section C.1.2.d of Addendum3 Vol4

The conclusions of the meeting were as follows:

4. **Data on preparations:** Galera

5. **Classification and labelling:** R43

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

7. **Reference List:** Not discussed

Areas of concern: None

Appendix 1: Discussion table: PICLORAM

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Picloram (Hb)

2. Mammalian toxicology

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 0.4 RMS to provide a summary table of the different toxicological studies performed with the different derivatives of picloram (with doses converted in picloram acid equivalents), in order to compare their toxicity profile. See reporting table 0(5)	The values in the DAR and in the list of endpoints are given as equivalent free acid. The toxicology endpoints relate to the acid. The 21-day dermal study and ADME study in rat was performed with the potassium salt and the developmental studies were performed with the potassium and TIPA salt. See answer to a message from Section 1 below.	Open point closed.
	Open point: 2.1 Application of R43 to be discussed by the experts, taking into consideration - the limitations of the available Buehler test - the results of the EPA evaluation: negative for picloram acid, positive for the potassium salt, the isooctyl ester and the TIPA salt. See reporting table 2(3)	The RMS presented information on the limitations of the Buehler test, and on the studies evaluated by the US EPA (these studies were not submitted to the RMS but were evaluated by the EPA –[RED 1995] and are published information). The EPA studies performed with 2 salts and one ester of picloram were positive and the EPA study performed with the picloram acid was negative. The available test in the DAR (Buehler test with 3 inductions) was negative but had limitations (only 10 animals used in the test group, dry material applied, dressing not fully occluded and limitations with comparability of the positive control group). As a precaution the experts proposed to classify picloram acid as R43. This proposal is supported by the data available with the salts and ester published by the EPA. It was mentioned that Aminopyralid is structurally similar to picloram (one additional chlorine in picloram). Both the salt and the acid form of Aminopyralid were found to be negative in the maximization test (M&K).	Open point fulfilled. R43 is proposed for picloram acid.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Open point fulfilled.	
	Open point: 2.2 The relevant short-term NOAEL in the rat (13-wk study) has to be confirmed by the experts. (similar findings were observed in the liver in the 2-year rat study) See reporting table 2(4)	The experts agreed that the target organ in rats is the liver and the liver findings at the high dose (500 mg/kg/day) were considered as adverse. They also agreed that the short-term study should be considered with the long-term (2-year rat) study. See further discussion in open point 2.3. Open point closed.	Open point closed. See open point 2.3.
	Open point: 2.3 Based on the relevance of the liver and pancreas findings, the systemic NOAEL of the 2-yr rat study (Landry, 1986) has to be discussed by the experts. (similar liver findings were observed in the 13-wk rat study) See reporting table 2(5)	Liver - In the first 2-yr rat study (Landry, 1986), the liver findings at 200 mg/kg bw/day (increase in liver weight of >10% and clear dose response with respect to histopathology) were considered adverse. In the second 2-yr rat study (Cosse, 1992), there were no histopathological findings in the liver at the terminal sacrifice of the high dose group (500 mg/kg bw/day) but an increase in liver weight of 12% in females. Pancreas - The data on the pancreas were not reported in the DAR for the 90-day study. The RMS reported that examination of the pancreas was only conducted at 0 (O incidence of pancreas atrophy among 10 male and 10 female animals) and 500 mg/kg bw/day (incidence of pancreas atrophy: 0 out of 10 in males and 2 out of 10 in females). In the first long-term rat study there was no increased incidence of pancreas atrophy but increased severity when compared with the controls. For the second 2-yr rat study, the incidences of pancreatic atrophy were presented by the RMS – the findings were considered to be inconsistent. The RMS provided further information with regard to the historical background range on pancreas findings which should be reported in an addendum to the DAR (together with further data on the second 2-yr rat study and 90-day rat study). Based on these studies the RMS proposed a NOAEL for the long-term rat study as 60 mg/kg/day (based on the same study the EPA derived a NOEL of 20 mg/kg/day) –	Open point fulfilled. The NOAEL in the 2-yr rat study is 60 mg/kg bw/day. The NOAEL in the 13-week rat study is 300 mg/kg bw/day. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		this was agreed by the experts based on the liver findings at 200 mg/kg bw/day. In the 13-week rat study the NOAEL proposed was 300 mg/kg bw/day – this was agreed by experts. Open point fulfilled. New open point proposed – RMS to provide further information on the pancreas findings (including historical control range) in sub chronic and chronic studies in an addendum to the DAR.	
	New open point: 2.12 RMS to provide further information (including historical control range) on the pancreas findings in sub chronic and chronic studies in an addendum to the DAR.		Open point open.
	Open point: 2.4 MS experts to discuss the carcinogenic potential of picloram based on the published article by Reuber Melvin Dwaine (J. of Tox. and Env. Health, 7:207-222, 1981). See reporting table 2(6)	The RMS presented findings of the NCI study (1978) evaluated by Reuber (but also by US EPA/NTP). The findings reported were inconsistent and the study design had limitations. The experts agreed that the conclusions in the DAR relating to the two recent rat studies conducted by the notifier should be used. Based on the data reported in the DAR the experts agreed that picloram has no carcinogenic potential. Open point fulfilled. New open point proposed – RMS to provide further information on why the Reuber evaluation was rejected (show the inconsistencies in reporting between Reuber and US EPA/NTP).	Open point fulfilled. The experts agreed that picloram has no carcinogenic potential. New open point proposed, see below.
	New open point: 2.13		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	RMS to provide further information on why the Reuber evaluation regarding the carcinogenic potential of picloram was rejected (show the inconsistencies in reporting between Reuber and US EPA/NTP).		
	Open point: 2.5 The derivation of the developmental NOAEL in rats based on the foetal findings in both studies has to be discussed by the experts. See reporting table 2(7)	The first rat developmental study was performed with the potassium salt of picloram. There was a single fetus at the mid dose of 430 mg picloram acid/kg bw/day with malformations (cleft palate and facial cleft – on external evaluation). No findings were observed at the highest dose. By checking the study the RMS also found one control foetus with cleft palate (on internal evaluation). The experts agreed that the NOAEL for the developmental effect was 860 mg picloram acid/kg bw/day and for maternal toxicity 430 mg picloram acid/kg bw/day based on clinical signs (salivation). The second rat developmental study was performed with the TIPA salt of picloram. There was one fetus with malformations at the top dose (cranial facial defects – no cleft palate and no facial cleft) and there were also similar findings in one control. Therefore, the RMS proposed that this was not of concern. Three fetuses from one litter at the high dose had subcutaneous hemorrhages, but in the absence of any other findings this was considered by the RMS not to be of concern. There were two top dose fetuses in different litters with dilated lateral brain ventricles, but they were considered by the experts not to be of concern (the RMS reported that one control fetus had a dilated third brain ventricle). The experts agreed that the NOAEL for developmental effects was 560 mg picloram acid/kg bw/day and for maternal findings 280 mg picloram acid/kg bw/day based on clinical signs (salivation). The experts agreed that the overall maternal NOAEL in rats should be 280 mg picloram acid/kg bw/day and the overall developmental NOAEL should be 560 mg picloram acid/kg bw/day (based on the worst case and taking into account the	Open point fulfilled. Rat developmental study (K salt): - developmental NOAEL is 860 mg picloram acid/kg bw/day - maternal NOAEL is 430 mg picloram acid/kg bw/day based on clinical signs (salivation). Rat developmental study (TIPA salt) - developmental NOAEL is 560 mg picloram acid/kg bw/day - maternal NOAEL is 280 mg picloram acid/kg bw/day based on clinical signs (salivation). The experts agreed that the overall maternal NOAEL in rats should be 280 mg picloram acid/kg bw/day and the overall developmental NOAEL should be 560 mg picloram acid/kg bw/day (based on the worst case and taking into account the LOAEL of the second study).

