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REPORT OF EPCO EXPERT MEETING 21

FOLPET

Rapporteur Member State: Italy

Specific comments on the active substance in the section

4. Environmental Fate and Behaviour

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**
17 November 2004	RMS/Italy	Folpet consultation report
22 December 2004	RMS/Italy	Folpet reporting table rev1-1
March 2005	RMS/Italy	Folpet addendum vol3 B8
23 March 2005	RMS/Italy	Folpet list of end points fate
23 March 2005	RMS/Italy	Folpet evaluation table rev0-1

3. Documents tabled at the meeting:

Date	**Supplier**	**File Name**
07 April 2005	RMS/Italy	Folpet supported uses

The conclusions of the meeting were as follows:

4. **Data on preparations:** Folpan 80 WDG.

5. **Classification and labelling:** readily biodegradable, no labelling proposed.

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

7. **Reference List**

Areas of concern: not at the moment. New FOCUS PEC groundwater modelling still pending.

Appendix 1: EPCO discussion table: FOLPET

Appendix 2: Evaluation table

RMS informs on amendments in the table of intended uses as the notifier does not want to support one of the uses (North EU winter wheat) any longer. EFSA confirmed that any longer supported uses should be maintained in the table of representative uses and labelled in grey.

Appendix 1: Discussion Table, FOLPET (Fu)

4. Environmental Fate and Behaviour

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.1: RMS to amend the list of end points to give number of studies and range of r2 and specify parameters used for FOCUS modelling (mean or median DT50 normalised to 1okPa of pF2, 20oC with Q10 of 2.2). (see reporting table 4(2))	The RMS amended the list of end points. Due to outcome of the meeting regarding the FOCUS modelling (see open point 4.15) the list of end points need to be amended again. Therefore the experts agreed to set a new open point: Remove FOCUS gw modelling from the list of end points until new FOCUS modelling has been provided (see new data gap 4.6).	Open point fulfilled. The list of end points was amended. The experts agreed to set a new open point (see new open point 4.19): Remove FOCUS gw modelling from the list of end points until new FOCUS modelling has been provided (see new data gap 4.6).
	Open point 4.2: RMS to clarify if folpet or metabolites are found in the sediment in an addendum. (see reporting table 4(4))	The notifier states in the evaluation table that Folpet was not found in sediment at any time point in either sediment/water system. No metabolite was detected in the sediment at levels approaching 10% of the applied amount. The RMS agrees with the notifier and provided the information in an addendum. The list of end points was amended. NL question whether phthalimide metabolite content is only a peak or still raising after the last sampling. The experts checked in the DAR. The experts agreed to set a new open point: RMS to check if phthalimide metabolite in the sediment is still increasing at the end of study and to give the day of occurrence of maximum value in the sediment in the list of end points.	Open point fulfilled. Folpet or metabolites are not found in the sediment at levels approaching 10% of the applied amount. The experts agreed to set a new open point 4.20: RMS to check if phthalimide metabolite in the sediment is still increasing at the end of study and to give the day of occurrence of maximum value in the sediment in the list of end points.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	New open point 4.20: RMS to check if phthalimide metabolite in the sediment is still increasing at the end of study and to give the day of occurrence of maximum value in the sediment in the list of end points.	This open point was proposed at EPCO 21.	Open point still open.
	Open point 4.3: RMS to report in the list of end points the rate of degradation of the metabolites phthalamic acid and phthalic acid. (see reporting table 4(9))	The RMS amended the list of end points. The experts agreed.	Open point fulfilled. The list of end points was amended.
	Open point 4.4: RMS to indicate units of PEC sw in the list of end points. (see reporting table 4(16))	The RMS amended the list of end points. The experts agreed.	Open point fulfilled. The list of end points was amended.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
4.1	Notifier to give more details on bound residues and on identity of the absorbed residue in the sediment. (see reporting table 4(18))	The notifier gave the following information in the evaluation table: It appears likely that the non-extracted residue in the sediment/water systems consisted of phthalic acid type moieties covalently bound to sediment which were then more slowly partially degraded in the anaerobic layers of the sediments to release methane and carbon dioxide. … As such, there would not appear to be any concern with respect to the bioavailability of the residue over time. The RMS answered on this information in the addendum on page 16/17 and concluded that the nature of the non-extracted sediment residue appears not to constitute a risk to sediment dwelling organisms. The experts agreed. No further concerns on bound residues and on the identity of the absorbed residue in the sediment.	Data requirement fulfilled. The information was presented and the experts have no further concerns on bound residues and on the identity of the absorbed residue in the sediment.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.5: The need for PEC sw and PEC sediment taking into account run-off and drainage to be discussed in an expert meeting. (see reporting table 4(19))	The notifier does not consider it necessary to conduct FOCUS surface water evaluations for annex 1 listing because at the time when the dossier was submitted this was not a requirement. The RMS states in the evaluation table: Given the short soil DT_{50} for folpet there is unlikely to be any significant movement to surface water through run-off or drainage. Unrealistic worst case PECsw values for metabolites from run-off have already been calculated and included in the DAR. Given the GAP for folpet uses (spring/summer applications) drainage will not be a significant exposure route for metabolites either. PEC sw including run off was addressed but not for drainage. The meeting took note of the fact that entry via run off has already been addressed and the meeting discussed the question whether entry via drainage could be disregarded. One expert disagrees and reminds on the North European uses in winter wheat. Thus the meeting does not agree to disregard drainage considering North European uses in winter wheat and taking into account the number of applications in Southern Europe. Therefore the experts agreed to identify a data gap: Calculation of PEC sw with consideration of drainage needs to be done. Reference was made to the discussion on captan. However the use was different with a high number of applications for folpet, so comparability is not given. The experts decided to send a message to the ecotox section: For runoff exposure only initial worst case estimation of PEC sw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required.	Open point fulfilled. New data gap identified 4.5: Calculation of PEC sw with consideration of drainage needs to be done. The experts decided to send a message to the ecotox section: For runoff exposure only initial worst case estimation of PEC sw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required.
4.5	New data gap: Calculation of PEC sw with consideration of drainage needs to be done.	This data gap was identified at EPCO 21.	Data gap identified.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Message to the ecotox section (EPCO 22): For runoff exposure only initial worst case estimation of PEC sw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required.		Answer EPCO 22: The metabolites are not regarded as relevant.
	Open point 4.6: RMS to amend the list of end points to give the average/median value for the Koc as requested according to the guidance on the list of end points. (see reporting table 4(20))	The RMS amended the list of end points. The experts agreed. (see also open point 4.12 and 4.13)	Open point fulfilled. The list of end points was amended.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.7: RMS to revise to 1st order DT50 values for phthalimide in an addendum to be discussed in an expert meeting. (see reporting table 4(26))	The addendum was presented by the RMS. A first order degradation rate for phthalimide was calculated for the purpose of calculating FOCUS PEC_{GW} values and reported. The data from day 5 to day 120 was analysed and a rate of degradation of 28.2 days derived, at 25°C. It was evident that this value was an over-estimation because the formation and decline of phthalimide was not taken into account, but it was the best fit value that could be obtained. The list of end points was amended accordingly by the RMS. The experts agreed.	Open point fulfilled. The addendum was presented and the list of end points was amended.
	Open point 4.8: RMS to clarify amount of bound residues taking into account fulvic and humic acid in an addendum to be discussed in an expert meeting. (see reporting table 4(27))	The addendum was presented by the RMS. One expert noted that fulvic acid can leach, they are not really bounded residues. RMS proposed that fulvic and humic acid components should be regarded as part of the non-extractable residues. The experts agreed.	Open point fulfilled. The addendum was presented.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.9: RMS to clarify which aerobic/anaerobic studies are acceptable and essential for the assessment in an addendum to be discussed in an expert meeting. (see reporting table 4(28) and 4(23))	RMS agrees with the notifier that the two aerobic studies (Daly, D. 1991a, and Crowe, A. 2001) are the essential soil degradation studies necessary for assessment purposes. Further studies under anaerobic conditions are regarded supplementary but results should be presented in the list of end points. Open point fulfilled with regard to clarification. However the open point is still open for including anaerobic study details in list of end points.	Open point fulfilled with regard to clarification. However the open point is still open for including anaerobic study details in list of end points (see open point 4.19).

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.10: RMS to provide r^2 for each determination and normalised DT_{50} in an addendum to be discussed in an expert meeting. (see reporting table 4(30))	A Table has been provided by the NOT which includes r^2 values (taken from the relevant reports) and re-calculated first order DT50 values (taken from Mackay, N. 2002), for those studies considered relevant for the assessment process. The table was assessed in the addendum presented. One expert raised a point to be discussed regarding mean and median which differ greatly in this example. He thinks with such a small data set the calculation and use of a median is not appropriate. See addendum page 9 and 21: Folpet: 1.05 days (median of five measurements in four soils) Phthalimide: 1.04 days (median of five measurements in four soils) One expert states that the old guidance recommended to use the worst case value between the mean and median values. The meeting discussed if the study Daly, D. 1991a (25°C) overestimates the DT50 and finally agreed not to disregard the DT50 from the study Daly, D. 1991a (25°C). The meeting agreed to use the mean value instead of the median. Remark from the meeting: The experts agree that the medians should not be used and to disregard the DT50 values derived from the study conducted at 10°C for the calculation of the mean because the same soil was used as for one of the studies at 20°C.	Open point fulfilled. The information was provided and assessed in the addendum. The experts agreed to set a new open point 4.21: With respect to aerobic DT50: A new mean should be recalculated excluding DT50 value from the study conducted at 10 ºC. Mean should be used in the risk assessment and therefore median should be removed form the list of end points (see open point 4.19).

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	New open point 4.21: With respect to aerobic DT50: A new mean should be recalculated excluding DT50 value from the study conducted at 10 ºC. Mean should be used in the risk assessment and therefore median should be removed form the list of end points.	This open point was proposed at EPCO 21.	Open point still open.
	Open point 4.11: RMS to provide an addendum with a summary of studies that address the fate of side chain of folpet. Formation of thiophosgen should be addressed. Addendum to be discussed in an expert meeting. (see reporting table 4(31))	The notifier states in the evaluation table that two captan studies wit the trichloromethyl - ^{14}C label are most relevant for addressing the fate of the captan and folpet common side chain. The results of these studies strongly imply that thiophosgen would not be expected to be a significant product of folpet degradation. The RMS agrees with the notifier. The addendum was presented. The experts discussed the molecular structure of folpet and captan. The side chain with $NSCCl_3$ was considered to be in similar molecular environment. Based on the molecular structure similarities, the meeting agreed that the studies on captan can also be used to address the fate of the side chain for folpet. However it can not be excluded that traces of thiophosgen may occur. The same message that was sent to the tox section on this issue for captan should be reiterated for folpet.	Open point fulfilled. The addendum was presented. The same message that was sent to the tox section on this issue for captan should be reiterated for folpet.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Message of EPCO 21 to tox section (EPCO 23): It cannot be excluded that traces of thiophosgene occur in the air.		
	Open point 4.12: RMS to provide an addendum with Koc estimation of phthalamic acid and phtalic acid an assessment of its reliability to be discussed in an expert meeting. (see reporting table 4(32))	The notifier states in the evaluation table that the PCKOC programme (within the EPIWIN suite of programs) was used to estimate the KOC values for phthalic acid and phthalamic acid. Further details of this programme were provided to the RMS in a new report by the notifier. RMS states: No sorption/desorption studies have been conducted with phthalamic and phthalic acid. As these degradation products only occurred briefly above 10% in soil degradation studies they were considered to be transient. The rapid formation and degradation of these secondary degradation products suggested that it was appropriate to employ estimates of sorption characteristics in order to assess the potential mobility. The PCKOC programme was used to estimate the K_{OC} values for phthalic acid (73.06) and phthalamic acid (10) (Mackay, N. 2002). The description of the estimation program has been provided and assessed. One expert is of the opinion that this approach is not acceptable in general, but in this case it is acceptable as there is a very fast transition. Normally in this case a column leaching study would be required (SCP opinion: SCP/KOC/002-Final[1]). The experts agreed with the RMS proposal. Remark by the meeting: Due to rapid degradation and transient nature in this case it is acceptable but not in general.	Open point fulfilled. The addendum was presented. The assessment is accepted by the meeting in this case due to rapid degradation and transient nature but not in general.

[1] Opinion of the Scientific Committee on plants on methods fort he determination of the organic carbon adsorption coefficient (Koc) for a plant protection product active substance in the context of council directive 91/414/EEC. (Opinion adopted by the Scientific Committee on Plants, 18 July 2002).

