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

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 1 Data requirements: ***1*** Open points: ***12***			Section 1 Data requirements: ***3*** Open points: ***0***
	Open point 1.1 RMS should consider using the current harmonised version of the list of end points. See reporting table 0(1).		The Endpoints have been re-formatted updated using the Sept 05 guidance. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
1.1	Data requirement The applicant should justify the minimum purity of the active substance given that the batch data suggest that 980 g/kg would be reliable. It should be noted that the applicant has stated that QC data has been sent to the rapporteur on 6 June 2007. See reporting table 1(1).	Quality control data on technical cyflufenamid produced on an industrial scale manufacturing plant, together with analysis of 5 representative batches of such material, support a minimum purity of 980 g/kg of the active substance in the industrial scale technical product. The Applicant confirms that the data was provided to RMS (UK PSD) on 6 June 2007.	Quality control data support a minimum purity of 980 g/kg, the endpoints have been amended. Addressed	PRAPeR 36 (27. – 30.11.2007): Data requirement fulfilled. New open point proposed, see open point 1.13
	New open point 1.13: The meeting agreed that the		RMS - 15.02.2008: Open point addressed, revised	PRAPeR 36 (27. – 30.11.2007):

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
	5-batch data supported a minimum purity of 980 g/kg. QC data were not required. RMS should consider including this information in an addendum to the DAR.		minimum purity has been incorporated in Addendum 4 to the Confidential information (Volume 4).	Open point open. Written procedure: Revised minimum purity has been incorporated in Addendum to the Vol.4). Open point fulfilled
	Open point 1.2 The CIPAC number 759 should appear in the list of end points. See reporting table 1(3).	Agreed. The CIPAC number for cyflufenamid is 759.	RMS: Endpoints have been updated Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.3 The method of analysis with regard too the LOQ should be discussed in a meeting of experts. The applicant has stated that a report will be available September 2007. See reporting table 1(5).	A study is being conducted to identify the LOQs in the method of analysis of the impurities in the technical active substance. The Applicant confirms that the report is expected to be available in December 2007 and will be provided to the RMS.	The study referenced in column B was not available to the RMS at the time of writing this comment, but will be evaluated once it is received. RMS - 15.02.08: The need for these data was discussed at PRAPeR 36. The comments of the RMS given in 1(36) of the reporting table were accepted at the meeting and it was agreed that further data were not required.	PRAPeR 36 (27. – 30.11.2007): 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 1.4 Rapporteur to update the list of references relied on to remove the references to solubility and partition co-efficient for the metabolites. See reporting table 1(8).		The studies have been deleted from the updated references relied on list Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.5 UV spectra. The rapporteur to add all the molar coefficients to the list of end points. See reporting table 1(9).		Endpoints have been updated Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.6 Rapporteur to update the references relied on. See reporting table 1(17).		The studies have been deleted from the updated references relied on list.	PRAPeR 36 (27. – 30.11.2007): 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 1.7 A final assessment of the air method is not possible until a residue definition is set. See reporting table 1(20).	The Applicant considers that the residue definition in air is the parent compound alone, cyflufenamid.	The method reported in the DAR is acceptable for the determination of the active substance in air. There is currently no residues definition proposed for air. If a residue definition for air is set as something other than cyflufenamid, then a further method will be required. RMS - 15.02.2008: Fate meeting confirmed the residues definition for air is parent only, therefore the submitted method is acceptable and no further data are required. Open point fulfilled.	PRAPeR 36 (27. – 30.11.2007): Open point still open. Written procedure: Fate meeting confirmed the residues definition for air is parent only, therefore the submitted method is acceptable and no further data are required. Open point fulfilled.
	Open point 1.8 Rapporteur to amend the list of references relied on to remove the reference to impurity methods that are not required. See reporting table 1(21).		The study of Unemoto, T, 2000, which makes reference to the analysis of hexane, has been deleted form the list of references relied on. The study of Unemoto, T, 2000a, which makes reference to the determination of toluene and Isopar G has not been removed from the list of references relied on, as this study was relied on to determine the analytical profile of batches used in Tox testing. Addressed	PRAPeR 36 (27. – 30.11.2007): 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 1.9 For the residue methods the analyte should be mentioned in the LOEP. See reporting table 1(26).		The list of end points has been amended to include this information. Addressed	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled.
	Open point 1.10 From the comment made by the rapporteur in column 3 of the reporting table it would appear that there was some communication between the primary lab and the lab that conducted the ILV such that initially the method did not work. This is not correct procedure and this issue should be discussed in a meeting of experts. The applicant has stated that a justification will be provided. 6 June 2007. See reporting table 1(32).	With respect to the ILV of analytical methods for residues in plant, plant products, foodstuff and feedingstuff, the current version of the guidance document on residue analytical methods (SANCO/825/00 rev.7, 17/03/2004), states that "where the chosen laboratory requires communication with developers of the method to carry out the analysis, this must be reported". Therefore, communication between the primary laboratory and that chosen for the ILV, which was documented in the study report, is acceptable. The Applicant confirms that this justification was provided to RMS on 6 June 2007.	As noted by the Notifier, the current guidance on the conduct of ILV studies states only that any communication between the independent laboratory and the developers of the method must be documented. It does not state that such communication is not acceptable. The RMS considers that the communication and subsequent minor modifications to the method do not invalidate the ILV study; however we do accept that it would be helpful for the details regarding batch size and storage of extracts to be incorporated into the analytical procedure as they do appear to be critical to the acceptability of the method.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled. New data requirement, see 1.2 An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier.