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		LOAEL of the second study). Open point fulfilled. New open point proposed – RMS to provide information regarding the cranial facial malformations in the rat studies in an addendum to the DAR.	New open point proposed, see below.
	New open point: 2.14 RMS to provide information regarding the cranial facial malformations in the rat studies in an addendum to the DAR.		Open point open.
	Open point: 2.6 The relevant developmental NOAEL in the rabbit developmental studies has to be discussed by the experts, based on the incidence of the foetal findings observed in the different studies at the high dose. See reporting table 2(14)	The first rabbit developmental study with the potassium salt showed at the highest dose an increased incidence of malformations. In the low and mid dose groups there were no effects. The notifier has requested that the developmental NOAEL is set at 400 mg/kg bw/day as this rabbit strain has a high background history of malformations. The experts agreed that the NOAEL for the developmental effect was 200 mg picloram acid/kg bw/day. The second rabbit developmental study with the TIPA salt was carried out in 2 phases, the second phase included an additional low dose. Malformations in the first phase were of low frequency or fell within the historical data as did the data in the additional phase. The experts were however concerned about the structural fetal findings at the highest dose in both phases of the study. The experts agreed that the NOAEL for the developmental effects in the second study was 300 mg picloram acid/kg bw/day based on adverse foetal findings at the highest dose.	Open point fulfilled. In the rabbit developmental study with the K salt, the developmental NOAEL is 200 mg picloram acid/kg bw/day. In the rabbit developmental study with the TIPA salt, the developmental NOAEL is 300 mg picloram acid/kg bw/day based on adverse foetal findings at the highest dose. No classification for developmental effects was proposed.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		The experts discussed whether the findings triggered R63 – it was agreed that classification was not triggered. Open point fulfilled.	
	Open point: 2.7 The relevant maternal NOAEL in the developmental rabbit studies has to be discussed by the experts, based on the changes in body weight (gain). (in the DAR, this NOAEL is proposed as the basis for the ADI). See reporting table 2(17)	In the first developmental rabbit study (with the K salt) the experts agreed on a maternal NOAEL of 40 mg picloram acid/kg bw/day and in the second study (with the TIPA salt), a maternal NOAEL of 30 mg picloram acid/kg bw/day was agreed. The RMS proposed an overall maternal NOAEL of 30 mg picloram acid/kg bw /day, and this was agreed by the experts (to be consistent with the proposal made for the rat studies). Open point fulfilled.	Open point fulfilled. The overall maternal NOAEL in the rabbit developmental studies is 30 mg picloram acid/kg bw/day (based on the study with the TIPA salt)
	Open point: 2.8 The derivation of the ADI has to be discussed by the experts. See reporting table 2(20)	The RMS proposed an ADI based on the maternal NOAEL in the developmental rabbit study with the TIPA salt of 30 mg picloram acid equivalent/kg bw/d and supported by the NOAEL of 35 mg/kg bw/d from the 1-year dog study with the free acid. The resulting ADI was 0.3 mg/kg bw/day with the use of a safety factor of 100. This was agreed by the experts. Open point fulfilled.	Open point fulfilled. ADI agreed as 0.3 mg/kg bw/day
	Open point: 2.9 The need for ARfD has to be discussed by the experts (and the derivation if needed).	The ARfD was considered needed based on the maternal effects during the first 3 days of the developmental rabbit study and supported by the 1 year dog study (initial weight loss during the first week of treatment). The same value is agreed for the ARfD as the ADI = 0.3 mg/kg bw. Open point fulfilled.	Open point fulfilled. ARfD agreed as 0.3 mg/kg bw