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.13: Acceptability of Koc for soils loam EUROSOIL 3 and sand soil LUFA2.1 to be discussed in an expert meeting. (This point relates to the metabolite phthalimide) (see reporting table 4(34))	This point relates to the metabolite phthalimide. The RMS agrees with the proposal of the notifier to remove the Koc derived from the more alkaline LUFA soils from the consideration. The meeting discussed the question whether the observed deviation from linear sorption could be related to the pH value of the soils. Thus it was proposed that the meeting should decide which soils to be used. One expert would also like to consider pH-dependency. The pH of LUFA soils was different from EUROSOIL soils. One of the EUROSOIL soils was quite acid. One expert questions if organic content is a factor. The experts agreed to disregard Koc values from two LUFA but to use only Koc values from EUROSOILS. The meeting remarks that the sentence in the addendum on page 22 “Putting this specific assessment aside, it appears, generally, that use of Koc rather than Kfoc is a more common practice.“ seems to be wrong as it is more common practice to use Kfoc. The experts agreed that the Kfoc values should be used instead of the Koc values in this case. Therefore a new open point was set: RMS to amend the list of end points accordingly.	Open point fulfilled. The experts agreed to disregard Koc values from two LUFA but use Koc values from EUROSOILS. The experts agreed that the Kfoc values should be used instead of the Koc values in this case. The list of end points should be amended accordingly (see new open point 4.19).
	Open point 4.14: RMS to provide an addendum to clarify and assess kinetic models employed to evaluate water sediment studies to be discussed in an expert meeting. (see reporting table 4(35))	A brief description of the kinetic model used to evaluate the results in the sediment/water study was presented in a study report provided by the notifier. Explanation on it was given by the RMS in the addendum (page 18). The experts agreed that the clarification is sufficient. The experts agreed to set a new open point: RMS is asked to give the parameter on the goodness of fittings (eg. r^2) in the list of end points.	Open point fulfilled. The addendum was presented and the experts agreed that the clarification is sufficient. The experts agreed to set a new open point (see new open point 4.19): RMS is asked to give the parameter on the goodness of fittings (eg. r^2) in the list of end points.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.15: RMS to provide an addendum with an expanded summary of FOCUS gw modelling and recalculations if necessary to be discussed in an expert meeting. (see reporting table 4(37))	A summary of the PEC_{GW} report (Mackay, N. 2002) was presented by the notifier, in which the justification for the selection of parameters is also given. RMS refers to the addendum page 18-22. CHAIR confirms with RMS that this was not a recalculation but only a expanded explanation. Reference to discussion on median and mean values (see open point 4.10) was made. One expert proposes that the list of end points should state which scenarios are used. The experts agreed and therefore set a new open point: RMS to amend in the list of end points including the scenarios used for FOCUS gw modelling. Resulting from the discussions in open point 4.13 und 4.10 a new data gap was identified. New FOCUS modelling is required with the mean values for DT 50 instead of median (Disregard DT50 values derived from the study conducted at 10° for calculation of mean – see open point 4.10) and with Koc value for phthalimide metabolite derived from 3 EUROSOILS. One expert questions if the degradation is pH dependent. RMS answer: no. Therefore it does not need to be considered in the gw modelling.	Open point fulfilled. The addendum was presented. The experts agreed to set a new open point (see new open point 4.19): RMS to amend in the list of end points including the scenarios used for FOCUS gw modelling. Data gap identified 4.6: New FOCUS modelling is required with the mean values for DT 50 instead of median (Disregard DT50 values derived from the study conducted at 10° for calculation of mean – see open point 4.10) and with Koc value for phthalimide metabolite derived from 3 EUROSOILS.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
4.6	New data gap: New FOCUS modelling is required with the mean values for DT 50 instead of median (Disregard DT50 values derived from the study conducted at 10° for calculation of mean – see open point 4.10) and with Koc value for Phthalimide metabolite derived from 3 EUROSOILS.	This data gap was identified at EPCO 21.	Data gap identified.
4.2	Notifier to submit PEC surface water for the metabolites. (see reporting table 4(39))	See new data gap identified 4.5. This point will be covered by the new data gap.	This data requirement is replaced by the new data gap identified 4.5.
4.3	Notifier to submit PEC sediment calculations. (see reporting table 4(41))	Data requirement fulfilled. Because no major metabolites occur in the sediment.	Data requirement fulfilled. No major metabolites occur in the sediment.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
4.4	Notifier to assess potential relevance of thiophosgene in the air compartment. (see reporting table 4(43))	Related to open point 4.11. Already covered by the discussion there and also discussion on captan. It can not be excluded that traces of thiophosgen may occur.	Data requirement fulfilled. However it can not be excluded that traces of thiophosgen may occur.
	Open point 4.16: MS to discuss the DT90 in surface water is < 3d in an expert meeting. Open point relates to open point 1.9 (comment 1(18) in the reporting table) (see reporting table 4(46))	DT50 in surface water is less than 3 days The experts agreed to send a message to EPCO 25 (phys chem section).	Open point fulfilled. The experts agreed to send a message to EPCO 25 (phys chem section): EPCO 21 confirms that the DT50 in surface water is less than 3 days.
	Message of EPCO 21 to EPCO 25: EPCO 21 confirms that the DT50 in surface water is less than 3 days.		

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.17: MS to discuss the residues definition in an expert meeting. (see reporting table 4(47))	Soil: Folpet and three metabolites phthalimide, phthalic acid, phthalamic acid. GW: Active substance and, pending on outcome of new calculation, further metabolites. SW: Folpet and phthalimide, phthalic acid, phthalamic acid, benzamide and 2-cyanobenzoic acid. Sediment: No residues. Air: Folpet.	Open point fulfilled. Residues were defined.
	Open point 4.18: RMS to clarify which studies of captan are used in the assessment of folpet and if these studies have actually been submitted in the folpet dossier. Open point relates to open point 4.11 (comment 4(31) in the reporting table) (see reporting table 4(48))	Only the two captan studies Diaz, D. and Lay, M.M. 1992 and Pack, D.E. and Verrips, I.S. 1988 are required to aid in the assessment of folpet. Makhteshim Chemical Works Ltd is the notifier for both folpet and captan. Hence, the use of these captan studies to support folpet is agreed by the notifier. Therefore there is no problem with data protection. EFSA remarks that the studies should be attached to the dossier. RMS answers that this was done in the addendum. The experts agreed.	Open point fulfilled. Only the two captan studies are required to aid in the assessment of folpet and there are no concerns on data protection by the notifier.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 4.19 RMS to revise the list of end points according to the amendments proposed by EPCO 21.	Remove FOCUS gw modelling from the list of end points until new FOCUS modelling has been provided (see open point 4.1). Give value of phthalimide metabolite in the sediment at the end of study and to give and the day of occurrence of maximum value in sediment (see open point 4.20). RMS to include anaerobic study results (see open point 4.9). Kfoc values should be used instead of the Koc values in the case of phthalimide (see open point 4.13) RMS is asked to give the parameter on the goodness of fittings (eg. r^2) of the kinetic models employed to evaluate water sediment studies (see open point 4.14). RMS include the scenarios used for FOCUS gw modelling (applicable when new modelling will be available) (see open point 4.15). With respect to aerobic DT50: median should be removed form the list of end points (see open point 4.10)	Open point still open.

Appendix 2: Evaluation table

4. Environmental Fate and Behaviour

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Section 4 Data requirements: ***4*** Open points: ***18***			Section 4 Data gaps: ***2*** Open points: ***4***
	Open point 4.1: RMS to amend the list of end points to give number of studies and range of r2 and specify parameters used for FOCUS modelling (mean or median DT50 normalised to 1okPa of pF2, 20oC with Q10 of 2.2). (see reporting table 4(2))	Normalised parameters for use in calculating PECgw were presented in the report: *Mackay, N. (2002). Predicted Environmental Concentrations of folpet and its degradation products in groundwater in the European Union using the FOCUS groundwater scenarios.*	list end point amended	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The list of end points was amended. The experts agreed to set a new open point (see new open point 4.19): Remove FOCUS gw modelling from the list of end points until new FOCUS modelling has been provided (see new data gap 4.6).
	Open point 4.2: RMS to clarify if folpet or metabolites are found in the sediment in an addendum. (see reporting table 4(4))	Folpet was not found in sediment at any time point in either sediment/water system. No metabolite was detected in sediment at levels approaching 10% of applied.	RMS agrees with notifier	EPCO 21 (11. – 14.04.2005): Open point fulfilled. Folpet or metabolites are not found in the sediment at levels approaching 10% of the applied amount. The experts agreed to set a new open point 4.20: RMS to check if phthalimide metabolite in the sediment is still increasing at the end

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	continued Open point 4.2: RMS to clarify if folpet or metabolites are found in the sediment in an addendum.			of study and to give the day of occurrence of maximum value in the sediment in the list of end points.
	New open point 4.20: RMS to check if phthalimide metabolite in the sediment is still increasing at the end of study and to give the day of occurrence of maximum value in the sediment in the list of end points. This open point was proposed at EPCO 21.			EPCO 21 (11. – 14.04.2005): Open point still open.
	Open point 4.3: RMS to report in the list of end points the rate of degradation of the metabolites phthalamic acid and phthalic acid. (see reporting table 4(9))		list end point amended	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The list of end points was amended.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.4: RMS to indicate units of PEC sw in the list of end points. (see reporting table 4(16))		list end point amended	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The list of end points was amended.
4.1	Notifier to give more details on bound residues and on identity of the absorbed residue in the sediment. (see reporting table 4(18))	The sediment phases in the study were exhaustively extracted. Following separation of the water and sediment phases, the latter was then extracted with acetonitrile/acetic acid (98:2, v/v) by shaking for 1 hour. The extracted sediment was then further extracted by refluxing in glacial acetic acid for 16 hours. This second extraction should be regarded as extraction under harsh conditions. The extracted sediment samples from the 100 day sampling point were further processed to estimate fulvic acid, humic acid and humin fractions. It is evident from this last fractionation that the unextracted residue was mostly associated with the humin fraction. Given the severity of the sequential extraction procedures employed it is reasonable to conclude that the vast majority of the non-extracted sediment residue was covalently associated with the sediment (rather than being simply adsorbed) and that this residue was not readily released from the sediment, except as carbon dioxide or methane. It appears	It is agreed that the nature of the non-extracted sediment residue appears not to constitute a risk to sediment dwelling organisms.	EPCO 21 (11. – 14.04.2005): Data requirement fulfilled. The information was presented and the experts have no further concerns on bound residues and on the identity of the absorbed residue in the sediment.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	continued Notifier to give more details on bound residues and on identity of the absorbed residue in the sediment. (see reporting table 4(18))	likely that the non-extracted residue in the sediment/water systems consisted of phthalic acid type moieties covalently bound to sediment which were then more slowly partially degraded in the anaerobic layers of the sediments to release methane and carbon dioxide. As such, there would not appear to be any concern with respect to the bioavailability of the residue over time.		
	Open point 4.5: The need for PEC sw and PEC sediment taking into account run-off and drainage to be discussed in an expert meeting. (see reporting table 4(19))	It is not considered necessary to conduct FOCUS surface water evaluations for annex 1 listing as when the dossier was submitted this was not a requirement. In addition, an assessment of risk to surface waters has been included in the DAR for run-off and for folpet for spray drift. A new report: *Terry, A. (2005). Predicted Environmental Concentrations of Metabolites of Folpet in Surface Water and Sediment arising from Spray Drift, in the European Union.* has been submitted giving PECs for folpet metabolites. Drainage is not an exposure route of relevance for folpet as products are only used late spring/summer and soil DT50 values for folpet and its metabolites are between 0.8 and 28.2 days, only.	Given the short soil DT_{50} for folpet there is unlikely to be any significant movement to surface water through run-off or drainage. Unrealistic worst case PECsw values for metabolites from run-off have already been calculated and included in the DAR. Given the GAP for folpet uses (spring/summer applications) drainage will not be a significant exposure route for metabolites either.	EPCO 21 (11. – 14.04.2005): Open point fulfilled. New data gap identified 4.5: Calculation of PEC sw with consideration of drainage needs to be done. The experts decided to send a message to the ecotox section: For runoff exposure only initial worst case estimation of PEC sw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
4.5	New data gap: Calculation of PEC sw with consideration of drainage needs to be done. This data gap was identified at EPCO 21.			EPCO 21 (11. – 14.04.2005): Data gap identified.
	Message to the ecotox section (EPCO 22): For runoff exposure only initial worst case estimation of PEC sw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required.			Answer EPCO 22: The metabolites are not regarded as relevant.
	Open point 4.6: RMS to amend the list of end points to give the average/median value for the Koc as requested according to the guidance on the list of end points. (see reporting table 4(20))		List end points amended	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The list of end points was amended.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.7: RMS to revise to 1st order DT50 values for phthalimide in an addendum to be discussed in an expert meeting. (see reporting table 4(26))	The relevant first order DT50 value for pthalimide was calculated for use in calculating PECgw and was presented in the report: *Mackay, N. (2002). Predicted Environmental Concentrations of folpet and its degradation products in groundwater in the European Union using the FOCUS groundwater scenarios.*	The Notifier has submitted the following (ref: Terry, A. 2005a. Responses to questions raised in the Reporting Table on fate and behaviour of folpet): The degradation of phthalimide can be calculated from the data reported in study 7.1.1.1.1/01 (Daly, D. 1991a), in which the degradation of folpet was investigated. A first order degradation rate for phthalimide was calculated for the purpose of calculating FOCUS PEC_{GW} values and reported (in Mackay, N. 2002). The data from day 5 to day 120 was analysed and a rate of degradation of 28.2 days derived (with an r^2 value of 0.83), at 25°C. It was evident that this value was an over-estimation because the formation and decline of phthalimide was not taken into account, but it was the best fit value that could be obtained. RMS agrees	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented and the list of end points was amended.
	Open point 4.8: RMS to clarify amount of bound residues taking into account fulvic and humic acid in an addendum to be discussed in an expert meeting. (see reporting table 4(27))	In the report concerned, the fulvic and humic acid fractions were reported in a way which implied they were equivalent to a standard extraction, which they are not. It is agreed that fulvic and humic acid components should be regarded as part of the non-extractable fraction.	Agree	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.9: RMS to clarify wich aerobic/anaerobic studies are acceptable and essential for the assessment in an addendum to be discussed in an expert meeting. (see reporting table 4(28) and 4(23))	The study 7.1.1.1.1/01 (Daly, D. 1991a) was conducted in a sandy loam soil (pH 5.4) with [U-phenyl-^{14}C] labelled folpet at 25°C and 75-80% of FC. The fate of folpet and its major soil metabolites was determined. In the more recently conducted study 7.1.1.1.1/03 (Crowe, A. 2001) the degradation of [U-phenyl-^{14}C] labelled folpet was investigated in three soils; loamy sand, silty loam and clay loam (pH 4.8, 6.2 and 7.5) at 20°C (and one soil at 10°C), and 40% WHC. The rate of degradation of folpet, phthalimide, phthalic acid and phthalamic acid was calculated. Together then, these two studies provide sufficient information to characterise the fate and behaviour of folpet in soil under aerobic conditions. These two studies were also sufficient to derive representative normalised (to pF 2.0 and 20°C, according to FOCUS guidance) rates of degradation for folpet and its major degradation metabolites (see Mackay, N. 2002). As such, it is proposed that these two studies (Daly, D. 1991a, and Crowe, A. 2001) are the only soil degradation studies submitted that are necessary for assessment purposes. All other studies should be regarded as providing supplemental information.	Agree	EPCO 21 (11. – 14.04.2005): Open point fulfilled with regard to clarification. However the open point is still open for including anaerobic study details in list of end points (see open point 4.19).

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.10: RMS to provide r^2 for each determination and normalised DT_{50} in an addendum to be discussed in an expert meeting. (see reporting table 4(30))	A Table has been provided to the RMS which includes r2 values (taken from the relevant reports) and re-calculated first order DT50 values (taken from Mackay, N. 2002), for those studies considered relevant for the assessment process.	The table was provided and assessed	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The information was provided and assessed in the addendum. The experts agreed to set a new open point 4.21: With respect to aerobic DT50: A new mean should be recalculated excluding DT50 value from the study conducted at 10 ºC. Mean should be used in the risk assessment and therefore median should be removed form the list of end points (see open point 4.19).
	New open point 4.21: With respect to aerobic DT50: A new mean should be recalculated excluding DT50 value from the study conducted at 10 ºC. Mean should be used in the risk assessment and therefore median should be removed form the list of end points. This open point was proposed at EPCO 21.			EPCO 21 (11. – 14.04.2005): Open point still open.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.11: RMS to provide an addendum with a summary of studies that address the fate of side chain of folpet. Formation of thiophosgen should be addressed. Addendum to be discussed in an expert meeting. (see reporting table 4(31))	Two captan studies are most relevant for addressing the fate of the captan and folpet common side chain: *Aerobic metabolism of [trichloromethyl -14C] captan in soil. (Diaz, D. and Lay, M.M. 1992; IIA, 7.1.1.1.1/04)* and *Aerobic soil metabolism of [trichloromethyl -14C] captan. (Pack, D.E. and Verrips, I.S. 1988; IIA, 7.1.1.1.1/05)*. The results of these studies strongly imply that thiophosgen would not be expected to be a significant product of folpet degradation.	The studies were provided and assessed. RMS agrees with the notifier	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented. The same message that was sent to the tox section on this issue for captan should be reiterated for folpet.
	Message of EPCO 21 to tox section (EPCO 23): It cannot be excluded that traces of thiophosgene occur in the air.			