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
1.2	New data requirement: An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier		RMS - 15.02.2008: The Notifier has provided the following information. The batches consisted of 2 control and 5 recovery samples and the extracts should only be stored in GPC solvent (cyclohexane/ethyl acetate) prior to GPC clean up, in a refrigerator. The Notifier needs to incorporate these details in to a revised procedure.	PRAPeR 36 (27. – 30.11.2007): Data requirement open. Written procedure: An amendment to the primary method regarding batch size and storage of extracts should be done and added to the dossier Data requirement still open
	Open point 1.11 The high RSD values for the residues in food method should be discussed in a meeting of experts and in general the level of validation in accordance with SANCO/825/00 should be considered. The applicant has stated that a justification will be provided. 6 June 2007. See reporting table 1(33).	The RSD values for the determined residues in food are within the limits specified in the EU guidance document for analytical methods (SANCO/825/00 rev.7, 17/03/2004), i.e. <20% per commodity and level. Furthermore, the mean recovery at each fortification level for each commodity was in the specified range of 70-110%. Although there was some variability in the initial determinations in the ILV study, subsequently modifications gave recovery and RSD values that met the above SANCO document. The Applicant confirms that this justification was provided to RMS (UK PSD) on 6 June 2007.	Communication between the independent laboratory and the developers of the method as described in open point 1.10 above took place after the independent laboratory had analysed three batches and obtained unacceptable results. After incorporating the minor changes proposed by the developers of the method, the two subsequent batches of data were acceptable. The RMS considers that the results of the first three batches can be disregarded. The results of batches 5 and 6 are within the acceptable limits described in SANCO/825/00.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled. See open point 1.10.

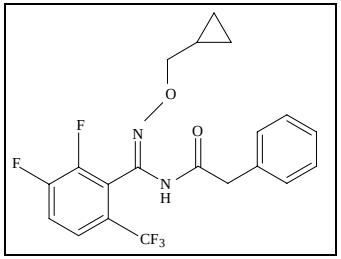
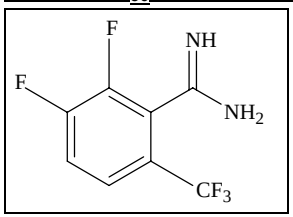
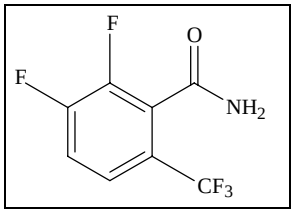
No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point 1.12 It should be discussed by a meeting of experts if the validation data for the confirmatory drinking water method is acceptable. See reporting table 1(37).		The RMS welcomes a discussion on this point at a meeting of experts. RMS - 15.02.2008: The study of Brewin, S.A., 2000, NOD 137/002147, report no.RD-II2006 was summarised in Volume 3, Section 4 of the dossier but was not included as the enforcement method in the DAR as it was used to support pre-registration studies. The method determines residues of cyflufenamid and metabolites in leachate water at levels down to 0.05 µg/L. In this exceptional case, the validation data in the study report were assessed by the experts at the meeting and the method was deemed acceptable as a confirmatory method for enforcement. The meeting agreed that the study reference should be included in the references relied on against Annex point 4.2.3.	PRAPeR 36 (27. – 30.11.2007): Open point fulfilled. New open point proposed, see open point 1.14

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 1.14: Reference to this study should be included with the correct Annex point.		RMS - 15.02.2008: The reference to this study and a summary of the method have been included in Addendum 3 to Volume 3 and also in the End points. Open point fulfilled	PRAPeR 36 (27. – 30.11.2007): Open point open. Written procedure: The reference to this study and a summary of the method have been included in Addendum 3 to Volume 3 and also in the list of end points. Open point fulfilled
	New open point 1.15: RMS to amend the list of end points according to the discussions during the PRAPeR 36 meeting.		RMS - 15.02.2008: The list of end points has been updated. Open point fulfilled.	PRAPeR 36 (27. – 30.11.2007): Open point open. Written procedure: The list of end points has been updated. Open point fulfilled
	(New data requirement transferred from the Residues section - 3.2) Analytical method for animal commodities is required for the following residue definition: sum of cyflufenamid, the E isomer and metabolite 149-F1.		RMS - 15.02.2008: The Notifier has stated that a method will be available in June 2008. Data requirement still open	PRAPeR 40 (12 – 13 December 2007): Data requirement open. Written procedure: Analytical method for animal commodities is required for the following residue definition: sum of cyflufenamid, the *E* isomer and metabolite 149-F1 Data requirement 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
	A clarification concerning the isomers determined in the analytical method proposed for enforcement of plant residues is required. If the current method is not appropriate for the revised residue definition, then a new method will be required.		RMS - 15.02.2008: The report of the residues meeting concludes that the *E* isomer of cyflufenamid should be included in the residues definition for plants and that the notifier should submit confirmatory information concerning the analytical method(s) used in the residues trials and the methods proposed for monitoring with regard to whether the methods are able to separate the isomers or not. The data gap that appeared in the evaluation table only specified clarification for the methods used in the residues trials. The reference to the enforcement method was missing. The RMS has therefore transferred the request for clarification with respect to the enforcement method to this section and has also updated the End points to reflect the revised residue definition. The information has been requested from the notifier but has not yet been submitted. The Notifier has stated that this will be available in June 2008. Data requirement still open.	PRAPeR 40 (12 – 13 December 2007): Data requirement open Written procedure: A clarification concerning the isomers determined in the analytical method proposed for enforcement of plant residues is required. Data requirement still open