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 2(22)		
	Open point: 2.10 The derivation of the systemic AOEL has to be discussed by the experts. See reporting table 2(24)	For the AOEL the same value as the ADI is proposed (based on the same studies) = 0.3 mg/kg bw. Open point fulfilled.	Open point fulfilled. AOEL agreed as 0.3 mg/kg bw/day
	Open point: 2.11 Dermal absorption values to be discussed by the experts, taking into account the weaknesses of the *in vivo* rat study and the findings in the human volunteer study. See reporting table 2(29)	The *in vivo* study was discussed by the experts as the dilution and concentrate showed the same pattern at the application site - the amount of test substance (either with concentrated or diluted product) on the treated skin area remained high when excretion levels were low/stopped (the substance remains in the skin). Once excretion stopped the guidance says what is on the skin can be ignored. The experts agreed that the amount available on the skin is not bioavailable. The RMS's proposal of 3% for the concentrate and 0.1% for the dilution was discussed. For the dilution, the experts agreed to base the dermal absorption value on the rat study results. For the concentrate, in order to correct for a low recovery, the experts discussed adding a correction value to the proposal of the RMS or assigning the default value of 10% given the limitations of the study. The experts agreed 10% (default) for the concentrate and 0.1% for the dilution. Open point fulfilled. New open point proposed – RMS to provide an addendum to the DAR with revised operator and worker exposure estimates taking into account the revised dermal absorption value agreed for the concentrate.	Open point fulfilled. The experts agreed 10% (default) for the concentrate and 0.1% for the dilution. New open point proposed, see below.
	New open point: 2.15 RMS to provide an		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	addendum to the DAR with revised operator and worker exposure estimates taking into account the revised dermal absorption value agreed for the concentrate.		
	Message from section 1 (Phys-chem) to section 2: Please consider the information on the toxicological batches presented in Addendum 3 to Vol. 4. The Ames study should not be considered in the peer review (new study).	The RMS distributed at the meeting a revised section C.1.2.d of Addendum 3 to Vol. 4. The evaluation of a new Ames test was also provided in Addendum 1 (July 2007). In view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, this new test could not be considered in the peer review. However, the experts could reach a conclusion without identifying a data gap for an Ames test. The experts highlighted differences in the impurity profile between the batches used for genotoxicity and carcinogenicity studies and the technical specification agreed at PRAPeR 66. The tested batches generally had lower levels of some impurities and apparently lacked other impurities. It was considered that the structures of the impurities were similar to the parent and no additional structures of clear toxicological concern were observed. Therefore the proposed levels were considered toxicologically acceptable. The impurities HCB and sulphuric acid were considered as relevant impurities, but not of concern at the proposed levels of 0.9% w/w for sulphuric acid and 0.005% w/w for HCB. It was noted that HCB had been tested in the carcinogenic studies up to a level of 0.02% w/w. Open point fulfilled. New open point proposed: The revised section C.1.2.d ‘Purity of test material used in toxicity studies’ of Addendum 3 Vol4, including comparison of the batches with the technical specification, has to be presented by the RMS in a confidential addendum.	Answer: The proposed levels of impurities in the technical specification presented in Addendum 3 Vol4 were considered toxicologically acceptable. New open point proposed, see below.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	New open point: 2.16 The revised section C.1.2.d 'Purity of test material used in toxicity studies' of Addendum 3 Vol4, including comparison of the batches with the technical specification, has to be presented by the RMS in a confidential addendum.		Open point open.

Appendix 2: Evaluation table

2. Mammalian toxicology

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 2 Open points: ***12*** Points for clarification: ***0*** Data gaps: ***0***			Section 2 Open points: ***5*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 0.4 RMS to provide a summary table of the different toxicological studies performed with the different derivatives of picloram (with doses converted in picloram acid equivalents), in order to compare their toxicity profile. See reporting table 0(5)	DAS: No further comment	RMS: 08.04.09 This is not a useful exercise as most of the package has been conducted with picloram acid, with the exception of the teratology studies which were conducted with either the potassium salt or the triisopropanolamine. Open point addressed.	PRAPeR 69 (4 – 8 May 2009): Open point closed. See answer to the message from section 1.
	Open point: 2.1 Application of R43 to be discussed by the experts, taking into consideration - the limitations of the available Buehler test - the results of the EPA evaluation: negative for picloram acid, positive for the potassium salt, the isooctyl	DAS: The notifier supports the RMS position in the Draft Assessment Report that picloram acid is negative for dermal sensitization.	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. R43 is proposed for picloram acid.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	ester and the TIPA salt. See reporting table 2(3)			
	Open point: 2.2 The relevant short-term NOAEL in the rat (13-wk study) has to be confirmed by the experts. (similar findings were observed in the liver in the 2-year rat study) See reporting table 2(4)	DAS: The observations at 300 mg/kg/day include small increases (<10%) in liver and kidney weight and "increased size of hepatocytes often accompanied by altered tinctorial properties" graded as slight to very slight. The notifier supports the RMS conclusion that the findings at this dose-level were non-adverse. The NOAEL is therefore considered to be 300 mg/kg/day	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point closed. See open point 2.3.
	Open point: 2.3 Based on the relevance of the liver and pancreas findings, the systemic NOAEL of the 2-yr rat study (Landry, 1986) has to be discussed by the experts. (similar liver findings were observed in the 13-wk rat study) See reporting table 2(5)	DAS: The notifier supports the RMS conclusion from the Draft Assessment Report that the histopathological liver and pancreas findings at 60 mg/kg/day were non-adverse (not toxicologically significant). The NOAEL is therefore considered to be 60 mg/kg/day.	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. The NOAEL in the 2-yr rat study is 60 mg/kg bw/day. The NOAEL in the 13-week rat study is 300 mg/kg bw/day. New open point proposed, see below.
	New open point: 2.12			PRAPeR 69 (4 – 8 May 2009):