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.12: RMS to provide an addendum with Koc estimation of phthalamic acid and an assessment of its reliability to be discussed in an expert meeting. (see reporting table 4(32))	The PCKOC programme (within the EPIWIN suite of programs) was used to estimate the KOC values for phthalic acid and phthalamic acid. Further details of this programme has been provided to the RMS in the new report: *Terry, A. 2005. Responses to questions raised in the Reporting Table on fate and behaviour of folpet*.	No sorption/desorption studies have been conducted with phthalamic and phthalic acid. As these degradation products only occurred briefly above 10% in soil degradation studies they were considered to be transient. The rapid formation and degradation of these secondary degradation products suggested that it was appropriate to employ estimates of sorption characteristics in order to assess potential mobility. The PCKOC programme (within the EPIWIN suite of programs) was used to estimate the K_{OC} values for phthalic acid (73.06) and phthalamic acid (10) (Mackay, N. 2002). The description of the estimation program has been provided and assessed.	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented. The assessment is accepted by the meeting in this case due to rapid degradation and transient nature but not in general.
	Open point 4.13: Acceptability of Koc for soils loam EUROSOIL 3 and sand soil LUFA2.1 to be discussed in an expert meeting. (see reporting table 4(34))	The acceptability of the data from the two soils with atypical 1/n values has been investigated in the report: *Mackay, N. (2002). Predicted Environmental Concentrations of folpet and its degradation products in groundwater in the European Union using the FOCUS groundwater scenarios* and a pragmatic approach for use of the data advanced.		EPCO 21 (11. – 14.04.2005): Open point fulfilled. The experts agreed to disregard Koc values from two LUFA but use Koc values from EUROSOILS. The experts agreed that the Kfoc values should be used instead of the Koc values in this case. The list of end points should be amended accordingly (see new open point 4.19).

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.14: RMS to provide an addendum to clarify and assess kinetic models employed to evaluate water sediment studies to be discussed in an expert meeting. (see reporting table 4(35))	A brief description of the kinetic model used to evaluate the results in the sediment/water study was presented in the study report: *Folpet. Degradability in the water/sediment system. (Crowe, A. 1999; IIA, 7.2.1.3.2/01)* see page 33.		EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented and the experts agreed that the clarification is sufficient. The experts agreed to set a new open point (see new open point 4.19): RMS is asked to give the parameter on the goodness of fittings (eg. r^2) in the list of end points.
	Open point 4.15: RMS to provide an addendum with an expanded summary of FOCUS gw modelling and recalculations if necessary to be discussed in an expert meeting. (see reporting table 4(37))	It is believed that a more detailed consideration of the PECgw report (*Mackay, N. (2002). Predicted Environmental Concentrations of folpet and its degradation products in groundwater in the European Union using the FOCUS groundwater scenarios*) will indicate that the various parameters required to appropriately calculate PECgw values have been derived according to current guidance as provided by FOCUS. It is not expected that re-calculation will be considered necessary.	Agree	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The addendum was presented. The experts agreed to set a new open point (see new open point 4.19): RMS to amend in the list of end points including the scenarios used for FOCUS gw modelling. Data gap identified 4.6: New FOCUS modelling is required with the mean values for DT 50 instead of median (Disregard DT50 values derived from the study conducted at 10° for calculation of mean – see open point 4.10) and with Koc value for phthalimide metabolite derived from 3 EUROSOILS.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
4.6	New data gap: New FOCUS modelling is required with the mean values for DT 50 instead of median (Disregard DT50 values derived from the study conducted at 10° for calculation of mean – see open point 4.10) and with Koc value for Phthalimide metabolite derived from 3 EUROSOILS. This data gap was identified at EPCO 21.			EPCO 21 (11. – 14.04.2005): Data gap identified.
4.2	Notifier to submit PEC surface water for the metabolites. (see reporting table 4(39))	A new report: *Terry, A. (2005). Predicted Environmental Concentrations of Metabolites of Folpet in Surface Water and Sediment arising from Spray Drift, in the European Union.* has been submitted giving PECsw for folpet metabolites.	The Notifier has submitted a new appropriate report	EPCO 21 (11. – 14.04.2005): This data requirement is replaced by the new data gap identified 4.5.
4.3	Notifier to submit PEC sediment calculations. (see reporting table 4(41))	A new report: *Terry, A. (2005). Predicted Environmental Concentrations of Metabolites of Folpet in Surface Water and Sediment arising from Spray Drift, in the European Union.* has been submitted giving PECsed for folpet metabolites.	The Notifier has submitted a new appropriate report	EPCO 21 (11. – 14.04.2005): Data requirement fulfilled. No major metabolites occur in the sediment.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
4.4	Notifier to assess potential relevance of thiophosgene in the air compartment. (see reporting table 4(43))	The results of the two captan studies most relevant to the fate of the common captan and folpet side chain strongly imply that thiophosgen would not be expected to be a significant product of folpet degradation in soil. Therefore, it is believed that thiophosgene is not of relevance in the air compartment.	Agree	EPCO 21 (11. – 14.04.2005): Data requirement fulfilled. However it can not be excluded that traces of thiophosgen may occur.
	Open point 4.16: MS to discuss the DT90 in surface water is < 3d in an expert meeting. Open point relates to open point 1.9 (comment 1(18) in the reporting table) (see reporting table 4(46))	The rate of hydrolysis of folpet was found to be extremely rapid in water at all pH values. The longest DT50 was at pH 5 (2.6 hours) which corresponds to a DT90 of 8.6 hours. Therefore, DT90 in water <3 days.	agree	EPCO 21 (11. – 14.04.2005): Open point fulfilled. The experts agreed to send a message to EPCO 25 (phys chem section): EPCO 21 confirms that the DT50 in surface water is less than 3 days.
	Message of EPCO 21 to EPCO 25: EPCO 21 confirms that the DT50 in surface water is less than 3 days.			

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.17: MS to discuss the residues definition in an expert meeting. (see reporting table 4(47))	A more detailed evaluation of the PECgw report (*Mackay, N. (2002). Predicted Environmental Concentrations of folpet and its degradation products in groundwater in the European Union using the FOCUS groundwater scenarios*) will indicate that the generated PECgw calculations show that neither folpet nor any of its degradation products are likely to exceed 0.1 μg/L. As such, it is proposed that the residue in groundwater should be considered to be folpet only (although based on the modelling folpet would not occur in groundwater). Surface water: metabolites are all of low toxicity to aquatic organisms. Hence, they should not be included in the residue definition. Soil: Studies on earthworms for folpet would have included exposure to major soil metabolites. Low toxicity was observed in these studies. Hence, metabolites should not be included in the residue definition for soil.	Agree	EPCO 21 (11. – 14.04.2005): Open point fulfilled. Residues were defined.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 4.18: RMS to clarify which studies of captan are used in the assessement of folpet and if these studies have actually been submitted in the folpet dossier. Open point relates to open point 4.11 (comment 4(31) in the reporting table) (see reporting table 4(48))	Only the two captan studies*: Aerobic metabolism of [trichloromethyl -14C] captan in soil. (Diaz, D. and Lay, M.M. 1992; IIA, 7.1.1.1.1/04)* and *Aerobic soil metabolism of [trichloromethyl -14C] captan. (Pack, D.E. and Verrips, I.S. 1988; IIA, 7.1.1.1.1/05)* are required to aid in the assessment of folpet. Makhteshim Chemical Works Ltd is the Notifier for both folpet and captan. Hence, the use of these captan studies to support folpet is agreed.	See comment open point 4.11	EPCO 21 (11. – 14.04.2005): Open point fulfilled. Only the two captan studies are required to aid in the assessment of folpet and there are no concerns on data protection by the notifier.
	Open point 4.19 RMS to revise the list of end points according to the amendments proposed by EPCO 21.			EPCO 21 (11. – 14.04.2005): Open point still open.

REPORT OF EPCO EXPERT MEETING 22

FOLPET

Rapporteur Member State: Italy

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:

None.

2. Documents submitted for meeting:

Date	Supplier	File Name
17 November 2004	RMS/Italy	Folpet consultation report
22 December 2004	RMS/Italy	Folpet reporting table rev1-1
March 2005	RMS/Italy	Folpet addendum vol3 B9
23 March 2005	RMS/Italy	Folpet list of end points ecotox
23 March 2005	RMS/Italy	Folpet evaluation table rev0-1

3. Documents tabled at the meeting:

Date	Supplier	File Name
07 April 2005	RMS/Italy	Folpet supported uses

The conclusions of the meeting were as follows:

4. **Data on preparations:** 'Folpan' 80 WDG

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

6. **Recommended restrictions/conditions for use:** buffer zones for the aquatic.

7. **Reference List**

Areas of concern: None

Appendix 1: EPCO discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

5. Ecotoxicology

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 5.1: RMS to prepare an addendum with an evaluation of the revised risk assessment for birds and mammals presented by the notifier. (see reporting table 5(1))	RMS: Folpet is of low toxicity to birds and mammals and its degradation rate is rapid. Long term TERs values are moreover based on the highest doses tested in reproduction studies, where no effects were determined. The risk to birds and mammals is considered as acceptable. MS stated that the endpoint for birds is based on a screening study which didn't address all concerns. However the study might not be needed at all. Acute risk assessment of birds: General: it is unclear if the a.s. was applied in the late growth stage. A confirmation is needed. RMS offers to check this. Short term risk assessment of birds: Meeting accepted the risk assessment. Long-term risk assessment of birds: The endpoint of the mallard is lower than for the bobwhite quail. Thus the risk assessment has to be revised using the lower value for the endpoint. The multiple application factor of 2.5 has been used for the grape application. This is for 8 applications. In the GAP list 10 applications are stated and therefore this has to be corrected.	<u>EPCO 22 (11.04.-15.04.2005)</u>: Open point closed New open point: RMS to evaluate the risk to herbivorous birds and mammals in cereals.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
		MS commented this risk assessment. The screening study will not address the risk. No new study is needed because the other studies are sufficient. MS stated that the study is not sufficient to cover the long-term risk for the foreseen ten applications. Because the degradation time in plants is long. New open point: The risk assessment is not valid: The whole risk assessment has to be performed with a NOEC of 78 mg as/kg bw. Why is this value used although the study should not be sufficient ? The meeting agreed that the refined risk assessment should be conducted with a RUD value of 29. PT value was questioned. It is not clear why the same PT was used for vines as for orchards. It is relevant for orchards but it is not effective for cereals. Is the study acceptable for grapes? Meeting accepted the approach as worst case. The TER values for insectivorous birds are 4 in winter wheat, 2 in grapes and 2.4 in tomatoes in a first tier risk assessment. However, the meeting considered the long term risk to insectivorous birds as low because: - no refinement of the PD values was conducted - a PT value of 0.6 was used which is considered as worst case to the crops under consideration - the NOEC value used in the risk assessment derive from toxicity tests where no effects were observed at the highest dose tested -dissipation was not taken into account Toxicity value for mammals is questioned. A low endpoint from the two generation study can be used instead of questioning the study.	New open point: RMS to perform the long term risk assessment for birds with a NOEC of 78 mg a.s./kg bw. For the refinement of the long term risk assessment for birds a RUD value of 29 should be used. New open point RMS to revise the NOEL and if necessary revise the long-term risk assessment for mammals.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
		Same approach like for captan. RMS to clarify a lowest relevant reproductive NOEL. The endpoint from offspring growth is relevant either. For a MS there is not enough argumentation available. RMS: after the 2-generation study toxicity is regarded as low. EFSA: first it was not regarded as teratogenic and now it is? Acute risk for mammals: EFSA: The crop interception factor of orchards and grapes. 50% interception factor has been used. There should be added some clarifications on the presence/absence of leafs. This might change the factor. 40% is the lowest factor which should be used. Meeting regarded the average (50%) as acceptable, because of the long application period. Long-term risk for mammals: No refinement was conducted because the risk assessment was higher than the trigger. Pending on the revision of the long-term NOEC value the long-term risk can be regarded as addressed or a refinement is needed. On page 14 of the addendum a typing error. Table 14 is said that results refer to herbivorous mammals but It refers to herbivorous birds.	New open point RMS to amend the typing error on table 14 of the addendum.
	Open point 5.2: RMS to amend the list of endpoints for birds and mammals (values in daily dose, long term endpoint mammals). (see reporting table 5(1))	Done. The meeting accepted the amendment.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 5.3: RMS to amend the list of endpoints regarding the endpoints for NTA (control mortality *C. septempunctata*). (see reporting table 5(4))	Done. The meeting accepted the amendment	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.4: RMS to amend the list of endpoints for terrestrial plants. (see reporting table 5(7))	Done. The meeting accepted the amendment	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
5.1	Notifier to submit the study byMoll, M., Bützler, R (2004). Effects of Folpan 80 WDG on the parasitoid *Aphidius rhopalosiphi*, extended laboratory study, aged residue test. Unpublished report. IBACON project number 18201003. Date: 13 January 2004. (Company file R-16400). (see reporting table 5(11))	Study was submitted and has been evaluated and accepted. Discussion see open point 5.5	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
5.2	Notifier to submit the study byMoll, M (2004). Effects of Folpan 80 WDG on the ladybird beetle Coccinella septempunctata, extended laboratory study, aged residues test. Unpublished report. IBACON project number 18203013. Date: 13 January 2004. (Company file R-16402). (see reporting table 5(11))	Study was submitted and has been evaluated and accepted. Discussion see open point 5.5	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
5.3	Notifier to submit the study byRosenkranz, B. (2004a). Effects of Folpan 80 WDG on the predatory mite *Typhlodromus pyri*, extended laboratory study, aged residues test. Unpublished report. IBACON project number 18202060. Date: 27 January 2004. (Company file R-16401). (see reporting table 5(11))	Study was submitted and has been evaluated and accepted. Discussion see open point 5.5	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
5.4	Notifier to submit the study by Rosenkranz, B. (2004b). Effects of Folpan 80 WDG on the lacewing *Chrysoperla carnea*, extended laboratory study, aged residues test. Unpublished report. IBACON project number 18204048. Date: 27 January 2004. (Company file R-16398). (see reporting table 5(11))	Study was submitted and has been evaluated and accepted. Discussion see open point 5.5	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.
5.5	Notifier to submit revised risk assessment by Norman, S. (2004). EU Review of folpet: Non-target arthropods: Updated risk assessment incorporating new extended laboratory studies at higher application rates than previously tested." (see reporting table 5(11))	Study was submitted and has been evaluated and accepted. Discussion see open point 5.5	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 5.5: RMS to revise the risk assessment for NTA in an addendum to be discussed in an expert meeting. (see reporting table 5(11)	The risk assessment was based on the new studies. Enough species were tested and the tested dose rate was regarded as sufficient. MS: List of endpoints: The tested dose rate of the field studies should be added	EPCO 22 (11.04.-15.04.2005): Open point fulfilled. New open point The tested dose rate of the field studies should be added in the list of endpoints.
	Open point 5.6: MS to discuss the risk to earthworms in an expert meeting. (see reporting table 5(12))	RMS: According to these results TERs for acute and long-term risks are all above the triggers. The notifier submitted a new study with the a.s. with earthworms. In the study a reduced peat moss content was used in the artificial substrate. A higher NOEC value was derived from this new study. However, the different feeding regime were applied in these new studies. Since the new study was not directly comparable to the older studies the meeting agreed that it was not clearly shown that the peat moss content did not influence the test results and therefore the lowest observed NOEC value should be used for the risk assessment. A correction factor of 2 should be applied to the NOEC of 5.18 mg a.s./kg since the standard peat moss content of 10% was used in the study. Therefore the meeting agreed that the risk assessment for earthworms presented in the addendum is correct..	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.7: MS to discuss the risk to non target plants in an expert meeting. (see reporting table 5(14))	RMS: Folpet data are available. The risk is regarded as addressed with the presented information.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 5.8: MS to discuss the risk to birds in an expert meeting. (see reporting table 5(20))	Reporting table 5(20): The reproductive NOEC is less than 100 ppm. RMS: (in agreement with study author) the 3% difference from the control in mean hatchling weight is not biologically significant. There is no dose response visible with higher concentrations. This effect is not treatment related. Meeting agreed that the NOEC is 1000 ppm.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.9: MS to discuss the risk to aquatic organisms in an expert meeting. (see reporting table 5(30))	Main difference between captan and folpet is related to the metabolites. As for captan the focus for aquatic risk assessment should be on the acute risk assessment. The risk assessment is based on 6 fish species. The safety factor was reduced from 100 to 10. Comment see reporting table 5(30): Lack of a proper analytical concentration during the test. Some of the test concentration have been too low to be measurable. It is dissolving in water very fast. P 21 addendum Table 17: results of the fish studies. In any case the concentration was measured initially. Meeting accepted the argumentation and that the endpoint expressed is in nominal concentrations. At the end of the studies the concentration is below 80 percent. This is accepted from the meeting. see reporting table 5(31):RMS: TER long-term values have been omitted due to short DT50 of 24 minutes in the water phase. It is proposed that this omission does not affect the outcome of the risk assessment, which should be focused on acute effects. RMS: The persistence is too short in water to do a chronic exposure. MS: Long-term risk assessment should have been performed because of the repeated applications.	EPCO 22 (11.04.-15.04.2005): Open point closed New open point: RMS to conduct a long-term risk assessment for aquatic organisms based on NOEC