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 Data requirements: **-** Open points: ***4***			Section 2 Data requirements: **-** Open points: ***0***
	Open point 2.1 MSs to discuss the relevance of metabolites 149-F1 and 149-F6. See reporting table 2(33).		The relative toxicity of these two metabolites is considered in the DAR in Section B.6.8.2.3. It is suggested that the increased acute toxicity will only be relevant to high dose levels (evidence being the nervous system effects seen at high dose levels only). 149-F1 and 149-F6 are both rat metabolites, and 149-F1 in particular is excreted in significant amounts (14% in urine), with 149-F6 up to 3% in urine. The significant *in situ* generation of these metabolites means that the toxicity of these metabolites should have been taken into account in the long-term studies with cyflufenamid. If it was necessary to perform a risk assessment for these metabolites then the ADI and ARfD for cyflufenamid should be appropriate since these metabolites will have contributed to the toxicity driving these reference values. Since residues are expected to be at low levels for the supported uses (e.g. up to 0.02 mg/kg in wheat, 0.07 mg/kg in barley, <0.01 mg/kg for animal products) it may not be necessary to	PRAPeR 39 (10– 13 12.2007): 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
			include these metabolites in residue definitions. Cyflufenamid LD_{50} >5000 mg/kg bw  149-F1 LD_{50} 434 ♂, 349 ♀  149-F6 LD_{50} 686 ♂, 686 ♀  For discussion at Expert meeting	
	Open point 2.2	With respect to the brain vacuolation,	The expert report for neurotoxicity was	PRAPeR 39 (10– 13 12.2007):

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
	Reference values to be discussed in an experts' meeting, taking into account relevant effects (in particular the occurrence of brain vacuolation) See reporting table 2(40).	an international panel of expert neurotoxicologists and neuropathologists independently reviewed all the neurotoxicological information on cyflufenamid, including original study reports and the histopathological slides. They concluded that a clear NOELneurotoxicity for the brain lesion in the dog was 97 and 93 mg/kg bw/day (2000 ppm) based on the 28-day dog toxicity study in the dog. See Open point 2.3 for further information.	addressed at Point 2(54) in the Reporting Table, and has been reproduced in Addendum 2. For the ADI it is necessary to clarify what safety margin is appropriate over the NOAEL for brain vacuolation, and following from that which NOAEL and safety factor should be used for the ADI. This is discussed in Point 2(41) in the Reporting Table, at Section B.6.10.1 in the DAR and summarised in Addendum 2. For the ARfD it is necessary to resolve the conflicting findings in the two rabbit developmental studies. A dose of 10 mg/kg bw/d was the LOAEL in one study, but an NOAEL in the other study (same lab, same test material a short time apart, almost identical methods, same strain but different source of animals). The RMS proposal is to take the conservative approach in view of the uncertainty (clear NOAEL of 5 mg/kg bw/d, leading to ARfD=0.05). The alternative value would be 0.1. The brain vacuolation effect is not relevant to setting the ARfD since an ARfD based on the NOAEL for this effect in the shortest study would be similar to or higher than an ARfD based on the developmental studies. For the AOEL it is necessary to clarify what safety margin is appropriate over	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 NOAEL for brain vacuolation – as is the case for the ADI. Following this the appropriate NOAEL and safety factor can be decided. It is then necessary to determine the appropriate oral absorption value, which in turn will be dependent on which NOAEL is selected to derive the AOEL (i.e. whether based on liver effects or not). This issue is discussed in detail at Point 2(44) in the Reporting Table with alternative proposals for oral absorption ranging from 18% up to 70%. The issues around the setting of the reference values (and also the revised dermal penetration values) are summarised in Addendum 2. For discussion at Expert meeting RMS 15.02.08: A revised Operator exposure risk assessment which uses the revised AOEL of 0.03 mg/kg bw/day agreed at the Expert meeting is presented in Addendum 3. The End points have also been updated.	
	Open point 2.3 The relevance of brain vacuolation to be discussed	An international panel of expert neurotoxicologists and neuropathologists independently reviewed all the neurotoxicological	The expert report for neurotoxicity was addressed at Point 2(54) in the Reporting Table, and has been	PRAPeR 39 (10– 13 12.2007): 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
	in a meeting of experts. See reporting table 2(45).	information on cyflufenamid, including original study reports and the histopathological slides. They concluded that high dose levels produced a unique pattern of toxic damage to oligodendrocytes and oedema of myelin in the white matter in certain areas of the brain of dogs. The effect was dose-related and resolved slowly after cessation of dosing. There was a clear NOELneurotoxicity for the lesion which was 97 and 93 mg/kg bw/day (2000 ppm) in the 28-day dietary toxicity study. The cause of the brain lesion in the dog was not known. The rat and mouse were not affected. The Applicant confirms that this independent expert report was submitted to the RMS (UK PSD).	reproduced in Addendum 2. It is necessary to clarify what safety margin is appropriate over the NOAEL for brain vacuolation, since this impacts on the setting of both the ADI and the AOEL. The issues surrounding the significance of this effect are covered at Section B.6.10.1 in the DAR and at Point 2(41) in the Reporting Table. For discussion at Expert meeting	
	Open point 2.4 MSs to agree on the representativeness of batches used in tox studies to the proposed specification. See reporting table 2(53).		The batch of cyflufenamid used in most of the toxicology studies was of lower purity than the proposed minimum specification, and hence may represent the 'worst-case' with respect to impurities. For the impurity present in the technical specification at 1% a case can be made for structural similarity (isomerisation) and there are data available (LD_{50} >5000 mg/kg bw, negative Ames test, tentative identification in the rat metabolism study) to address any concerns with	PRAPeR 39 (10– 13 12.2007): 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
			this impurity. For the impurity present at 0.3% in the technical specification there is evidence that it is a rat metabolite of cyflufenamid, that it is naturally occurring in rats and there are data available in the open literature (e.g. LD_{50} >2000 mg/kg bw). The RMS considers that there are no concerns regarding this impurity at 0.3% (see Appendix 4A in the DAR). For discussion at Expert meeting.	