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	RMS to provide further information (including historical control range) on the pancreas findings in sub chronic and chronic studies in an addendum to the DAR.			Open point open.
	Open point: 2.4 MS experts to discuss the carcinogenic potential of picloram based on the published article by Reuber Melvin Dwaine (J. of Tox. and Env. Health, 7:207-222, 1981). See reporting table 2(6)	DAS: the notifier highlights that the two guideline GLP rat bioassays were included in the original submission and provide a more robust assessment of the carcinogenic potential of picloram. These two guideline rat bioassays were both negative for carcinogenicity as indicated by the RMS in the Draft assessment report. The following document provides additional information and justification as to why the published article by Reuber Melvin Dwaine (J.of Tox and Env. Health, 7:207-222, 1981) should not be considered under the 91/414 evaluation of picloram.	RMS: 08.04.09 Comment noted. The information provided by the notifier has been presented in Addendum 3 (Confidential information).	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. The experts agreed that picloram has no carcinogenic potential. New open point proposed, see below.
	New open point: 2.13 RMS to provide further information on why the Reuber evaluation regarding the carcinogenic potential of picloram was rejected (show the inconsistencies in reporting between Reuber and US EPA/NTP).			PRAPeR 69 (4 – 8 May 2009): Open point open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point: 2.5 The derivation of the developmental NOAEL in rats based on the foetal findings in both studies has to be discussed by the experts. See reporting table 2(7)	DAS: The notifier highlights that there were no treatment-related effects on development evident in either study.	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. Rat developmental study (K salt): - developmental NOAEL is 860 mg picloram acid/kg bw/day - maternal NOAEL is 430 mg picloram acid/kg bw/day based on clinical signs (salivation). Rat developmental study (TIPA salt) - developmental NOAEL is 560 mg picloram acid/kg bw/day - maternal NOAEL is 280 mg picloram acid/kg bw/day based on clinical signs (salivation). The experts agreed that the **overall maternal NOAEL in rats** should be **280 mg picloram acid/kg bw/day** and the **overall developmental NOAEL** should be **560 mg picloram acid/kg bw/day** (based on the worst case and taking into account the LOAEL of the second study). New open point proposed, see below.
	New open point: 2.14 RMS to provide information regarding the cranial facial			PRAPeR 69 (4 – 8 May 2009): Open point open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	malformations in the rat studies in an addendum to the DAR.			
	Open point: 2.6 The relevant developmental NOAEL in the rabbit developmental studies has to be discussed by the experts, based on the incidence of the foetal findings observed in the different studies at the high dose. See reporting table 2(14)	DAS: For the K-salt study, the Notifier affirms that the NOAEL for developmental effects should be > 400 mg/kg (Picloram Acid Equivalents). The two incidences of forelimb flexure at the top dose were limited to a tendon anomaly and importantly were confined to a single litter. Also supporting that the effects were non-treatment related, similar findings were not observed in the rabbit teratology study with the TIPA salt. For the study on the TIPA salt, the notifier supports the RMS position that there were not treatment-related foetal findings in the study. The developmental NOAEL is therefore considered to be >558 mg/kg/day.	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. In the rabbit developmental study with the K salt, the developmental NOAEL is 200 mg picloram acid/kg bw/day. In the rabbit developmental study with the TIPA salt, the developmental NOAEL is 300 mg picloram acid/kg bw/day based on adverse foetal findings at the highest dose. No classification for developmental effects was proposed.
	Open point: 2.7 The relevant maternal NOAEL in the developmental rabbit studies has to be discussed by the experts, based on the changes in body weight (gain). (in the DAR, this NOAEL is proposed as the basis for the	DAS: For the K-salt study, the notifier agrees with the RMS supported maternal NOAEL of 40 mg/kg/day. For the TIPA-salt study, the observed effect on body weight gain at 180 mg/kg/day is not considered to be toxicologically meaningful due to the mild nature (<1% change) and transient duration (only observed at one interval) of the observation. The	RMS: 08.04.09 In the TIPA-salt study there were clear effects on bodyweight gain and even a bodyweight loss at 180 mg/kg/day (a.e. of 100 mg/kg/day) which was observed in both phases of the study.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. The overall maternal NOAEL in the rabbit developmental studies is 30 mg picloram acid/kg bw/day (based on the study with the TIPA salt)