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
		EFSA: A chronic study under semi static conditions mimics the repeated exposure. Therefore a risk assessment for the chronic risk to fish could be conducted with the NOEC value from the rainbow trout (28 d) study. This value can be compared with the initial peak PECsw value. The meeting agreed that a safety factor of 10 should be applied in the chronic risk assessment since only one species (rainbow trout) was tested for chronic effects. In addition rainbow trout was less sensitive to the a.s. compared to brown trout. 5 (33): This comment is related to the lowering of the trigger value. If 5 species are tested than the trigger can be lowered. But only if just one specie has a higher sensitivity than this approach can not be used. Thus the largest buffer zone has to be used. MS doesn't agree to take the endpoint for *Daphnia* at 48 h. Observer: The 24 h is a lower endpoint than at 48 h because *Daphnia* can recover from immobilisation at 24 h. Thus 24 h endpoint is the worst case. After a check of the data set it can be concluded 20 mg/l is an unrealistic value. The static test is also not addressing the point. A 21 day semi static test in *Daphnia* should be made available to address the risk. Consistent with the fish approach. MS proposes to use the long-term study of the fish as most sensitive species might be sufficient. But the studies of *Daphnia* have both shortcomings. Thus the meeting can not be sure if fish are the most sensitive. When the data becomes available the data have to be evaluated.	values from chronic studies and the initial peak PECsw . New open point: The acute toxicity endpoint for brown trout (*Oncorhynchus mykiss*) should be added to the list of endpoints <u>Data gap identified:</u> Notifier to repeat the 21 d *Daphnia* study under semi static conditions. The study should be conducted according to OECD guidelines.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 5.10: MS to discuss the risk to mammals in an expert meeting. (see reporting table 5(37))	See open point 5.1	EPCO 22 (11.04.-15.04.2005): Open point closed.
	Open point 5.11: RMS to summarise and evaluate the study by Nengel 1996c on bees in an addendum and revise the risk assessment for bees accordingly. (see reporting table 5(44))	The missing summary has been reported in the addendum. The risk was regarded as acceptable. Meeting accepted the explanation.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.12: RMS to transfer the information on earthworms from column 3 of the reporting table to an addendum. (see reporting table 5(55))	Done. The meeting accepted the approach.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Message EPCO 21 to EPCO 22:	For runoff exposure only initial worst case estimation of PECsw for metabolites is given. If refinement is needed for risk assessment a recalculation will need to be required. (open point 4.5)	EPCO 22 (11.04.-15.04.2005): The metabolites are not regarded as ecotoxicological relevant.
	Residue definition	Soil: the metabolites are less toxic than the parent. Water: no metabolites of ecotoxicological concerns were found. Groundwater: still open depending on the outcome of the new calculations.	

Appendix 2: Evaluation table

5. Ecotoxicology

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Section 5 Data requirements: ***5*** Open points: ***12***			Section 5 Data requirements: 0 Open points: 7 Data gaps: 1
	Open point 5.1: RMS to prepare an addendum with an evaluation of the revised risk assessment for birds and mammals presented by the notifier. (see reporting table 5(1))		Notifier has presented a new risk assessment according to the EU Guidance document SANCO /414/2000. It should be noted that GAP was changed (removal of North EU cereals). Endpoints chosen for birds risk assessment were: >2510 mg/kg/bw (acute), > 764 mg /kg/bw/day (short term), 90.0 mg/kg/bw (long term). For mammals toxicity endpoints were: >2000 mg/kg bw/day (acute), 548.6 mg /kg bw/day (long term). Tier 1 risk assessment The long term TERs for insectivorous mammals in cereals and herbivorous mammals in grapes and tomatoes are all greater than the Annex VI trigger of 5. Tomato foliage is not an attractive food source for birds or mammals and these scenarios should be considere unrealistic. Overall there is a low long term risk to mammals.	EPCO 22 (11.04.-15.04.2005): Open point closed. New open point (5.13) New open point (5.14): New open point (5.15) New open point (5.16)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	continued Open point 5.1: RMS to prepare an addendum with an evaluation of the revised risk assessment for birds and mammals presented by the notifier. (see reporting table 5(1))		Long term TERs for insectivorous birds (all uses) were less than 5 indicating a need for further refinement. Tier 2 risk assessment. The following assumptions were used: a) refinement of long term toxicity endpoint for birds (from 90 to 769 mg a.s./kg/bw day) based on absence of species sensitivity. b) RUD on insects was 5.1 mg/kg.; c) PT= 0.61 (based on blue tits behaviour in orchards) . Under these assumptions all the calculated TERs are above the triggers (more than one order of magnitude). Folpet is of low toxicity to birds and mammals and its degradation rate is rapid. TERs long term values are moreover based on no effect of the highest doses tested in reproduction studies, the risk to birds and mammals is considered acceptable.	
	New open point 5.13: RMS to evaluate the risk to herbivorous birds and mammals in cereals. See open point 5.1. This open point was proposed at EPCO 22			EPCO 22 (11.04.-15.04.2005): Open point still open.
	New open point 5.14:			EPCO 22 (11.04.-15.04.2005):

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	RMS to perform the long term risk assessment for birds with a NOEC of 78 mg a.s./kg bw. For the refinement of the long term risk assessment for birds a RUD value of 29 should be used. See open point 5.1. This open point was proposed at EPCO 22.			Open point still open.
	New open point 5.15: RMS to revise the NOEL and if necessary revise the long-term risk assessment for mammals. See open point 5.1. This open point was proposed at EPCO 22			EPCO 22 (11.04.-15.04.2005): Open point still open.
	New open point 5.16: RMS to amend the typing error on table 14 of the addendum. See open point 5.1. This open point was proposed at EPCO 22			EPCO 22 (11.04.-15.04.2005): Open point still open.
	Open point 5.2: RMS to amend the list of endpoints for birds and mammals (values in daily dose, long term endpoint mammals).		List of endpoints amended	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	(see reporting table 5(1))			
	Open point 5.3: RMS to amend the list of endpoints regarding the endpoints for NTA (control mortality *C. septempunctata*). (see reporting table 5(4))		List of endpoints amended	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.4: RMS to amend the list of endpoints for terrestrial plants. (see reporting table 5(7))		List of endpoints amended	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
5.1	Notifier to submit the study byMoll, M., Bützler, R (2004). Effects of Folpan 80 WDG on the parasitoid *Aphidius rhopalosiphi*, extended laboratory study, aged residue test. Unpublished report. IBACON project number 18201003. Date: 13 January 2004. (Company file R-16400). (see reporting table 5(11))	Study submitted.	Folpan 80WDG was applied (foliar spray) to bean plants at 1.64, 3.38, 5.25 kg a.s./ha with a control and a reference item. Leaves were removed 30-40 min or 14 days after application (aged residues). Leaves were used as a substrate in laboratory bioassay. For fresh dry residues, at 1.64 and 3.38 kg a.s./ha effects were below the Escort 2 trigger (50%). At the highest dose the effect on survival was > 50% (75%). For 14 days aged residues there was no mortality at any treatment level reduction in paratization at the maximum dose was < 50%. Overall	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
			effects were less than the Escort 2 trigger of 50% for fresh residues at 1.64 and 3.38 kg a.s./ha and for 14 days aged residues at 5.25 Kg a.s./ha. The study is acceptable	
5.2	Notifier to submit the study byMoll, M (2004). Effects of Folpan 80 WDG on the ladybird beetle Coccinella septempunctata, extended laboratory study, aged residues test. Unpublished report. IBACON project number 18203013. Date: 13 January 2004. (Company file R-16402). (see reporting table 5(11))	Study submitted.	Folpan 80WDG was applied (foliar spray) to bean plants at 0.31, 1.64, 3.38, 5.25 kg a.s./ha with a control and a reference item. Leaves were removed 30-40 min after application. There was no need for testing aged residue leaves on the basis of the results obtained with fresh residues. Leaves were used as a substrate in laboratory bioassay. For fresh dry residues, corrected mortality was below the Escort 2 trigger (50%) for all the groups; there was no adverse effect on reproduction (fertile eggs per female) at any treatment level. There were also >2 fertile eggs/female in all groups indicating no effect. Overall there were no negative effects > 50 % The study is acceptable	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.
5.3	Notifier to submit the study byRosenkranz, B. (2004a). Effects of Folpan 80 WDG on the predatory mite *Typhlodromus pyri*, extended laboratory study, aged residues test. Unpublished report. IBACON project	Study submitted	Folpan 80WDG was applied (foliar spray) to bean plants at 1.64, 3.38, 5.25 kg a.s./ha with a control and a reference item. Leaves were removed 30-40 min after application. There was no need for testing aged residue leaves on the basis of the results obtained with fresh residues. Leaves were used as a substrate in laboratory bioassay. For	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	number 18202060. Date: 27 January 2004. (Company file R-16401). (see reporting table 5(11))		fresh dry residues, there were no significant effects on survival or reproduction at all treatment level. Overall there were no negative effects > 50 % The study is acceptable	
5.4	Notifier to submit the study byRosenkranz, B. (2004b). Effects of Folpan 80 WDG on the lacewing *Chrysoperla carnea*, extended laboratory study, aged residues test. Unpublished report. IBACON project number 18204048. Date: 27 January 2004. (Company file R-16398). (see reporting table 5(11))	Study submitted	Folpan 80WDG was applied (foliar spray) to bean plants at 1.64, 3.38, 5.25 kg a.s./ha with a control and a reference item. Leaves were removed 60-65 min after application. There was no need for testing aged residue leaves on the basis of the results obtained with fresh residues. Leaves were used as a substrate in laboratory bioassay. For fresh dry residues, there were no significant effects on survival or reproduction at all treatment level. Overall there were no negative effects > 50 % The study is acceptable	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.
5.5	Notifier to submit revised risk assessment by Norman, S. (2004). EU Review of folpet: Non-target arthropods: Updated risk assessment incorporating new extended laboratory studies at higher application rates than previously tested." (see reporting table 5(11))	Risk assessment submitted.		EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	Open point 5.5: RMS to revise the risk assessment for NTA in an addendum to be discussed in an expert meeting. (see reporting table 5(11)		A new risk assessment including the results of new studies covering the highest application rates notified in the dossier ha been submitted by the notifier. Four new additional extended laboratory studies (see 5.1 5.2,5.3,5.4) on Aphidius rhopalosiphi, Typhlodromus pyri, Coccinella septempunctata and Chrysoperla carnea have been presented as a complete data set under Escort 2 requirement. The highest rate in the new studies (5.25 kg a.s./ha including MAF) cover the worst case (use on grapevines 1.5 kg/ha x 10) At this rate there were no significant effect on T.Pyri, C. septempunctata or C. carnea. A. rhopalosiphi gave 76% mortality at 5.25 kg a.s. /ha for fresh residues (> 50%) . For 14 days aged residues, at 5.25 kg/ha, there were no effects on A. rhopalosiphi indicating that the Escort 2 criterion for potential for recovery/recolonization within 1 year is satisfied. Overall it can be concluded that there is a low risk to non target arthropods in-field and off- field.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled. New open point (5.17). The tested dose rate of the field studies should be added in the list of endpoints.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	New open point 5.17: The tested dose rate of the field studies should be added in the list of endpoints. See open point 5.5. This open point was proposed at EPCO 22			EPCO 22 (11.04.-15.04.2005): Open point still open.
	Open point 5.6: MS to discuss the risk to earthworms in an expert meeting. (see reporting table 5(12))	The Notifier supports the Comments of the RMS in the Reporting Table (5(53), 5(55). The EPPO correction factor of 2 for the existing long term endpoint is not necessary. In addition, a new earthworm reproduction study has been submitted (Gobman, 2005). This study used half the percentage of organic matter (5% peat) compared with the standard approach (10% peat). Hence, the EPPO correction factor of 2 is not necessary when using the NOEC from this study. The NOEC is also higher than the previous study which used 10% peat. Therefore, this is clear experimental evidence that in this case toxicity is not related to soil organic matter content. Using the NOEC from the new study, a low risk can be concluded for all uses.	The notifier has submitted a new earthworm reproduction study to investigate the effect of a reduced organic matter content of the artificial soil on the toxic effect of folpet in order to support the removal of the need for the correction factor of 2. The results show no statistically significant effect on adult survival feeding, growth or number of offsprings at any treatment level. The NOEL was 6.4 kg folpet/ha.(the highest dose tested) equivalent to 8.53 mg s.a./kg soil. According to these results TERs for acute and long-term risks are all above the triggers.	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.7: MS to discuss the risk to non target plants in an expert meeting.	Folpet is not a herbicide. Hence, there is no reason to discuss risk to non-target plants.		EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	(see reporting table 5(14))			
	Open point 5.8: MS to discuss the risk to birds in an expert meeting. (see reporting table 5(20))	A risk assessment according to SANCO 4145 has been submitted (Norman and Wyness, 2003).	See.point 5.1	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	Open point 5.9: MS to discuss the risk to aquatic organisms in an expert meeting. (see reporting table 5(30))	The Notifier supports the risk assessment in the DAR. A higher tier risk assessment for acute risk to fish has been presented (based on studies on 6 fish species). The lowest LC50 (brown trout, 98 µg/L) should be used together with a TER trigger of 10. Hence, the Ecological Acceptable Concentration (EAC) is 9.8 µg/L. In addition, Member States which support use of Species Sensitivity Distributions (SSD) at national level, should also have the option to use this approach at re-registration. In which case, the HC5 of 26.2 µg/L for fish is proposed as an alternative EAC.		EPCO 22 (11.04.-15.04.2005): Open point closed New open point (5.18) New open point (5.19) Data gap identified (5.6):
	New open point 5.18: RMS to conduct a long-term risk assessment for aquatic organisms based on NOEC values from chronic studies and the initial peak PECsw . See open point 5.9. This open point was			EPCO 22 (11.04.-15.04.2005): Open point still open.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	proposed at EPCO 22.			
	New open point 5.19: The acute toxicity endpoint for brown trout (*Oncorhynchus mykiss*) should be added to the list of endpoints. See open point 5.9. This open point was proposed at EPCO 22.			EPCO 22 (11.04.-15.04.2005): Open point still open.
5.6	New data gap: Notifier to repeat the 21 d *Daphnia* study under semi static conditions. The study should be conducted according to OECD guidelines. See open point 5.9. This data gap was identified at EPCO 22.			EPCO 22 (11.04.-15.04.2005): Data gap identified.
	Open point 5.10: MS to discuss the risk to mammals in an expert meeting. (see reporting table 5(37))	A risk assessment according to SANCO 4145 has been submitted (Norman and Wyness, 2003).	See point 5.1	EPCO 22 (11.04.-15.04.2005): Open point closed.
	Open point 5.11: RMS to summarise and	For information, this study on Folpan 80 WDG shows a low toxicity to bees (acute oral and contact LD50 of >179	The missing summary has been reported in the addendum. There were no significant mortalities at any dosage	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the evaluation group
	evaluate the study by Nengel 1996c on bees in an addendum and revise the risk assessment for bees accordingly. (see reporting table 5(44))	and >160 µg a.s./bee, respectively).	or route of administration. Based on the highest application rate of 1500 g a.s./ha HQ values are < 8.4 (oral) and <9.4 (contact). The risk is acceptable	
	Open point 5.12: RMS to transfer the information on earthworms from column 3 of the reporting table to an addendum. (see reporting table 5(55))		See point 5.6	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