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 Data requirements: **-** Open points: ***2***			Section 3 Data requirements: ***0*** Data requirement***s: 2*** Open points: ***0***
	Open point 3.1 RMS to elaborate further on whether isomerisation into the Z-isomer has taken place and if so, to clarify the impact on the risk assessment in an addendum See reporting table 3(3).		It seems that it is isomerisation from parent (z isomer) to the E isomer during plant metabolism studies that is in question. The applicant has not addressed any implications of isomerisation on risk assessment in their submission. The reports on plant metabolism do not provide further significant clarification on whether isomerisation has occurred. The applicant does include the E isomer of cyflufenamid in their proposed metabolic pathway (Figure B.7.1). It can only be assumed so as the peak for radiochemical purity determination was named 'NF-149' which is the z-isomer. Therefore it is possible that a limited amount of isomerisation has occurred in the plant metabolism to account for the amounts of 149-(E)-FB reported as found in the plant metabolism studies. It is not considered that the findings of 149-(E)-FB reported (expected to be on the basis of isomerisation) need to	PRAPeR 40 (12 – 13 December 2007): 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
			be considered from a risk assessment perspective on the basis that the amounts formed ranged in straw from 0.5% to 4% TRR only, and that the highest mg/kg amount of E isomer of cyflufenamid (149-(E)-FB) reported in the 1N rates of study was 0.013 mg/kg in straw, only a small amount above 0.01 mg/kg and insignificant compared to amounts of parent (z isomer). Mg/kg amounts of 149-(E)-FB were generally only slightly higher (compared to straw) in forage (up to 0.21 mg/kg) and in the range of 2-3% TRR. Addressed (suggest point is discussed in residues Expert meeting)	
	Open point 3.2 To be discussed in an experts' meeting whether a, and if so what, residue definition for risk assessment and monitoring for food of animal origin should be proposed The meeting consider aspects such as fat solubility of parent compound, toxicological relevance of metabolites 149-F1, 149-F6 (higher acutely toxic)		With regard to the DE comment and the RMS response to point 3(5) in the reporting table, there seems to be agreement that animal product residues are not expected as a result of the currently proposed use. On this basis a residue definition is not currently proposed by the RMS. However if the Residues Expert meeting considers that a residue definition is required, then a rationale for a residue definition proposal for animal products for cyflufenamid and metabolite 149-F1 for monitoring	PRAPeR 40 (12 – 13 December 2007): 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 3(5).		purposes and risk assessment is provided by the RMS in column 3 of the reporting table point 3(5). All columns of Reporting table points 3(5), 3(6), 3(7), 3(8), 3(9), 3(10), 3(11) provide relevant considerations (e.g. on fat solubility). UK RMS toxicologist advice is that metabolite 149-F1 is of relevance toxicologically compared to parent, at least on an acute basis, and metabolite 149-F1 is of higher acute toxicity than metabolite 149-F6. However, the EFSA comment seems to state that 149-F6 has a higher acute toxicity, so this is an aspect that needs to be resolved in discussion. Addressed (suggest point is discussed in toxicology and residues Expert meetings).	
3.1	New data requirement A clarification concerning the analytical methods used in the residue trials to be submitted.		RMS - 15.02.2008: Data requirement transferred to Section 1	PRAPeR 40 (12 – 13 December 2007): Data requirement open. Written procedure: Data requirement remains open.
3.2	New data requirement to be transferred to the phys-chem section. Analytical method for animal commodities is required for		RMS - 15.02.2008: Data requirement transferred to Section 1	PRAPeR 40 (12 – 13 December 2007): Data requirement open (see phys-chem) Written procedure:

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 following residue definition: sum of cyflufenamid, the E isomer and metabolite 149-F1.			Data requirement remains open.
	New open point 3.3: RMS to amend the list of end point according to the discussions during the PRAPeR 40.		RMS - 15.02.2008: Open point addressed, revised chronic risk assessment has been incorporated in to Addendum 3. Further amendments to the End points may be required following the outcome of the evaluation of data gap 3.1.	PRAPeR 40 (12 – 13 December 2007): Open point open. Written procedure: Open point fulfilled. Updated version of list of end points has been submitted in February 2008.

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 Data requirements: ***3*** Open points: ***6***			Section 4 Data requirements: ***0*** Open points: ***6***
4.1	Data requirement Applicant to provide further details on the monitoring study on phenyl acetic acid (PAA) in soil performed in Japan, to support the reported natural background concentrations in soil. In the comments received on the reporting table, the applicant stated that the study has been submitted to RMS on 6 June 2007. See reporting table 4(3).	A report (number RD-01179) on the determination of the levels of phenylacetic acid (PAA) in Japanese soil shows that the PAA content was 0.076 mg/kg of soil which is 1.6 times higher than the maximum theoretical residue that could be formed from cyflufenamid (NF-149). The Applicant confirms that the report of this study was submitted to RMS on 6 June 2007.	The report has been briefly evaluated in Addendum 2 (Yamasaki, 2001, report number RD-01179). In the opinion of the RMS the study provided evidence of limited quality only on the determination of PAA in soil. However, despite the shortcomings of the study the RMS considers it highly plausible that PAA is a naturally occurring compound and that the potential formation of such a substance from applied cyflufenamid would have an insignificant effect on the naturally occurring levels of this substance derived from alternative sources. The RMS considers the data requirement fulfilled.	PRAPeR 37 (03. – 06.12.2007): Data requirement fulfilled.
	Open point 4.1 RMS to add in the LoEP the mean/median value for parent DT50lab and for metabolites (as they were		The LoEP has been updated. Actual and TWA values for the individual metabolites over time have been removed from the LoEP. This is	PRAPeR 37 (03. – 06.12.2007): 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
	used for PECsoil calculations) and to specify that the reported mean values for metabolites (normalised for FOCUS modelling) refer to arithmetic mean. See reporting table 4(4).		because the RMS does not consider it valid to calculate these based on a degradation DT50 (a dissipation DT50 should really be used).	New open point proposed, see open point 4.7
	New open point 4.7: RMS to recalculate PECaccumulation for 149-F1 and 149-F6 using max DT50 lab values, and to provide clarification on DT50 calculation (decline from maximum observed) in the LoEP.		RMS - 15.02.2008: Open point fulfilled. New theoretical accumulated PECsoil values have been included in the LOEP for 149-F1 and F6. In the absence of reliable data on dissipation from maximum observed for each metabolite seen in the parent studies, the maximum degradation DT50 values from the metabolite laboratory degradation studies have been used. The calculations are based on residues in the top 5cm following repeated applications for up to 7 years for 149-F1 and up to 40 years for 149-F6. Given the relatively low Koc values of both metabolites the assumptions used are considered by the RMS to represent a sufficiently conservative approach.	PRAPeR 37 (03. – 06.12.2007): Open point open. Written procedure: Open point still open EFSA note: new theoretical accumulated PECsoil values should be included in an addendum.
4.2	Data requirement Applicant to provide further information to support the	The trial sites and soils used in the field dissipation study were selected in accordance with the recommendations	The Applicant has provided further clarification regarding the selection of sites for the field dissipation study and	PRAPeR 37 (03. – 06.12.2007): Data requirement 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
	choice of field trial sites, specifically with regard %OC content, to cover the wide range of European conditions. In the comments received on the reporting table, the applicant stated that the study has been submitted to RMS on 6 June 2007. See reporting table 4(5).	of SETAC-1995 procedures for assessing the environmental fate and ecotoxicity of pesticides. The soil types chosen were specifically located in areas of N. and S. Europe with soil types representative of crop production areas of the intended uses of NF-149 EW. Furthermore, information from field trials experts is that organic matter in typical cereal growing areas in the EU has a **maximum** of 3-5% organic matter. Although in laboratory studies there was a tendency for a long DT_{50} to be associated with high organic matter content, this was not seen in the field dissipation study. In the field study, the shortest DT_{50} value (10.2 days) was associated with an intermediate level of organic matter content (1.89%) and the longest DT_{50} value corresponded with the lowest content (1.38%). The Applicant confirms that the justification that the maximum organic matter content in typical cereal growing areas in the EU (3-5%) was provided to the RMS on 6 June 2007.	this information is assessed in Addendum 2. Given the very wide range of DT_{50} values observed in the laboratory soils, and the potential relationship between DT_{50} and soil OM%, the RMS considers it would have been useful to have tested soils with a wider range of OM% under field conditions. However the RMS considers that the submitted field dissipation data meets the data requirements and does not consider it necessary to request any further information. For further reassurance the RMS has simply re-run the groundwater exposure assessment using a simple worst case laboratory DT50 of 412 d in place of the original value of 19.4 d used in the DAR. All other input parameters were as per the modelling in the DAR. Even with this conservative value the cyflufenamid PECgw was still 0.000µg/l according to FOCUS PELMO simulations, indicating no risk to groundwater even using the most conservative degradation input parameter. Therefore the RMS considers that no	