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	ADI). See reporting table 2(17)	notifier therefore considers the maternal NOAEL to be 180 mg/kg/day (a.e. of 100 mg/kg/day).		
	Open point: 2.8 The derivation of the ADI has to be discussed by the experts. See reporting table 2(20)	DAS: The Notifier supports the proposed ADI of 0.35 mg/kg/day derived from the NOAEL of 35 mg/kg/day in the 1 year dog study. This exposure limit is based on the most suitable toxicological endpoint available and is health protective. The proposed ADI values of 0.3 and 0.2 mg/kg/day are based on endpoints of a transient nature and/or are of questionable toxicological significance.	RMS: 08.04.09 The weight loss and reduced bodyweight gain in the rabbit teratology study must be considered as adverse.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. ADI agreed as 0.3 mg/kg bw/day
	Open point: 2.9 The need for ARfD has to be discussed by the experts (and the derivation if needed). See reporting table 2(22)	DAS: The Notifier maintains the active substance picloram has low acute hazard potential (LD50 > 4000 mg/kg bw), is not teratogenic, and other toxicological alerts (FAO/WHO, 2000) that would trigger the establishment of an ARfD have not been demonstrated.	RMS: 08.04.09 There are several studies where reduced bodyweight gain is evidence after a few days of dosing. Therefore an ARfD is required.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. ARfD agreed as 0.3 mg/kg bw
	Open point: 2.10 The derivation of the systemic AOEL has to be discussed by the experts. See reporting table 2(24)	DAS: The Notifier supports the derivation of the AOEL from the TIPA-salt rabbit developmental study as the salts are considered toxicologically equivalent to picloram. The maternal NOAEL is considered to be 100 mg/kg/day in this study rather than 30 mg/kg/d (discussed in point 2.7) resulting in an AOEL of 1 mg/kg/day.	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. AOEL agreed as 0.3 mg/kg bw/day

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point: 2.11 Dermal absorption values to be discussed by the experts, taking into account the weaknesses of the *in vivo* rat study and the findings in the human volunteer study. See reporting table 2(29)	DAS: The default assumptions associated with the dermal absorption of covalent bounded compounds may not always be applicable to salts of acids as is the case of the olamine salt of picloram. Decrease in %absorption with increased dilution is unusual, but reflects the difference in the disassociation of the active substance at the concentration in the formulation and dilute spray dilution. The human volunteer study (B6.1.1) confirms this point with low absorption of the acid. A recent OECD 428 guideline compliant study on an olamine salt with the structurally related clopyralid – olamine demonstrated again that the absorption from a dilute spray solution was less than that from the neat formulation. Van Burgsteden (2007) In vitro percutaneous absorption of 14C Clopyralid formulated as EF-1136 and field dilutions through human skin membranes using flow through diffusion cells. A copy of this study was provided as supplementary information only to verify the conclusions regarding the validity of	RMS: 08.04.09 Comment noted.	PRAPeR 69 (4 – 8 May 2009): Open point fulfilled. The experts agreed 10% (default) for the concentrate and 0.1% for the dilution. New open point proposed, see below.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		the proposed dermal values. DAS: The OECD Guideline 427 specifies that recoveries <90% are acceptable if justified. The OECD guidance 28 recommends wash off at 6 hours , the contact time in the study was24 hours, combined with the high wash off percentages, (ca. 70%) the missing 5% would have no impact on the absorption. The specific activity and conc. of the picloram dictated that a 500 fold dilution was the maximum conc. that could be studied. 2x difference will not impact on % absorption. Neither of these criteria warrant part inclusion of the application site. No movement from the application site was observed over 72 hours.		
	New open point: 2.15 RMS to provide an addendum to the DAR with revised operator and worker exposure estimates taking into account the revised dermal absorption value agreed for the concentrate.			PRAPeR 69 (4 – 8 May 2009): Open point open.
	Message from section 1 (Phys-chem) to section 2: Please consider the			PRAPeR 69 (4 – 8 May 2009): Answer:

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	information on the toxicological batches presented in Addendum 3 to Vol. 4. The Ames study should not be considered in the peer review (new study).			The experts highlighted differences in the impurity profile between the batches used for genotoxicity and carcinogenicity studies and the technical specification agreed at PRAPeR 66. The tested batches generally had lower levels of some impurities and apparently lacked other impurities. It was considered that the structures of the impurities were similar to the parent and no additional structures of clear toxicological concern were observed. Therefore **the proposed levels were considered toxicologically acceptable**. The impurities HCB and sulphuric acid were considered as relevant impurities, but not of concern at the proposed levels of 0.9% w/w for sulphuric acid and 0.005% w/w for HCB. It was noted that HCB had been tested in the carcinogenic studies up to a level of 0.02% w/w. New open point proposed, see below.
	New open point: 2.16 The revised section C.1.2.d 'Purity of test material used in toxicity studies' of Addendum 3 Vol4, including comparison of the batches with the technical specification, has to be presented by the RMS in			PRAPeR 69 (4 – 8 May 2009): Open point open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	a confidential addendum.			

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REPORT OF PRAPeR EXPERT MEETING 70

PICLORAM

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
April 2009	UK	Picloram addendum 2 Vol 3 B2_B3_B5_B6_B7_B8_B9 (April 2009).doc
2009-04-09	UK	Picloram evaluation table rev1-0 (2009-04-09).doc
April 2009	UK	Picloram addendum3 Vol4 (April 2009) cover page.doc
2009-02-12	UK	Picloram reporting table rev 1-1 (2009-02-12).doc
June 2008	UK	Picloram studies relied on v2 June 2008.doc
April 2009	UK	Picloram updated list of endpoints (April 2009).doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** GALERA

5. **Classification and labelling:** none

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

7. **Reference List:** not discussed

Areas of concern: none

Appendix 1: Discussion table: PICLORAM

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Picloram (Hb)