REPORT OF EPCO EXPERT MEETING 23

FOLPET

Rapporteur Member State: Italy

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
17 November 2004	RMS/ Italy	Folpet consultation report (17-11-2004)
27 April 2005	RMS/ Italy	Folpet Addendum Vol3 B6 2005-04-27
22 Dezember 2004	RMS/ Italy	Folpet reporting table rev1-1 (22-12-2004)
08 April 2005	RMS/ Italy	Folpet list of endpoints tox 2005-04-27
08 April 2005	RMS/ Italy	Folpet supported uses (08-04-2005)
27 April 2005	RMS/ Italy	Folpet evaluation table rev.0-1 tox 2005-04-27

3. Documents tabled at the meeting:

Date	Supplier	File Name
13.05.2005	Chairman	Folpet JMPA paper 2004

The conclusions of the meeting were as follows:

4. **Data on preparations:** A data set has been submiotted for Folpan 80 WDG.

5. **Classification and labelling:** Xn, R 20, R 40, R 41, R 43

6. **Recommended restrictions/conditions for use:** appropriate PPE is needed for the operator and probably for the worker

7. **Reference List: ---**

Areas of concern: carcinogenicity at cytotoxic doses, incomplete information on developmental toxicity.

Appendix 1: EPCO discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

2. Mammalian Toxicology

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
			Section 2 Data requirements: ***4*** Open points: ***16***
	Open point 2.1: RMS to provide more detailed summary of short term oral toxicity for discussion of short term NOAEL at an expert meeting. (see reporting table 2(1))	The value has been proposed to be 10 mg/kg bw/day from the 1 year dog study based on decreased cholesterol and albumin (LOAEL 60 mg/kg bw/day). This was supported by the experts. However, EFSA stated that tables should have been added to the addendum presenting the detailed figures for the dog study to ease the evaluation and discussion. On the limited information presented in the addendum a conclusion could almost not be made.	<u>EPCO 23 (10 – 13.5.2005):</u> Open point fulfilled. Relevant short term NOAEL 10 mg/kg bw/day from the 1-year dog study.
	Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	This issue is discussed in the addendum page 8. Irritation was observed, but no evidence of carcinogenicity in the rat. The NOAEL is 190 ppm (= about 10 mg/kg bw/day) based on the 2 year rat study. Tumours in the duodenum have been observed in the mouse study. Therefore category 3, R 40 has been proposed for the classification, which has been supported by the majority of the experts. The NOAEL is 150 pmm = about 20 mg/kg bw/day) based on the 2 year mouse study.	<u>EPCO 23 (10 – 13.5.2005):</u> Open point fulfilled. Classification: category 3, R 40 based on effects in the mouse study.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
2.1	Notifier to submit the position paper by Gordon E., 2004 and the study Moore and Creasey (2004). (see reporting table 2(4))	The information has been submitted and the evaluation has been presented in the addendum (p 11ff) Acute effects have been observed. Therefore an ARfD should be proposed, see open point 2.3 below.	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.
	Open point 2.3: RMS to provide more detailed summary of the studies which lead to the derivation of the ARfD for discussion at an expert meeting. (see reporting table 2(4))	The developmental toxic effects might be relevant for the acute exposure. Therefore an ARfD has been proposed, based on the NOAEL of 10 mg/kg bw/day in the developmental toxicity study in rabbit, resulting in 0.1 mg/kg. SF 100	EPCO 23 (10 – 13.5.2005): Open point fulfilled. ARfD: 0.1 mg/kg, SF 100, (developmental study in rabbit)
2.2	The notifier to send position paper regarding reproductive toxicity and teratogenicity of folpet to the RMS. (see reporting table 2(5))	The information has been submitted and the evaluation has been presented in the addendum. The evaluation of the developmental toxicity study will be discussed together with the setting of the ARfD	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 2.4: RMS to provide more detailed summary of the 2-generation reproduction toxicity study for derivation of NOAEL and discussion in an expert meeting. (see reporting table 2(5))	The summary has been provided in the addendum (p. 18 ff) The meeting agreed ith the proposals from the RMS. Overall NOAEL values: 3600 ppm resulting in 180 mg/kg bw/day (fertility) 800 ppm resulting in 14 mg/kg bw/day (parental, offspring) based on the two 2-generation study in the rat..	<u>EPCO 23 (10 – 13.5.2005):</u> Open point fulfilled. NOAEL (fertility): 3600 ppm = 180 mg/kg bw/day NOAEL (parental, offspring): 800 ppm = 14 mg/kg bw/day
	Open point 2.5: MS to agree on the AOEL at an expert meeting. (see reporting table 2(6))	The rabbit developmental study has been proposed by the RMS to be the main basis for the AOEL instead of the dog study, which has been concluded to be supportive only. The meeting agreed to proposed 10 mg/kg bw/day based on the developmental study in rabbit. AOEL: 0.1 mg/kg (developmental rabbit), SF 100	<u>EPCO 23 (10 – 13.5.2005):</u> Open point fulfilled. AOEL: 0.1 mg/kg (developmental rabbit, SF 100)
	Open point 2.6: RMS to provide more detailed summary of studies leading to the derivation of the ADI value to be discussed at an expert meeting. (see reporting table 2(8))	The ADI will be based on the 1 year dog study, which is supported by the 2 year rat study, which will result in 0.1 mg/kg with a SF 100.	<u>EPCO 23 (10 – 13.5.2005):</u> <u>Open point fulfilled.</u> ADI: 0.1 mg/kg, SF 100, based on the1 year dog supported by the 2-year rat.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
2.3	Notifier to submit the new toxicokinetic study Arndt and Dohn (2004). (see reporting table 2(14))	The information has been submitted and the evaluation has been presented in the addendum (p. 39ff)	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.
	Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	Due to the information presented in the DAR the experts agreed on the proposal for R41 Based on the available experimental data R37 (irritating to respiratory tract) was not considered justified.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. The proposal is R41
	Open point 2.8: MS to agree on NOAEL in rat 90-day study at an expert meeting. (see reporting table 2(17))	A short response on the comment from one MS has been presented in the addendum. The NOAEL for the 90 day rat study is < 1000ppm = 44,5 mg/kg bw/day. This value will not change the overall conclusions, because there has already been derived a NOAEL from the dog study.	EPCO 23 (10 – 13.5.2005): Open point fulfilled The NOAEL in the 90-day rat study is 44.5 mg/kg bw/day.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 2.9: The RMS to summarize the the study (Collins, 1972a) in an addendum. (see reporting table 2(18))	The study by Collins (1972) from is summarised and presented in the addendum. The study on in vivo toxicity in germ cells is from the open literature and not according to GLP.	EPCO 23 (10 – 13.5.2005): Open point fulfilled.
	Open point 2.10: MS to discuss the genotoxicity, also in relation to classification, and the need of additional studies to be performed at an expert meeting. (see reporting table 2(19))	Information on this point has been presented in the addendum. Folpet is positive in in vitro studies but there is no indication of DNA damage in vivo up to 2000 mg/kg bw/day with regard to the information submitted. Therefore there is no genotoxic potential for folpet in vivo.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. No genotoxic potential in vivo.
	Open point 2.11: MS to confirm the NOAELs in the long term studies at an expert meeting. (see reporting table 2(22))	This has already been done under open point 2.2	EPCO 23 (10 – 13.5.2005): Open point fulfilled. See open point 2.2

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	A study been submitted to JMPR, which is reported in the JMPR conclusion on folpet from 2004 should be submitted to the RMS for evaluation. This refers to a developmental toxicity rabbit study. The study should be evaluated by the RMS and a proposal for the classification and labelling made. Category 3 R63 has been proposed by two experts. So far the classification and labelling is an open issue as well as the NOAEL for maternal toxicity, which has been proposed to be 10 or 40 mg/kg bw/day The developmental NOAEL is 10 mg/kg bw/day.	EPCO 23 (10 – 13.5.2005): Open point still open
	Open point 2.13: MS to discuss the toxicity of the metabolites phthalimide and phthalic acid and their possible inclusion in the residue definition at an expert meeting. See also open point 3.2 (comment 3(12) in the reporting table). (see reporting table 2(30))	Both metabolites are also found in animal metabolism. These metabolites are covered by the ADI Additional information has been presented in the addendum for phthalic acid. “Phthalic acid is not mutagenic in Ames or other bacterial assays, but does act synergistically with some but not all heterocyclic amine mutagens. It is not carcinogenic based on negative rodent bioassays with phthalic anhydride (which converts to phthalic acid). The actual ground water concentrations are not available. Therefore a final conclusion on their toxicological relevance for ground water cannot be made.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Phtalimide and phtalic acid are present in the in vivo studies. The ADI for folpet cover the metabolites.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 2.14: MS to discuss the dermal absorption value at an expert meeting. (see reporting table 2(34))	The notifier proposed a dermal absorption value of 1%, mostly based on open literature, which did not present detailed information to conclude on. Within the DAR 2 in vitro studies and one in vivo study have been submitted. Based on these data the absorption is: about 10% for the concentrate about 10 – 20% for the dilution about 3% (human in vitro study, no data on residues on skin) Based on the available *in vivo* rat study a value of 10% has been proposed by the experts	<u>EPCO 23 (10 – 13.5.2005):</u> Open point fulfilled. Dermal absorption: 10% for the concentrate and the dilution based on the *in vivo* rat study.
2.4	The notifier to submit the study Wilson, 1990 (dermal absorption). (see reporting table 2(35))	The information has been submitted and the evaluation has been presented in the addendum (p 61 ff). A discussion on a second dermal absorption study has been added to the addendum	<u>EPCO 23 (10 – 13.5.2005):</u> Data requirement fulfilled.
	Open point 2.14: RMS to present an estimation of exposure in glass-houses in an addendum. (see reporting table 2(40))	This information has already been presented in the DAR (p 150). Since the value for the dermal absorption has been amended to 10% the exposure estimations have to be re-calculated for all uses.	<u>EPCO 23 (10 – 13.5.2005):</u> Open point still open A new estimation on operator exposure has to be submitted for all uses.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 2.15: The bystander exposure needs to be discussed at an expert meeting. (see reporting table 2(41))	This information has already been presented in the DAR (p 151). Even the value for the dermal absorption has been amended to 10% the exposure estimations shows probably safe uses. Nevertheless a new calculation taking into account the dermal absorption value of 10% has to be submitted	EPCO 23 (10 – 13.5.2005): Open point still open A calculation for bystander exposure taking into account the dermal absorption value of 10% has to be submitted
	Open point 2.16: MS to discuss available residue decline data with respect to worker exposure at an expert meeting. (see reporting table 2(43))	The information has already been presented in the DAR. Nevertheless new calculations have to be submitted taking into account the amended value for dermal absorption.	EPCO 23 (10 – 13.5.2005): Open point still open A calculation for worker and bystander exposure taking into account the dermal absorption value of 10% has to be submitted