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
			further information is required.	
4.3	Data requirement Applicant to provide the original study on PEC groundwater calculations. In the comments received on the reporting table, the applicant stated that the information on the calculation of PECgw has been submitted to RMS on 6 June 2007. See reporting table 4(12).	A separate study report on PECgw calculations is not available. This is not unusual as separate reports are not normally produced for other risk assessments (e.g. for assessing risks to avian, aquatic and other terrestrial vertebrates) as they are derived from information contained in the dossier. Calculations were carried out in accordance with recommendations of the FOCUS ground water scenarios group (FOCUS, 2000). FOCUS scenarios were implemented into 4 models. PELMO (version 2.2.2) was used to investigate the potential for contamination of groundwater by cyflufenamid and its 4 metabolites/degradates. Information on the calculation was presented in the EU dossier (Section 5, Point 9.2.1). Further information produced by the RMS (UK PSD) can be found in the watermarked Draft Assessment Report issued by EFSA. The Applicant confirms that this information was provided to RMS on 6 June 2007.	The RMS can confirm that the calculation of PECgroundwater provided by the Applicant was presented in their MIII summary document only, and therefore no specific reference to a separate study is included in the DAR. The RMS can also confirm that the values presented in the DAR were independently validated by the RMS by repeating the modelling using identical input parameters. The LoEP has been updated to ensure all information needed to re-run the FOCUS groundwater simulations has been included.	PRAPeR 37 (03. – 06.12.2007): Data requirement not fulfilled formally. However, since values were validated by RMS, it is agreed that the data requirement is not essential to finalise the assessment. Written procedure: Data requirement for the original study on PEC groundwater calculations (not essential to finalise the assessment).
	Open point 4.2 MS to discuss the suitability	The Applicant agrees with the opinion of the RMS (UK PSD) who states that “inputs to soil have been calculated	This issue is addressed in Addendum 2.	PRAPeR 37 (03. – 06.12.2007):

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 approach used to model the metabolites for groundwater contamination in a meeting of experts. EFSA note: the direct application of metabolites instead of using sequential degradation in the model would result in a best case as the amount of the leaching of metabolite during its formation from the parent is excluded in the modelling. Therefore this approach is not recommended. See reporting table 4(14).	assuming instantaneous input of the parent compound and considering the maximum accumulation of each metabolite in the laboratory degradation studies and the ratio of molecular weights of the parent and metabolites". This was an appropriate approach as it was not possible to produce a kinetic analysis of the formation fractions of metabolites in parent degradation studies. Importantly, a higher tier leaching study was conducted which showed that in spite of multiple worst case conditions (above average rainfall plus irrigation), there was no leaching of parent cyflufenamid down to 40 cm or any of the metabolites (149-F, 149-F1 or 149-F6) below 80 cm. Additionally, no quantifiable residues of the parent were detected in any soil water sample collected at depths of 40, 80 or 120 cm. Therefore it was considered that the potential of cyflufenamid and its metabolites to leach to groundwater at concentrations of 0.1 μg/ml of higher was negligible. The Applicant confirms that the above was provided to RMS on 6 June 2007.	The RMS accepts that the simplistic approach used in the original DAR ignores the potential for metabolite leaching to occur during the individual formation phases that would be simulated if a formation fraction approach had been used. For simplicity, the RMS has repeated the FOCUS groundwater assessment assuming a formation fraction of 100% for each stage of the metabolic pathway (i.e. parent → 149-F11 → 149-F → 149-F1 → 149-F6). This assumption is cleary worst case and the calculations are presented for illustrative purposes only. Results indicate that the method has no significant impact on parent or metabolites 149-F11 or 149-F. Higher concentrations of metabolites 149-F1 and 149-F6 are generated, however both these metabolites were subject to a relevance assessment in the original DAR. Revised results are presented in Addendum 2 for information. Overall the RMS considers that no further information is required.	Open point fulfilled. New open points proposed, see open points 4.8 and 4.9
	New open point 4.8: RMS to update the LoEP to		RMS - 15.02.2008: Open point fulfilled. The PECgw	PRAPeR 37 (03. – 06.12.2007):