3. Residues

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 3.1 RMS should provide the correct data relating to Table B7.2 in an corrigendum/ addendum as appropriate. See reporting table 3(1)	A revised table has been presented in Addendum 2 of the DAR. The corrected values do not change the evaluation.	Open point fulfilled. A revised table has been presented in Addendum 2 of the DAR.
	Open point: 3.2 RMS to present a re-evaluation of the rotational crop study, considering the correct application rate in an addendum. See reporting table 3(3)	As presented in Addendum 2 of the DAR, the overdosing factor has been corrected to 25 N instead of 285N. Using this factor of 25 residues above LOQ maybe expected in rotational crops. The experts discussed if additional rotational field studies have to be requested or if default MRLs could be derived from the submitted rotational crop metabolism study. The majority of the experts were of the opinion that using the available study could for the moment be a way forward in order to conduct a risk assessment and to propose MRLs for certain rotational crops. Nevertheless, rotational field crop studies should be submitted for national authorisations to either confirm the proposed MRLs or to modify the proposed MRLs if necessary (Point of clarification 3.1 becomes data gap). On the basis of the TRR observed in the ether partition fraction [worst case assumption for the residues of picloram free and conjugated] in the rotational crop study [table B.7.7, Addendum 2], the following provisional MRLs are proposed based on the residue definition for risk assessment as agreed under open point 3.3:	Open point fulfilled. Rotational crop study was re-evaluated and MRLs for rotational crops were proposed.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		0.07 mg/kg for fruiting vegetables, brassica vegetables, leafy vegetables, stem vegetables, herbal infusion and spices 0.02 mg/kg for legume vegetables, pulses, cereal grains 0.01* mg/kg for root vegetables and oilseeds	
	Comment in reporting table 3(9) and 3(10) 3(9): For future reference, to enable accurate comparison with the estimated livestock burden the administered dose in the study should be specified and expressed on a dry matter basis or mg/kg bw basis, respectively. If expressed on an 'as received' basis, the composition of the diet/ dry matter content of the diet used in the study needs to be reported for further conclusions. 3(10): For future reference, can the impurities of the active substance that showed the same chromatographic behaviour as the non-	On the basis of the proposed MRLs in rotational crops the experts considered livestock intake that was found to be significant for ruminants. Therefore the experts discussed two additional comments in the reporting table regarding the goat metabolism study (comment 3(9) and 3(10)) that had not been addressed but were found to be relevant for the assessment of the notified use. Based on the goat metabolism study a MRL for picloram of 0.2 mg/kg is proposed for kidney. This proposal is pending confirmation by the RMS upon re-evaluation of the animal intake considering residues in rotational crops and clarification of the dose rate in the metabolism study in an addendum to the DAR.	New open point proposed: In an addendum, RMS to provide animal intake calculations [on a dry matter basis] considering residues in rotational crops, and clarify the dose rate in the goat metabolism study [see 3(9) in the reporting table]. RMS to re-evaluate the goat metabolism study in order to propose MRLs for animal products. Data gap proposed: [based on reporting table 3(10)] Applicant to name impurities and to clarify the possible impact of the impurities that showed the same chromatographic behaviour as the non-polar components in the goat metabolism study.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	polar components in the goat studies be named? The increased ratio of impurities to picloram in the fat residue (47:45) could be an indication for preferential accumulation of those impurities in fatty matrices.		
	New open point: 3.6 [based on reporting table comment 3(9)]: In an addendum, RMS to provide animal intake calculations [on a dry matter basis] considering residues in rotational crops, and clarify the dose rate in the goat metabolism study [see 3(9) in the reporting table]. RMS to re-evaluate the goat metabolism study in order to propose MRLs for animal products.		Open point open.
	New data gap: 3.1 identified at PRAPeR 70 meeting [based on reporting table comment 3(10)]: Applicant to name impurities and to clarify		Data gap open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	the possible impact of the impurities that showed the same chromatographic behaviour as the non-polar components in the goat metabolism study.		