Appendix 2: Evaluation table

2. Mammalian Toxicology

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Section 2 Data requirements: 4 Open points: 16			Section 2 Data requirements: 0 Open points: 4
	Open point 2.1: RMS to provide more detailed summary of short term oral toxicity for discussion of short term NOAEL at an expert meeting. (see reporting table 2(1))	Text summarising short term oral toxicity for derivation of AOEL revised and included in new addendum under point IIA, 5.10.	April 2005 The text of the addendum correctly summarized the short term oral toxicity studies and the RMS agrees that the 1 year study in dogs (NOAEL 10 mg/kg b.w.) is the right term of reference to calculate the AOEL, i.e. 0.1 mg/kg b.w..	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Relevant short term NOAEL 10 mg/kg bw/day from the 1-year dog study.
	Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	The notifier's response to comments by Member States is given in the new addendum. (1) Sweden (SE) notes that Cancer Category 3* should be added, according to the list of classification and labelling (ref: Annex I of Directive 67/548/EEC. The risk phrase R-40, "Limited evidence of carcinogenicity"	April 2005 RMS on a basis of a pure hazard characterization we can agree with R 40 labelling of folpet. However, in the light of risk assessment for man the toxicology expert of RMS still believes that folpet does not require R40 in view of the fact that: i) folpet is not considered genotoxic and ii) mice tumours are species specific and	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Classification: category 3, R 40 based on effects in the mouse study.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	suggests that an uncertainty exists regarding the carcinogenic potential of folpet. There is no such uncertainty with folpet. Robust chemical/physical data, mechanistic data supporting a threshold MOA, and bioassays in rats, mice and dogs allow a judgment of no cancer risk to man with a high degree of certainty; accordingly, the risk phrase, R-40, is not required nor appropriate. Supporting this conclusion are the following: 1. Folpet is not carcinogenic to industrial or agricultural workers in that there is no systemic dose following dermal or inhalation exposure. 2. Folpet acts through a non-genotoxic threshold based mechanism. This MOA requires high oral doses that sustain a duodenal-specific proliferative response. 3. Persons ingesting captan residues have a margin of exposure (MOE) well over one million.	appear only above a dose that causes chronic toxicity. see above RMS supports the Notifier's response (see data presented in the addendum (table 10H)	

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	4. Folpet is not carcinogenic in rats or dogs; the gastrointestinal tumors (primarily in the duodenum) that appear in mice may well be species specific. Practically, folpet is not carcinogenic to industrial or agricultural workers in that it has been determined to act through a non-genotoxic threshold based mechanism that requires high oral doses that sustain a proliferative response of the duodenum. As the systemic exposure to captan is essentially zero from dermal and inhalation routes (due to the rapid degradation of captan and thiophosgene, half-life of folpet is 4.9 seconds and the half-life of thiophosgene is 0.6 seconds), there can be no adverse effects on the duodenum. Moreover, the mode of action is specific to irritation of the duodenal villi from the lumen side of the mucus membrane. Weight of evidence analysis concludes that folpet is not a human carcinogen as it is used in agriculture and that the risk phrase, R-40, is inappropriate.		

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	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	(2) Denmark suggests classification for carcinogenicity, based on the increased incidences of adenomas and carcinomas in the duodenum of male and female mice in two strains (CD-1 and B6C3F1). The highly reactive thiophosgene is most likely the metabolite responsible for duodenal tumor formation in mice. In rats, folpet was classified as a carcinogen in males based on an increase in the incidences of C-cell adenomas and carcinomas of the thyroid as well as interstitial cell tumors of the tests. There was no evidence of duodenal tumors in the rat; however, there was a dose related increase in incidence of severity of hyperkeratosis of the oesophagus and stomach, which may be due to thiophosgene. The increase in the incidence of duodenal adenocarcinomas in the CD 1 mouse study occurred at relatively high doses. A similar response was observed in a 2-year feeding study with B6C3F1 mice. Ascribing the carcinogenic effect of folpet in the mouse duodenum to		

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	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	thiophosgene is not supported. Folpet, not thiophosgene, is administered to mice. It is folpet that initially reacts with thiol groups of tissue proteins and induces irritation (e.g., villi disruption). In the process of this initial chemical interaction, thiophosgene is generated. Thiophosgene is reactive not only with thiol groups but an array of other functional groups, thus extending the irritation effects. It is the collective actions of folpet and thiophosgene that most likely are responsible for the duodenal irritation, loss of villi, and eventual induction of tumors. Folpet induces hyperkeratosis in the upper GI tract of rats but does not induce treatment related tumors. Folpet is not available systemically, regardless of the oral dose, due to the exponential degradation in blood (half-life of 4.9 seconds). There is no consistent pattern of tumors across studies (as there is with mice) and rat studies with captan, its sister fungicide with which it shares a common mechanism of toxicity do not show these same tumors (in contrast other non-treatment related tumors are seen).		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	(3) The UK notes the NOAEL in the chronic mouse study of East (1994) is considered to be 150 ppm as the histopathological findings in the gastrointestinal tract at 450 ppm are considered to be treatment –related. The study director cites hyperplasia (noted in the data) as well as a benign squamous cell papilloma at 450 ppm but cited a reference supporting his conclusion that these findings were fortuitous as “between one and three tumours of the squamous epithelium of the non-glandular stomach will be found during the course of a carcinogenicity study” (Faccini et al., (1990) Mouse Histopathology, A glossary for use in toxicity and carcinogenicity studies. Elsevier, Publisher, Amsterdam, New York, Oxford). Inspection of the data show the nature and severity of effects on the gastrointestinal tract. In both cases were there was hyperplasia noted at 450 ppm, there was an absence of hyperplasia at the next higher dose, 1350 ppm. The lack of dose response,		

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	continued: Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	the expected background incidence (citation, above) and the absolute numbers involved support the study director's judgment that the NOAEL for this study is 450 ppm The NOAEL of 450 ppm is supported.		
	Notifier to submit the position paper by Gordon E., 2004 and the study Moore and Creasey (2004). (see reporting table 2(4))	Summarised in new addendum. • Gordon E., (2004). Under point IIA, 5.10/01 **Conclusion:** Based on an evaluation of the toxicology database for folpet, an ARfD for folpet is not required. • Moore and Creasey (2004). Under point IIA, 5.8.2/06 **Conclusion**: Folpet administered by oral gavage at 900 mg/kg/bw or in the diet for 24 hours at 5000 ppm (as well as 500 ppm, 200 ppm, and 50 ppm) caused only minimal ("borderline") irritation of the	April 2005 Summaries provided in the addendum	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
		proximal duodenum. The initial finding of apparent irritation in the first study was shown likely due to artefacts upon thorough (eight step serial section) examination of the expanded second study. It was concluded that folpet was borderline for producing irritancy at 5000 ppm.		
	Open point 2.3: RMS to provide more detailed summary of the studies which lead to the derivation of the ARfD for discussion at an expert meeting. (see reporting table 2(4))	The notifier contends that an ARfD is not applicable. The arguments supporting this contention are presented in the paper by Gordon E., (2004) summarised in the new addendum, in Point IIA, 5.10/01, supported by Moore and Creasey (2004) under point IIA, 5.8.2/06.	April 2005 In principle RMS agrees Summaries provided. See below	EPCO 23 (10 – 13.5.2005): Open point fulfilled. ARfD: 0.1 mg/kg, SF 100, (developmental study in rabbit)
	The notifier to send position paper regarding reproductive toxicity and teratogenicity of folpet to the RMS. (see reporting table 2(5))	Position paper by Neal (2004) is summarised in the new addendum under Point IIA, 5.6/01. **Conclusion**: The paper concludes that the existing database provides adequate information regarding the reproductive and developmental toxicity of folpet to permit informed and conservative risk assessment. There is no evidence that there is any unique developmental susceptibility of the	April 2005 RMS whereas agrees with the Notifier that no additional useful information would be obtained from further reproduction studies, but deems desirable the accomplishment of new developmental toxicity studies in rabbit since it is not fully clarify whether the teratogenic effect is due to maternotoxicity elicited by Folpet administration.	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
		developing young to folpet. Further reproductive or developmental toxicity testing of folpet should not be required.		
	Open point 2.4: RMS to provide more detailed summary of the 2-generation reproduction toxicity study for derivation of NOAEL and discussion in an expert meeting. (see reporting table 2(5))	A more detailed summary of the 2-generation reproduction toxicity study is summarised in the new addendum under Point IIA, 5.6.	April 2005 A short summary has been provided in the addendum	EPCO 23 (10 – 13.5.2005): Open point fulfilled. NOAEL (fertility): 3600 ppm = 180 mg/kg bw/day NOAEL (parental, offspring): 800 ppm = 14 mg/kg bw/day
	Open point 2.5: MS to agree on the AOEL at an expert meeting. (see reporting table 2(6)) continued: Open point 2.5	The estimates of operator exposure demonstrate that the exposure of operators without PPE using the German model is less than an AOEL of 0.1 mg/kg bw/day. Notifier agrees with Germany that a new risk assessment for operators is not necessary, as the calculated values do not exceed the new AOEL.	April 2005 Noted	EPCO 23 (10 – 13.5.2005): Open point fulfilled. AOEL: 0.1 mg/kg (developmental rabbit, SF 100)
	Open point 2.6: RMS to provide more detailed summary of studies leading to the derivation of the ADI value to be discussed at an expert	More detailed summaries of the relevant studies for derivation of the ADI are presented in the new Addendum under Point IIA, 5.5.	April 2005 RMS supports the one year dog study NOAEL of 10 mg/kg b.w. and the Crown 1989 two year rat study of 190 ppm (nominal 250 ppm) equivalent to 9.55 mg/kg b.w. rounded to 10 mg/kg	EPCO 23 (10 – 13.5.2005): Open point fulfilled. ADI: 0.1 mg/kg, SF 100, based on the1

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	meeting. (see reporting table 2(8))		b.w. for the derivation of the ADI value.	year dog supported by the 2-year rat.
	Notifier to submit the new toxicokinetic study Arndt and Dohn (2004). (see reporting table 2(14))	Summarised in new addendum Under point 5.1/06. **Conclusion**: Thiophosgene disappears rapidly when added in excess (100 µg/mL) to human whole blood *in vitro.* The half-life was calculated to be 0.6 seconds.	April 2005 Study summarized in the addendum	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.
	Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	The data relating to acute inhalation toxicity and eye irritation are summarised in the new addendum. UK stated that consideration should be given to classification of folpet as R37 "irritating to respiratory system and R41 "risk of serious damage to eyes". **Conclusion**: The R37 risk phrase for folpet is not appropriate. The active substance will be classified as Xn R20 Harmful by inhalation, based on deaths in an acute (4-hour) inhalation toxicity study. The Directive (67/548, as amended by 2001/59) is quite clear in defining the criteria for	April 2005 RMS supports the Notifier's considerations.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. The proposal is R41

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	continued: Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	R37: there should be evidence that the substance or preparation can cause serious irritation to the respiratory system based on practical observations in humans, or positive results from appropriate animal tests. There are no recorded instances of inhalation irritation in humans, despite the active substance being manufactured and used in agriculture for few decades. In further defining positive results from animal tests, the Directive cites as examples histopathological data from the respiratory system, and that data from the **measurement** of experimental bradypnea may also be used to assess airway irritation. In specifically defining measurement i.e. accurate quantification by experimental means, the Directive does not cite cage-side observations from acute studies (and therefore implies that cage-side observations, made in every acute inhalation study, are insufficient). There were no adverse findings in the lung histopathology from the long-term toxicity studies, in which the finely-ground test material was administered in a mixture with powdered diet, to indicate any irritant effects on the lungs, yet the fine nature of the dietary		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	admixture inevitably results in some inadvertent inhalation of both diet and test material during feeding. It is important to recognise that there were also no irritance data from the buccal tissues in the chronic dietary studies. Secondly, during inhalation studies, irregular or slow respiration and gasping are standard responses to inhaling a harmful material: there were several deaths during and shortly following exposure. Moreover, the International Programme on Chemical Safety does not list folpet as irritating to the respiratory tract. The mode of action (MOA) of folpet centers on the chemical reaction of these compounds with thiol groups on the surface of tissues (e.g., mucus membranes) that they contact. This MOA results in the transient irritation seen in Cracknell (1993). Since both folpet and captan degrade rapidly (half-life in blood is 4.9 seconds for folpet ,the half-life for thiophosgene is 0.6 seconds), the irritation due to inhalation is restricted to the surface layers of epithelium only. The absence of treatment related findings in surviving animals are consistent with this MOA.		