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
	include the first approach for PECgw calculations presented in addendum (arithmetic mean DT50 for a.s. and metabolites) and delete the original DAR approach from the LoEP.		approach based on 100% formation fractions presented in the Addendum has been included in the LEOP.	Open point open. Written procedure: Open point fulfilled
	New open point 4.9: RMS to clarify what '149-F was an intermediate leacher' means or delete this information from the LoEP.		RMS - 15.02.2008: Open point fulfilled. The comment has been removed since the groundwater approach has been updated based on the assumption of 100% formation fractions.	PRAPeR 37 (03. – 06.12.2007): Open point open. Written procedure: Open point fulfilled
	Open point 4.3 MS to discuss the appropriate DT50 value to be used in FOCUSgw modelling in a meeting of experts. See reporting table 4(17).		This point is discussed further in Addendum 2. The selection of alternative DT50 values is not considered by the RMS to affect the conclusions of the existing FOCUSgw modelling. Overall the RMS considers that no further information is required.	PRAPeR 37 (03. – 06.12.2007): Open point fulfilled.
	Open point 4.4 RMS to provide explanations on the inconsistency between the timing of application as indicated in the GAP table and the actual dates of application used in the assessment.		This point is discussed further in Addendum 2. Information on application dates has been included in the Addendum and LoEP to demonstrate that there is in fact no significant inconsistency between the GAP and the application dates used in the exposure assessment.	PRAPeR 37 (03. – 06.12.2007): 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
	EFSA note: it is noted that in all field trials cyflufenamid was applied in late May or middle June. In addition, in FOCUS GW the crop interception factors were calculated based on applications to cereals at GS 20-39 and GS 40-89 (it was not possible to check the actual dates of application used in the modelling because the original report on FOCUS PECgw is not available). See reporting table 4(18).		Overall the RMS considers that no further information is required.	
	Open point 4.5 RMS to update the list of references relied on with respect the reference Brewin (2002). See reporting table 4(20).		The references relied on list has been updated. Addressed RMS - 15.02.2008: The correct reference is Brewin, S.A. (2000), Ref: RD-II02006. The references relied on list has been updated (February 2008). Addressed	PRAPeR 37 (03. – 06.12.2007): Open point still open. Written procedure: Open point fulfilled
	Open point 4.6		The references relied on list has been updated.	PRAPeR 37 (03. – 06.12.2007):

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	RMS to update the list of references relied on with a cross reference between the phys-chem and the fate section for the studies by Yamasaki (1999), Aikens (2001) and Aikens & Millais (2002) See reporting table 4(21).		Addressed RMS - 15.02.2008: The references relied on list has been updated (February 2008). Addressed	Open point still open Written procedure: Open point fulfilled
	New open point 4.10: RMS to amend the list of end points according to the discussions during the PRAPeR 37 meeting.		RMS - 15.02.2008: Open point fulfilled. The LOEP has been updated as recommended by the PRAPeR 37 meeting discussions.	PRAPeR 37 (03. – 06.12.2007): Open point open. Written procedure: Open point fulfilled

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 Data requirements: ***1*** Open points: ***5***			Section 5 Data requirements: ***0*** Open points: ***2***
	Open point 5.1 The toxicity endpoint for the long-term risk assessment for mammals to be discussed in an experts' meeting. See reporting table 5(5).		RMS - 22 Aug 2007 As previously stated the total litter resorption was considered to be a spontaneous treatment-unrelated incident. Abortions at the highest dose level (300 mg a.s./kg bw/d) were a consequence of severe maternal toxicity at unlikely environmental exposure levels. The NOEC selected was considered the most appropriate endpoint reflecting reproductive effects. Point to be discussed further at Expert meeting. RMS - 15.02.2008: The effects identified at 60 mg/kg bw/day in the rabbit study (resulting in the proposed NOEC of 10 mg/kg bw/day) are not considered to be relevant to the long-term risk assessment for mammals. The single incidence of total litter loss was likely to be a spontaneous finding (single spontaneous instances are not	PRAPeR 38 (03 – 07 12.2007): Question to mamtox: are the effects on foetal weight, ossification and litter resorption seen in the developmental study with rabbits likely to have been caused by the gavage dosing? Open point still open pending mamtox meeting.