3.1	Point of clarification for the notifier: Notifier to address the potential for residues in following crops as field trials in rotational crops seem to be triggered. See reporting table 3(3)	As already discussed in open point 3.2, the point of clarification 3.1 becomes a data gap. In the light of the proposed MRLs for rotational crops the respective monitoring methods will have to be available. Message to section 1: The residue experts have proposed MRLs for fruiting vegetables, brassica vegetables, leafy vegetables, stem vegetables, herbal infusion and spices, legume vegetables, pulses, cereal grains, root vegetables and oilseeds. Hence, a validated method of analysis for monitoring covering all the standard plant matrices and taking into account the message to section 1 on picloram conjugates (see open point 3.3) will be necessary. Message to section 1: A MRL for picloram of 0.2 mg/kg is proposed for kidney. Hence, a validated method of analysis for monitoring covering animal matrices is necessary.	Point of clarification turned into a data gap: Field rotational crop study is requested to confirm or if necessary to modify (refine) the proposed MRLs in rotational crops. Message 1 to section 1: A validated method of analysis for monitoring covering all the standard plant matrices and taking into account the message 3 to section 1 on picloram conjugates (see open point 3.3) will be necessary. Message 2 to section 1: A MRL for picloram of 0.2 mg/kg is proposed for kidney. Hence, a validated method of analysis for monitoring covering animal matrices is necessary.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 3.3 The issue on whether conjugated picloram should be included in the residue definition for risk assessment and whether the available data sufficiently address conjugated residues (primary and rotational crops) should be discussed by experts. See reporting table 3(8)	Picloram conjugates appear to account for a significant proportion of the total residue. Picloram residue level is higher after hydrolysis (Table B.7.8 in Addendum 2). These conjugates have to be taken into account in the residue definition for risk assessment. The experts have some doubts that the analytical method used in the supervised residue trials (Hastings, M.J.; draft method GRM 00.19) fully released the picloram conjugates. A final decision could not be taken and the experts were of the opinion that the applicant should provide validation data to demonstrate that the analytical method used in the residue trial is able to analyse the conjugates. For the time being, a decision on the residue definition for enforcement can not be taken as it is not clear whether and to what extent picloram conjugates will be determined with the methods currently proposed for enforcement/ monitoring purposes. Message to section 1: A decision on a plant residue definition for enforcement (in terms of whether picloram conjugates will have to be included) can currently not be taken since it is unknown whether the analytical method proposed for monitoring (GRM 00.19) does fully or partially analyse any conjugated picloram. If this were the case conjugated picloram will have to be considered in the residue definition for monitoring and MRL setting.	Open point fulfilled. Conjugated picloram should be included in the residue definition for risk assessment, i.e. the residue of concern for RA is defined as picloram, free and conjugated. New open point proposed, see below. Decision on residue definition for enforcement can currently not be taken as a decision depends on whether or not the analytical method for monitoring does analyse picloram conjugates. Message 3 to section 1: A decision on a plant residue definition for enforcement (in terms of whether picloram conjugates will have to be included) can currently not be taken, since it is unknown whether the analytical method proposed for monitoring (GRM 00.19) does fully or partially analyse any conjugated picloram.
	New open point: 3.7 Decision on residue definition for enforcement pending on confirmation whether or not the		Open point open.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	analytical method for monitoring does analyse picloram conjugates.		
	Open point: 3.4 Experts to consider whether the method used in residue trials is suitable to determine conjugated picloram (consider also extraction efficiency in releasing conjugated picloram) or whether further information or data should be required. See reporting table 3(14)	Refer to discussion in open point 3.3 Data gap: Applicant to provide validation data to demonstrate the efficiency of the analytical method used in the supervised residue trials in terms of the analysis of picloram conjugates.	Open point fulfilled. New data gap proposed, see below.
	New data gap: 3.2 identified at PRAPeR 70 meeting: Applicant to provide validation data to demonstrate the efficiency of the analytical method used in the supervised residue trials in terms of the analysis of picloram conjugates.		Data gap open.
	Open point: 3.5 Acceptability of storage	For the oil seeds, the storage stability study covers the storage period in the residue trials. The forage analyses were carried out at a slightly later time point than covered by the	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	stability data in terms of the sample storage time in the field trials to be agreed by experts. See reporting table 3(15)	storage stability data, but the experts agreed that for this short period the study is acceptable taking into account the overall stability of the active substance.	Storage stability data are acceptable taking into account the overall stability of the active substance.
	New open point: 3.8 RMS to update the LoEP according to the discussions at PRAPeR 70, including a new risk assessment.	The LoEP have to be updated accordingly.	Open point open.
	Message 1 to section 1: A validated method of analysis for monitoring covering all the standard plant matrices and taking into account the message No 3 to section 1 on picloram conjugates (see open point 3.3) is necessary.		
	Message 2 to section 1: A MRL for picloram of 0.2 mg/kg is proposed for kidney. Hence, a validated		