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	continued: Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	In conclusion, R37 is not appropriate because there is no evidence from humans, and no supporting scientific data from animal experiments. R20 should be sufficient to warn of the risks from inhalation. The notifier's conclusion is consistent with the conclusion of the RMS that R20 is appropriate for folpet but that R37 is not appropriate for folpet. The rabbit bioassay is a surrogate test system to assess human hazard. Experience with folpet and its sister fungicide, captan, shows that the rabbit study does not reflect the actual hazard of folpet and captan. Over 100 years of combined use (folpet and captan, taken together) does not support a R41 risk phrase. The mode of action (MOA) of these two fungicides centers on the rapid reaction with available thiol groups associated with mucus membranes. This chemical reaction is responsible for the severe eye irritation noted in rabbit studies. The collective eye irritation study data, however, do not support the "irreversible" nature of the		

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	continued: Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	adverse effects. The weight of evidence shows that eye damage is restricted to surface areas (including the cornea) but that these insults do recover. Analysis of the collective data on captan, the sister fungicide to folpet based on their common mechanism of toxicity, show that folpet and captan are not corrosive chemicals and that irreversible damage to the eye does not occur. The collective data both from non-clinical studies, where recovery from irritation (including corneal opacity) is always evident as well as clinical experience, where there is an absence of credible reports of eye injury argues against the issuance of R41. By example, as noted in “Captan and Folpet,” Gordon, E.B. (2001) In Handbook of Pesticide Toxicology (R. I. Krieger, ed., Volume 2, Agents, pp 1171-142, Academic Press, San Diego), a review of the literature for the years to 2001 did not indicate any reports of eye injury. Additionally,		

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	continued: Open point 2.7: MS to discuss the irritating properties, also in relation to classification, at an expert meeting. (see reporting table 2(15))	agricultural workers in California, USA who routinely reenter captan treated fields (e.g., strawberries) indicate there is not a problem with eye irritation (R. Krieger, personal communication). The notifier's conclusion is consistent with the conclusion of the RMS that R36 is appropriate for folpet.		
	Open point 2.8: MS to agree on NOAEL in rat 90-day study at an expert meeting. (see reporting table 2(17))	The data from the 90-day study are summarised in the new addendum. The notifier contends that the issue is not significant as this study is not used to derive any relevant end-point.	April 2005 RMS supports the Notifier's opinion.	EPCO 23 (10 – 13.5.2005): Open point fulfilled The NOAEL in the 90-day rat study is 44.5 mg/kg bw/day.
	Open point 2.9: The RMS to summarize the the study (Collins, 1972a) in an addendum. (see reporting table 2(18))	Summarised in new addendum under Point IIA, 5.4.3/04. **Conclusion:** Folpet did not adversely affect fertility or mean total implants per female following interperitoneal injection at up to 10 mg/kg/day or oral intubation at up to 200 mg/kg/day. Folpet caused a dose-related increase in mean early embryonic deaths per	April 2005 The relevance of the experimental findings of the study in relation to the assessment of genotoxicity of folpet in germ cells is doubtful: genetic damage mainly results in pre-implantation losses, with the reduction of the number of implants per pregnancy. In this study, an increased incidence of	EPCO 23 (10 – 13.5.2005): Open point fulfilled.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.9: The RMS to summarize the the study (Collins, 1972a) in an addendum. (see reporting table 2(18))	pregnancy and the mean percentage of litters with two or more deaths. A response to the comments by the UK is also included in the new addendum. This response concludes that consideration of Collins (1972) in light of the collective data on folpet (and captan, its sister fungicide that shares a common mechanism of toxicity) shows that folpet is not mutagenic *in vivo*.	early death is reported, with no concurrent reduction in the mean number of implants. It is noteworthy that both Folpet (Collins 1972) and Captan (Collins 1975) were reported positive using the Collins's experimental design and procedures but were negative when studied by other investigators. As Folpet and Captan share a common mechanism of toxicity, it is likely that whatever conditions that appear unique to the Collins studies, they affected the results with Folpet and Captan in a similar manner.	
	Open point 2.10: MS to discuss the genotoxicity, also in relation to classification, and the need of additional studies to be performed at an expert meeting. (see reporting table 2(19))	A new Comet assay study is summarised in new addendum under Point IIA 5.4. **Conclusion:** There was no DNA damage in the mouse duodenum following treatment with folpet at 1000 or 2000 mg/kg as measured by a Comet Assay test. In addition, responses to comments by Member States are included in the new addendum: (1) The UK notes that a number of additional studies of the genotoxicity of	April 2005 RMS: Folpet does not meet the EC classification criteria for mutagenicity (as laid down in Commission Directive 2001/59/EC). Classification on the basis of in vitro test results is only exceptionally considered, i.e. for substances with no in vivo data and structural resemblance with known mutagens/carcinogens. In vivo studies on Folpet are not contradictory but uniformly negative (apart from the questionable study by Collins 1972). The nuclear aberration assay used massive oral dose of Folpet and looked	EPCO 23 (10 – 13.5.2005): Open point fulfilled. No genotoxic potential in vivo

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.10: MS to discuss the genotoxicity, also in relation to classification, and the need of additional studies to be performed at an expert meeting. (see reporting table 2(19))	folpet *in vivo* are available. These include a mouse spot test (negative), a mouse dominant lethal assay (negative, but concerns about the study quality) and the rat dominant lethal assay, discussed above. All studies should be considered. The relevance of the tissues investigated in each study should also be considered, given the known rapid degradation of the folpet molecules and the likely reactive species. The tissues that are relevant for investigation of folpet's mutagenicity *in vivo* are those tissues that come into direct contact with the intact molecule or the reactive degradate, thiophosgene. *In vivo*, these tissues are the cells of the gastrointestinal tract. The remainder of the mammalian system is "off limits" to folpet and thiophosgene due to their rapid degradation in blood (folpet: 4.9 second half-life, thiophosgene: 0.6 second half-life, respectively). Further to the issue of relevant tissues, it is the permanent basal cells of the gastrointestinal tract that are the appropriate targets to investigate. The epithelial layer of the gastrointestinal	for aberrations (mainly micronuclei) in the crypt cells of the mouse duodenum. None were found. The Comet assay further confirmed the absence of any effect by harvesting individual crypt cells and showing normal DNA patterns after large dose of Folapet (1000 and 2000 mg/kg b.w.) RMS deems that no further testing is required.	

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		tract that comprises the villi is replaced every three to four days; thus, any mutagenic events taking place in this compartment are of no consequence. The appropriate tissue to investigate is the crypt cell compartment in the mouse, as this compartment gives rise to duodenal tumors that appear after oral exposure at doses of approximately 1000 ppm and higher in cancer bioassays. This tissue compartment has been investigated, *in vivo*, using the single cell Comet assay (Clay, 2004). The negative results confirm that folpet is not mutagenic *in vivo*. This finding is consistent with that for captan with which it shares a common mechanism of toxicity. (2) Denmark (DK) notes folpet induces a wide range of genotoxic events *in vitro* including gene mutations/DNA damage in bacteria and mammalian cells, chromosomal aberrations in mammalian cells and mitotic recombination in yeast (not present in DAR). Although folpet was active in both the +/-S9 activation, the response was generally more pronounced		
	continued: Open point 2.10: MS to discuss the genotoxicity, also in relation to classification, and the need of additional studies to be performed at an expert meeting. (see reporting table 2(19))			

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.10: MS to discuss the genotoxicity, also in relation to classification, and the need of additional studies to be performed at an expert meeting. (see reporting table 2(19))	without S9 activation. The notifier contends that S9 "activation" is not relevant to the mutagenic activity of folpet. The role S9 plays in bacterial assays is that of a supply of available thiol groups associated with the enzyme fractions. These thiols react chemically (not enzymatically) with folpet and result in its degradation. They also promote the degradation of folpet's reactive degradate, thiophosgene. The collective data on the mutagenicity of folpet supports the conclusion taken by other regulatory and expert bodies that evaluated the full data package and concluded that Folpet is not genotoxic (e.g., JMPR, USEPA, and Germany). An overall conclusion on genotoxicity is included in the new addendum. **Conclusion**: The experimental data and our understanding of the mode of action for folpet combine to provide absolute assurance that folpet does not pose a mutagenic or genotoxic risk to humans. The notifier's conclusion is consistent with the conclusion of the RMS that		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
		folpet does not meet the EC classification criteria for mutagenicity.		
	Open point 2.11: MS to confirm the NOAELs in the long term studies at an expert meeting. continued: Open point 2.11: MS to confirm the NOAELs in the long term studies at an expert meeting. (see reporting table 2(22))	Revised summaries of the following studies are included in new addendum under Point IIA 5.6 and IIA 5.5. B.6.3. one year dog study (Daly 1986) B.6.5 2-year rats study (Crown, 1989) B.6.6 2-generation reproduction , rat (Rubin, 1986) B.6.6. Teratogenicity study, rabbit, Rubin 1985c). A response to comments from the UK Member State is also included in the new addendum. (1) UK notes the endpoint used to determine the NOAEL in the study of Crown (1989) is considered to be appropriate; however, the demonstrated decomposition of folpet in the diet should be taken into consideration. The NOAEL for this study is therefore calculated to be 190 ppm (equivalent to 12 an 16 mg/kg bw/day in males and females, respectively. The notifier calculates the NOAEL 191 ppm, confirming the comment by the UK. (2) The UK considers the NOAEL in	April 2005 RMS agrees RMS agrees	EPCO 23 (10 – 13.5.2005): Open point fulfilled. See open point 2.2

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.11: MS to confirm the NOAELs in the long term studies at an expert meeting. (see reporting table 2(22))	the rat carcinogenicity study of Crown (1985) to be 500 ppm, based on hyperkeratosis of the forestomach epithelium at 1000 ppm. The notifier advises that 500 ppm appears to be the NOAEL At 1000 and 2000 ppm, findings included hyperkeratosis of the esophagus and non-glandular keratin layers, ulcerations in the gastric non-glandular mucosa and foci or areas of cellular alteration (basophilic cell type) in the liver.		
	Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	The notifier's response to comments by the EFSA and Member States is given in the new addendum. (1) The United Kingdom (UK) considers the maternal NOAEL in the rabbit developmental study (Rubin, 1995) to be 10 mg/kg bw/day based on the slight initial reduced body weight gain at 40 mg/kg bw/day. Developmental effects however are not serious enough to warrant further investigation in either rat or rabbit, and might be expected given the level of maternal toxicity seen.	April 2005 RMS: after considering that folpet might exert its developmental toxicity through its primary effect on the g.i.-tract of the dams and could disrupt the normal g.i. flora, causing nutritional deficiencies, RMS is not convinced to classify Folpet as R 63 and proposes to discuss this subject in an expert meeting.	EPCO 23 (10 – 13.5.2005): Open point still open

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	Folpet (and captan) exert their developmental toxicity through their primary irritancy effect on the gastrointestinal tract of the dams. In addition, these fungicides are bacteriostats and therefore are expected to disrupt the normal gastrointestinal flora present in the rabbit intestine. This flora is essential for proper nutrition in that rabbits rely on a fermentation process and coprophagia to obtain nutrients. To the extent that folpet (and captan) disrupt this natural cycle, nutritional deficiencies would occurs. In this regard, the rabbit test system is not appropriate as a surrogate for human hazard identification. (2) Denmark suggests classification for developmental toxicity. Folpet caused an increase in the incidence of hydrocephaly in fetuses with associated domed skull and irregularly shaped fontanelles in NZW rabbits in the presence of maternal toxicity. Both fetal and litter incidences of this malformation were increased.		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	There was also evidence of fetal effects (delayed ossification of the sternebrae) in rabbits at a lower dose than that causing maternal toxicity. Analysis of the collective rabbit data show that folpet does not cause an increase in hydrocephaly in rabbits. From an analysis of the folpet database (Gordon and Neal, 1997, PDF attached): At severely toxic or maternally lethal doses, folpet shows embryotoxicity in rabbits. A further developmental toxicity study showed a possible dose relationship with an increased incidence of hydrocephaly in New Zealand White rabbits only at a maternally toxic dose of 60 mg/kg bw/day administered on days 6-28 (Feussner et al, 1984, "Teratology study in rabbits, [redacted] Project No. 303-002). This finding (hydrocephaly) has a variable incidence in the New Zealand White rabbit strain and tends to occur in non-dose-related clusters (Christian, 1985, "Variations in the incidence of hydrocephalus observed in caesarean-delivered control new Zealand White rabbit fetuses, Journal of the American College of Toxicology, 4(2): 218). Further, the findings were not		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	replicated in a predictable manner on pulsed exposure to the same high dose of folpet in the same rabbit strain done by the same investigators (Feussner, 1985, 'Teratology study in rabbits with folpet technical using a 'pulse-dosing' regimen." [redacted] Project No. 303-004). Additionally other rabbit studies with folpet (e.g., Rubin, 1985, "Folpan: Teratology study in the Rabbit." [redacted] Report No. MAK/051/FOL) have not shown hydrocephaly associated with gestation exposure to folpet. On review of the complete developmental toxicity data on folpet, WHO-JMPR concluded that folpet is not teratogenic in rabbits, even at a dose that is clearly maternally toxic (WHO-FAO, 1986, cited in WHO-FAO Pesticide Residues in Food – 1990, folpet 51-62, JMPR 1986). An additional confounding factor in interpreting rabbit developmental toxicity studies is the indirect action on maternal nutritional status caused by disruption of the intestinal flora from the bacteriostatic action of folpet. This adverse effect of bacteriostatic agents, such as folpet and captan, in rabbits may contribute to maternal toxicity and		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued: Open point 2.12: Teratogenic properties, also in respect of classification and labelling, to be discussed at an expert meeting. (see reporting table 2(26))	thus promote secondary effects in fetuses. (3) The European Food Safety Authority (EFSA) notes that there seems to be evidence of teratogenic potential of folpet at maternal non-toxic doses both in rat and rabbit. Thus, Classification of R63 is proposed. R63 ("possible risk of harm to the unborn child") is not appropriate. A weight of evidence analysis of the collective data for folpet and captan show that these compounds do not pose a rise to the unborn child: 1) The uterus and developing fetus does not come into contact with folpet or captan due to their rapid disappearance in blood. 2) Developmental studies show folpet and captan are not frank teratogens. 3) Developmental effects in fetuses at doses that are maternally toxic, particularly in rabbits, does not warrant R63. 4) Rabbits are less than optimal for studying folpet or captan's developmental effects because these two fungicides are bacteriostatic and disruption of the intestinal flora in		