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
			uncommon in control animals). The minor effects on foetal weight and ossification are normal secondary consequences of the bodyweight effect in the maternal animals. Such minor effects would not be expected to persist beyond the early post-natal period and are not severe enough to impact on post-natal survival. The effects driving the proposed NOEC of 10 mg/kg bw/day would not be expected to have any impact at the wildlife population level. The NOEC of 57 mg/kg bw/day from the reproductive study is considered to be the appropriate endpoint. LOEPs have been amended. Addressed	
	Open point 5.2 RMS to clarify whether the LC_{50} for earthworms reported as 25 mg a.s./kg based on 'NF-149 EW' has been corrected for organic content in soil. The Notifier has indicated that a clarification will be provided by 6 June. See reporting table 5(11).	The LC_{50} value of NF-149 EW to earthworms presented in the study report and in the EU dossier was not corrected for the organic content of the soil because at the time the study was conducted there was not requirement for this in the prevailing testing guideline (OECD 2007, adopted 4 April 1984). In accordance with the current guidance, because the log Kow for cyflufenamid ranges from 4.55 to 4.71, the LC_{50} in the acute toxicity study to earthworms (>1000 ppm) has been	RMS - 22 Aug 2007. Relevant earthworm endpoints have been corrected in the revised LOEPs & TERs amended where appropriate. Low risk indicated for earthworms. Addressed.	PRAPeR 32 (15. – 19.10.2007): 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
		corrected using a factor of 2 for organic matter content (10%) in the artificial soil used in the study. The corrected LC_{50} value is >500 ppm. The Applicant confirms that the above reason and the corrected LC_{50} value were provided to RMS on 6 June 2007.		
5.1	Data requirement: Applicant to address the risk to soil micro-organisms from the metabolites. The statement in column 3 does not address the concern for 149-F. The DT_{50} of 9.1 days might be correct but it takes 44 days for the peak to be reached. The Notifier will provide further justification to RMS (UK PSD) on 6 June 2007. See reporting table 5(15).	The worst case maximum PECsoil for the metabolites (6.6 μg/kg) is more than 40-fold below the applied rate of 294 μg/kg of soil of cyflufenamid which had no effect on carbon and nitrogen transformations. As cyflufenamid and the metabolites 149-F1 and 149-F6 had no effect on soil micro-organisms, no risk to soil micro-organisms is expected from other metabolites (149-F and 149-F11). This is supported by their acute toxicity to soil macro-organisms e.g. earthworms. 149-F was only 4 times more toxic to earthworms than cyflufenamid (LC_{50} 149-F = 279 ppm; cyflufenamid LC_{50} >1000 ppm); 149-F1, 149-F6 and 149-F11 were of similarly low toxicity to earthworms as cyflufenamid. The Applicant confirms that the justification was provided to RMS (UK PSD) on 6 June 2007.	RMS - 22 Aug 2007 An approximate 19% decline in cyflufenamid over 28d is predicted from PECsoil values. In the soil microbial studies at the highest dose this represents approximately 0.056 mg cyflufenamid degradation. Assuming degradation follows the proposed soil pathway this represents formation of 0.045mg 149-F11, which with a DT50 of 2.5d, will have rapidly degraded to149-F. Thus it is likely that significant exposure to 149-F is probable in this study (max PECsoil 149-F= 0.0066 mg/kg) without effect on microbial activity. Furthermore, both 149-F and 149-F11 were considered not to significantly accumulate in soil (DAR B.8.3). Low risk to earthworms was indicated from 149-F11 and 149-F and its soil metabolite derivatives 149-F1 and 149-F6, the latter also without effect on soil microbial activity. Thus, overall, the RMS considered that the weight of	PRAPeR 38 (03 – 07 12.2007): Data requirement 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
			evidence, based on likely absence of toxicity and limited transient exposure, indicates that 149-F will be of low risk to soil organisms and processes. Point addressed	
	Open point 5.3 The reproduction test with Collembola to be discussed in an experts' meeting. There seems to be no formal data requirement for a Collembola study. However, since the study is available the validity and results should be discussed. See reporting table 5(17).	he cyflufenamid study with Collembola (*Folsomia candida*) was conducted in accordance with the draft version of the EU guidance document on terrestrial ecotoxicology (SANCO/10329) prevailing at the time the dossier was compiled and also in accordance with ESCORT 2. ecause the DT_{90f} in the field dissipation study with cyflufenamid ranged up to 350 days, this triggered an assessment of effects on soil macro-organisms according to the prevailing draft SANCO/10329 document. (For the same reason tests with 4 species of non-target arthropods were conducted; hazard quotients were not required in the prevailing draft of SANCO/10329).	RMS - 22 Aug 2007 According to SANCO/10329, for cyflufenamid (soil DT90 100-365d) the absence of risk to earthworm, NTAs and soil microbial activity is sufficient establish low risk to soil organisms and processes. Nevertheless, a Folsomia study was submitted using NF-149EW formulation. However, although considered acceptable by the RMS, due to absence of a clear dose vs. effect relationship between 0.00355 - 3.55 mg a.s./kg, a reliable NOEC cannot be determined and other evidence on NTAs and earthworms would suggest likely low toxicity. Point addressed	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	Open point 5.4 RMS to give the reference to the studies on which the statement "Cyflufenamid and its metabolites showed no fungicidal activity to non-crop		RMS - 22 Aug 2007 This information was given in the Biological Assessment Dossier. Prince, K.J. & Pickering, J.W (2002). Biological assessment dossier on the	PRAPeR 38 (03 – 07 12.2007): 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
	plants as this was specific to cereals and powdery mildew. In addition, neither the parent or its metabolites showed any herbicidal or insecticidal activity" as given in B.9.11was based on. See reporting table 5(19).		fungicidal product cyflufenamid to be used for the control of Powdery mildew in cereal crops. Agrisearch UK. Ltd for Nippon Soda The study referenced has been added to the references relied on list. Point addressed.	
	Open point 5.5 RMS to delete the two position papers by Kawai (2002a and b) from the reference list. See reporting table 5(22).		RMS - 22 Aug 2007 These two papers were not relied in the ecotox section and have been removed for the references relied on list. Point addressed	PRAPeR 38 (03 – 07 12.2007): Open point fulfilled.
	New open point 5.6: RMS to include the secondary poisoning and drinking water risk assessment for birds and mammals in the LoEP.		RMS - 15.02.2008: LoEPs have been amended to include the bird and mammal secondary poisoning and drinking water risk assessment. Low risk indicated. Point addressed	PRAPeR 38 (03 – 07 12.2007): Open point open.