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	method of analysis for monitoring covering animal matrices is necessary.		
	Message 3 to section 1: A decision on a plant residue definition for enforcement (in terms of whether picloram conjugates will have to be included) can currently not be taken, since it is unknown whether the analytical method proposed for monitoring (GRM 00.19) does fully or partially analyse any conjugated picloram.		

Appendix 2: Evaluation table

3. Residues

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 3 Open points: ***5*** Points for clarification: ***1*** Data gaps: ***0***			Section 3 Open points: ***3*** Points for clarification: ***0*** Data gaps: ***3***
	Open point: 3.1 RMS should provide the correct data relating to Table B7.2 in an corrigendum/ addendum as appropriate. See reporting table 3(1)	DAS: The ppm values for Day 84 – Stem in Table B.7.2 are correct but the %TRR value for Acetonitrile/water extract should be 4.0% (0.005/0.125 mg/kg), so that the total %TRR is 4.0% + 32.8% = 36.8%. Continuing with the TLC method in Table B.7.2, the picloram conjugates represent 0.051 mg/kg (correctly reported in Table B.7.2.) which would result in 40.8%TRR (91.1% of the extract). Combining the above two, 36.8% + 40.8% = 77.6% TRR identified as free or conjugated picloram. The diethyl ether extract followed acid and base hydrolysis of the post-extracted solids (PES), so these values can be considered to represent conjugated picloram that was released upon hydrolysis. Using the TLC analysis, 0.041 mg/kg was identified as	RMS: 08.04.09 A revised table has been presented in Addendum 2 of the DAR. Open point addressed.	PRAPeR 70 (5 – 8 May 2009): Open point fulfilled. A revised table has been presented in Addendum 2 of the DAR.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		picloram from hydrolysis of the PES, equivalent to 32.8% TRR.		
	Open point: 3.2 RMS to present a re-evaluation of the rotational crop study, considering the correct application rate in an addendum. See reporting table 3(3)	DAS: The notifier agrees with the comments made by the RMS in the reporting table that the correct N rate should be 28.2 N and not 285N	RMS: 08.04.09 A re-evaluation of the metabolism study has been presented in Addendum 2 of the DAR. Taking into consideration the revised rates it is noted that there is the potential for significant residues in leafy following crops at the shortest harvest interval studied. At the later plantback intervals residues in following crops are not expected to be significant. As discussed in the Addendum the Notifier has previously provided justification that the 30 day interval is not relevant to the proposed uses. The RMS is of the opinion that for the proposed use no further data on rotational crops are considered necessary. However, for other uses proposed in the future further data may be necessary.	PRAPeR 70 (5 – 8 May 2009): Open point fulfilled. Rotational crop study was re-evaluated and MRLs for rotational crops were proposed.
	New open point: 3.6 [based on reporting table comment 3(9)]: In an addendum, RMS to provide animal intake			PRAPeR 70 (5 – 8 May 2009): Open point open.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	calculations [on a dry matter basis] considering residues in rotational crops, and clarify the dose rate in the goat metabolism study [see 3(9) in the reporting table]. RMS to re-evaluate the goat metabolism study in order to propose MRLs for animal products.			
	New data gap: 3.1 identified at PRAPeR 70 meeting [based on reporting table comment 3(10)]: Applicant to name impurities and to clarify the possible impact of the impurities that showed the same chromatographic behaviour as the non-polar components in the goat metabolism study.			PRAPeR 70 (5 – 8 May 2009): Data gap open.
3.1	Point of clarification for the notifier: Notifier to address the potential for residues in following crops as field trials in rotational crops seem to be triggered.	DAS: Since the majority of the residue was identified as free or conjugated picloram, another study to confirm these results should not be required. No metabolite was present at levels greater than 0.148 mg/kg after hydrolysis (28.2 N), which would be less than 0.006 mg/kg at a 1N rate.	RMS: 08.04.09 RMS notes the comments from the Notifier. See also comments for open point 3.2 above.	PRAPeR 70 (5 – 8 May 2009): Point of clarification turned into a data gap: Field rotational crop study is requested to confirm or if necessary to modify (refine) the proposed MRLs in rotational crops.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 3(3)	The analytical methods will detect free and conjugated picloram. A field rotational crop study should not be required.		Messages 1 and 2 sent to section 1.
	Open point: 3.3 The issue on whether conjugated picloram should be included in the residue definition for risk assessment and whether the available data sufficiently address conjugated residues (primary and rotational crops) should be discussed by experts. See reporting table 3(8)	DAS: Both free and conjugated picloram were expected to be included in the residue definition for monitoring (MRLs) and dietary risk assessment. The analytical method involves hydrolysis of conjugates and measures both free and conjugated picloram, reported as total picloram.	RMS: 08.04.09 Comment noted.	PRAPeR 70 (5 – 8 May 2009): Open point fulfilled. Conjugated picloram should be included in the residue definition for risk assessment, i.e. the residue of concern for RA is defined as picloram, free and conjugated. New open point proposed, see below. Message 3 sent to section 1.
	New open point: 3.7 Decision on residue definition for enforcement pending on confirmation whether or not the analytical method for monitoring does analyse picloram conjugates.			PRAPeR 70 (5 – 8 May 2009): Open point open.
	Open point: 3.4 Experts to consider whether the method used in residue trials is suitable to determine	DAS: The plant metabolism studies (as submitted in the original dossier) describe the extraction procedures which were used to quantitatively extract and hydrolyze residues of	RMS: 08.04.09 Comment noted.	PRAPeR 70 (5 – 8 May 2009): Open point fulfilled. Refer to open point 3.3

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	conjugated picloram (consider also extraction efficiency in releasing conjugated picloram) or whether further information or data should be required See reporting table 3(14)	picloram. Very similar procedures (e.g., alkaline extraction with heat) were used in this metabolism study as well as in the residue methods. There is adequate proof in the metabolism reports that the extraction methods which are used in the methods are sufficient to extract the residues from the samples. Analytical method GRM 00.19 uses both basic and acidic conditions (sodium hydroxide and hydrochloric acid), and this is expected to hydrolyze any conjugated picloram present in the sample.		New data gap proposed, see below.
	New data gap: 3.2 identified at PRAPeR 70 meeting: Applicant to provide validation data to demonstrate the efficiency of the analytical method used in the supervised residue trials in terms of the analysis of picloram conjugates.			PRAPeR 70 (5 – 8 May 2009): Data gap open.
	Open point: 3.5 Acceptability of storage stability data in terms of the sample storage time in the	DAS: The storage stability data for oil seed rape seed was carried out for a period of 24 months (730 days) and residues were stable over this interval. The maximum period of frozen storage	RMS: 08.04.09 Comment noted. RMS agrees that the only samples stored for longer than 24 months before analysis were	PRAPeR 70 (5 – 8 May 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	field trials to be agreed by experts. See reporting table 3(15)	for residue study samples was approximately 810 days. This is only about 10% over the measured storage interval. Since there was no degradation during the 730 day interval, no appreciable degradation would be expected over the period of 80 additional days. Additionally, it is important to point out that the samples stored for about 800 days were whole plant samples, which are not used in the MRL. The seed samples were stored for a maximum period of time that was only within or nearly within the 730 day interval supported by the storage stability study.	the immature whole plants (i.e. not at harvest maturity)	Storage stability data are acceptable taking into account the overall stability of the active substance.
	New open point: 3.8 RMS to update the LoEP according to the discussions at PRAPeR 70, including a new risk assessment.			PRAPeR 70 (5 – 8 May 2009): Open point open.
	Message 1 to section 1: A validated method of analysis for monitoring covering all the standard plant matrices and taking into account the message No 3 to section 1 on picloram			

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	conjugates (see open point 3.3) is necessary.			
	Message 2 to section 1: A MRL for picloram of 0.2 mg/kg is proposed for kidney. Hence, a validated method of analysis for monitoring covering animal matrices is necessary.			
	Message 3 to section 1: A decision on a plant residue definition for enforcement (in terms of whether picloram conjugates will have to be included) can currently not be taken, since it is unknown whether the analytical method proposed for monitoring (GRM 00.19) does fully or partially analyse any conjugated picloram.			