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
		rabbits may have a deleterious effect on the health of the dams and, secondarily, on the fetuses. The conclusion of the notifier that R63 is not appropriate is consistent with the conclusion of the RMS.		
	Open point 2.13: MS to discuss the toxicity of the metabolites phthalimide and phthalic acid and their possible inclusion in the residue definition at an expert meeting. See also open point 3.2 (comment 3(12) in the reporting table). (see reporting table 2(30)) continued: Open point 2.13: MS to discuss the toxicity of the metabolites phthalimide and phthalic acid and their possible inclusion in the	A review of the toxicity potential of folpet metabolites (Seilfried 2000) is summarised in new addendum under Point II 5.8.1/01. **Conclusion:** The review concludes that folpet metabolites have a very low level of hazard to humans when exposed through the diet and to the environment compared to parent folpet. In addition a discussion paper by Gordon (2005) is summarised in new addendum under Point II 5.8.1/02. **Conclusion**: The discussion paper expands on the discussion of the toxicological significance of the degradates of folpet and concludes, based on the DG SANCO Guideline for Metabolism and Distribution in Plants (European Commission 1997) that they are not of toxicological significance and	April 2005 RMS agrees with the Notifier‘s conclusions.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Phtalimide and phtalic acid are present in the in vivo studies. The ADI for folpet cover the metabolites.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	residue definition at an expert meeting. See also open point 3.2 (comment 3(12) in the reporting table).	should not be included in the residue definition for risk assessment expression. The definition of the residue in plants and animal commodities is therefore folpet alone. This conclusion is consistent with the conclusion of the RMS.		
	Open point 2.14: MS to discuss the dermal absorption value at an expert meeting. (see reporting table 2(34))	Responses are given to comments made by Member States (Netherlands, Austria and UK) in the new addendum. The notifier contends that a value of 1% dermal absorption is appropriate. The argumentation supporting this contention is presented in the new addendum under Point IIIA 7.3. This conclusion is consistent with the conclusion of the RMS.	April 2005 RMS has some difficulties to support the Notifier view that "the biological availability of folpet from dermal exposure is essentially zero" based on the two studies of Shah 1987, and Wilson 1990. As a matter of fact even if the measurements of residual radioactivity in the skin (with folpet labeled on the ring) will reflect phthalimide and not Folpet, it does not mean that some material (no matter what) is passing throught the skin layers and is recovered in the urine in both the experiments. In the Shah paper, a study that uses Folpet labeled on the trichloromethylthio side-chain,skin absorption was up to 14.8% (low dose) whereas in the Wilson study, following dermal application of [U-phenyl-^{14}C] folpet, the fungicide and /or its labelled degradation products once absorbed were excreted via the urine (up to 13.2% of applied	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Dermal absorption: 10% for the concentrate and the dilution based on the *in vivo* rat study.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
			radioactivity), with a higher rate of excretion at lower doses.	
	The notifier to submit the study Wilson, 1990 (dermal absorption). continued: The notifier to submit the study Wilson, 1990 (dermal absorption). (see reporting table 2(35))	Summarised in new addendum under Point IIA 5.8.2/07. However, this study is not appropriate for the determination of dermal absorption for use in risk assessment. This is supported by a position paper by Gordon, E. (2005) summarised in the new addendum under Point IIA 5.8.2/08. The paper concludes that data developed from studies with folpet labelled on the ring (such as the Wilson study) should not be used as they reflect the presence of phthalimide (which is of no toxicological concern) not folpet. The study by Shah and co-workers used folpet labelled on the reactive side-chain which is responsible for the toxicity of folpet and therefore more appropriate. The appropriate dermal absorption factor for occupational risk assessment is 0%. **Conclusion:** Folpet absorption is approximately 1% based on traditional studies, but special mechanistic studies actually suggest this absorption is effectively much lower. For regulatory purposes, the notifier	April 2005 See above	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
		accepts a 1% absorption rate while this issue is further evaluated by EU scientists.		
	Open point 2.14: RMS to present an estimation of exposure in glass-houses in an addendum. (see reporting table 2(40))	This is already addressed in the DAR. Since there is a large margin of safety, even if inhalation exposure in greenhouses is higher than for outdoor crops (dermal exposure in greenhouses and outdoor crops would be similar), inhalation exposure is small (also folpet has low vapour pressure) and so any increase would not significantly increase total systemic exposure. There is therefore a wide margin of safety for spray operators in greenhouses. .	April 2005 RMS agrees	EPCO 23 (10 – 13.5.2005): Open point still open A new estimation on operator exposure has to be submitted for all uses.
	Open point 2.15: The bystander exposure needs to be discussed at an expert meeting. (see reporting table 2(41))	An estimate of dermal exposure of bystanders is presented in the DAR. This shows a wide margin of safety. Furthermore, the vapour pressure of folpet is low 2.1 x 10^{-5} Pa at 25^{o}C and so the inhalation risk to bystanders is considered to be negligible. Therefore, the overall risk to bystanders is considered to be negligible. This conclusion is consistent with the conclusion of the RMS.	April 2005 RMS agrees	EPCO 23 (10 – 13.5.2005): Open point still open A calculation for bystander exposure taking into account the dermal absorption value of 10% has to be submitted
	Open point 2.16: MS to discuss available	A new risk assessment to workers using decline data is summarised in	April 2005 RMS agrees	EPCO 23 (10 – 13.5.2005):

No.	Column A Conclusions of the EFSA \Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	residue decline data with respect to worker exposure at an expert meeting. continued: Open point 2.16: MS to discuss available residue decline data with respect to worker exposure at an expert meeting. (see reporting table 2(43))	new addendum under Point IIIA 7.2.3.1. **Conclusion**: The maximum exposure of workers in worst-case calculations (based on 10 applications to grapes at the maximum recommended rate) in the absence of protective gloves is 0.057 mg/kg bw/day (based on the German model) and 0.010 mg/kg bw/day (based on published data on captan, which is similar to folpet). Thus, exposure of workers is lower than an AOEL of 0.1 mg/kg bw/day. Consequently, the risk to workers is considered to be low and it is not necessary to set an additional re-entry period for workers harvesting treated grapes.		Open point still open A calculation for worker and bystander exposure taking into account the dermal absorption value of 10% has to be submitted

REPORT OF EPCO EXPERT MEETING 24

FOLPET

Rapporteur Member State: Italy

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:

None.

2. Documents submitted for meeting:

Date	Supplier	File Name
19 April 2005	RMS/Italy	Folpet Addendum residues 2005-04-19.doc
17 Nov 2004	RMS/Italy	Folpet consultation report (17-11-2004).doc
19 April 2005	RMS/Italy	Folpet evaluation table rev0-1 2005-04-19.doc
19 April 2005	RMS/Italy	Folpet list of endpoints res 2005-04-19.doc
22 December 2004	RMS/Italy	Folpet reporting table rev1-1 (22-12-2004).doc
08 April 2005	RMS/Italy	Folpet supported uses (08-04-2005).doc

3. Documents tabled at the meeting:

None.

The conclusions of the meeting were as follows:

4. **Data on preparations:** Not yet complete.

5. **Classification and labelling:** None.

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

7. **Reference List** None.

Areas of concern: acute intake

Appendix 1: EPCO discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

3. Residues

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 3.1: RMS to prepare an acute risk assessment in an addendum to be discussed in expert meeting. (see reporting table 3(3))	RMS presented the risk assessment in an addendum. However, the risk assessment has to be redone according to the new residue definition, which includes phthalimide. (see open points 3.2 and 3.3). Nevertheless, this open point was regarded as fulfilled by the meeting.	Acute risk assessment was presented by the RMS. Open point fulfilled.
3.1	Notifier to provide hydrolysis studies in representative hydrolytic conditions. (see reporting table 3(5))	RMS stated that data discussed in the position paper presented by the notifier do not fulfil the point. Specific studies are still required. Therefore, the meeting agreed that this data requirement is still open	The meeting confirmed that the specific hydrolysis studies are still required. Data requirement still open.
3.2	Notifier to provide a whole balance study for tomato washed, peeled and canned or used for juice, 3 follow-up studies in juice and canned tomato. (see reporting table 3(6))	RMS stated that the studies have been submitted and were summarised in an addendum. The conclusions of the main data submitter were accepted by the RMS. But, the studies need to be re-evaluated in the light of the new residue definition,(including phthalimide). Therefore, this data requirement is still open.	Studies need to be re-evaluated in the light of the new residue definition. Data requirement still open for formal reasons.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
3.3	Notifier to provide 2 greenhouse residue trials for tomatoes. (see reporting table 3(7))	Further results of new studies still have to be awaited. Therefore, data requirement is still open.	Results of studies have to be awaited. Data requirement still open.
	Open point 3.2: MS to discuss the residue definition for risk assessment in an expert meeting. RMS to prepare an assessment of the toxicological relevance of metabolites (including their contribution to the toxicological burden). (see reporting table 3(12))	RMS included the risk assessment in an addendum. RMS stated that metabolites phthalimide and phthalic acid have to be considered similar to THPI and THPAM with regard to the a.s. captan. In the addendum it is stated that phthalic acid is of no toxicological relevance and moreover it is present in the environment. Therefore, it should not be included in the residue definition. The meeting basically agreed and proposed that phtalic acid should not be taken into account. The NL expert stated that in residue trials also control treatments are tested. Therefore, by comparison to the folpet treatments the phthalic acid coming from folpet could be quantified. However, this view was not shared by other experts. The expert meeting on toxicology decided that a final conclusion on the toxicological relevance of phthalimide and phthalic acid can not drawn up (See report of EPCO 23, open point 2.13). Finally, after an extensive discussion, the meeting agreed to take only into account the metabolite phthalimide, as for captan only THPI and not THPAM was taken into account. The residue definition for plants is proposed as folpet + phthalimide expressed as folpet. Since folpet does not occur in products of animal origin, the residue definition for animals is defined as phthalimide expressed as folpet. The proposals applies to the definitions for monitoring and for risk assessment. The list of end points needs to be revised regarding the residue definition.	Open point fulfilled. Due to the change in the residue definition a new open point was proposed: New open point 3.4: RMS to go back to the available data set and make new evaluation of the available data so that the MRL proposals and the risk assessment can be done on the basis of the new residue definitions. The new calculations should be summarised in an addendum. Open point still open. RMS to amend the list of end points. (See new open point 3.5)

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 3.3: MS to discuss the residue definition for animal commodities, including the need for it, in an expert meeting. (see reporting table 3(13))	See discussion under open point 3.2.	Open point fulfilled. RMS to amend the list of end points. (See new open point 3.5)
	New open point 3.5: RMS to revise the list of end points according the amendments proposed by EPCO 24.	The residue definition to be revised as follows: - Plant residue definition for monitoring: sum of folpet and phthalimide expressed as folpet - Plant residue definition for risk assessment: sum of folpet and phthalimide expressed as folpet - Animal residue definition for monitoring: phthalimide expressed as folpet - Animal residue definition for risk assessment: phthalimide expressed as folpet	Open point still open.

Appendix 2: Evaluation table

4. Residues

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Section 3 Data requirements: ***3*** Open points: ***3***			Section 3 Data requirements: ***3*** Open points: ***2*** Data gaps: **-**
	Open point 3.1: RMS to prepare an acute risk assessment in an addendum to be discussed in expert meeting. (see reporting table 3(3))	The notifier contends that an ARfD for folpet is not necessary. This is supported by a position paper summarised in the new addendum under Point IIA 5.10/01.	Using the UK model for the determination of the acute intake, the ARfD for table grape is exceeded by the 807 % in toddler and by the 167% in adults. Other values are 17.8% of the ARfD for tomatoes in adults and 82.2% of the ARfD for tomatoes in toddler.	EPCO 24 (11.05. – 13.05.2005): Acute risk assessment was presented by the RMS. Open point fulfilled.
3.1	Notifier to provide hydrolysis studies in representative hydrolytic conditions. (see reporting table 3(5))	A position paper (Goodyear, 2004) is summarised in the new addendum under Point IIA 6.5.1/01. **Conclusion**: The position paper concludes that sufficient data already exist to predict the effect of processing hydrolysis on the nature of the residue and therefore new studies are not required.	Data discussed in the position paper do not fulfil the point. Specific studies are still required. Moreover we have been informed from the applicant that hydrolysis studies are on going and results will be available soon.	EPCO 24 (11.05. – 13.05.2005): The meeting confirmed that the specific hydrolysis studies are still required. Data requirement still open.

section 3 - Residues

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
3.2	Notifier to provide a whole balance study for tomato washed, peeled and canned or used for juice, 3 follow-up studies in juice and canned tomato. (see reporting table 3(6))	The results of a new balance study and three follow-up studies (Pollmann, 2005) are summarised in the new addendum under Point IIA 6.5.2/07. **Conclusion**: The studies show that there is no concentration of folpet residues in tomato juice and canned tomato fruit (human edible commodities).	Studies have been revised. The conclusions of the main data submitter are accepted.	EPCO 24 (11.05. – 13.05.2005): Studies need to be re-evaluated in the light of the new residue definition. Data requirement still open for formal reasons.
3.3	Notifier to provide 2 greenhouse residue trials for tomatoes. (see reporting table 3(7))	The results of the existing studies and arguments against the need for new studies are presented in the new addendum under Point IIA 6.3. **Conclusion:** The notifier contends that, since a EU MRL for folpet in tomatoes already exists, and since the existing value of 3 mg/kg is supported by the results of 10 trials carried out under worst-case conditions for residues, i.e. under greenhouse conditions, (of which 6 are validated by freezer storage study), it is not necessary to set a new MRL for folpet in tomato as part of the EU review of folpet. Therefore, it is concluded that as sufficient information is available, additional residue trials in greenhouse grown tomatoes are not required for the EU review of folpet.	Ten trials in greenhouse grown tomatoes treated according to the EU GAP were originally presented. In four trials, samples were stored for periods longer than the period tested in freezer storage stability studies and so were not accepted. According to the applicant, new freezer storage stability study in tomato fruit is underway to validate the residue studies in tomato which were not accepted, and results will be available at the beginning of 2006. The MRL for folpet in tomatoes of 3 mg/kg is therefore provisionally accepted, waiting for results of the above mentioned studies.	EPCO 24 (11.05. – 13.05.2005): Results of studies have to be awaited. Data requirement still open.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Open point 3.2: MS to discuss the residue definition for risk assessment in an expert meeting. RMS to prepare an assessment of the toxicological relevance of metabolites (including their contribution to the toxicological burden). (see reporting table 3(12))	A review of the toxicity of potential folpet metabolites is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/01. In addition a discussion paper by Gordon (2005) is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/02. **Conclusion**: The discussion paper expands on the discussion of the toxicological significance of the degradates of folpet and concludes, based on the DG SANCO Guideline for Metabolism and Distribution in Plants (European Commission 1997) that they are not of toxicological significance and should not be included in the residue definition for risk assessment expression. The definition of the residue in plants is therefore folpet alone. This conclusion is consistent with the conclusion of the RMS.	Assessment has been included in the addendum and is open for discussion. According to our opinion, folpet metabolites are of low toxicological significance compared to folpet. Residue definition for risk assessment should be therefore folpet alone.	EPCO 24 (11.05. – 13.05.2005): Open point fulfilled. Due to the change in the residue definition a new open point was proposed: New open point 3.4: RMS to go back to the available data set and make new evaluation of the available data so that the MRL proposals and the risk assessment can be done on the basis of the new residue definitions. The new calculations should be summarised in an addendum. RMS to amend the list of end points. (See new open point 3.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	New open point 3.4: RMS to go back to the available data set and make new evaluation of the available data so that the MRL proposals and the risk assessment can be done on the basis of the new residue definitions. The new calculations should be summarised in an addendum. This open point was proposed at EPCO 24.			EPCO 24 (11.05. – 13.05.2005): Open point still open.
	Open point 3.3: MS to discuss the residue definition for animal commodities, including the need for it, in an expert meeting. (see reporting table 3(13))	A review of the toxicity of potential folpet metabolites is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/01. In addition a discussion paper by Gordon (2005) is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/02. **Conclusion**: The discussion paper expands on the discussion of the toxicological significance of the degradates of folpet and concludes, based on the DG SANCO Guideline for Metabolism and Distribution in Plants (European Commission 1997) that they	A discussion has been included in the addendum. For animal commodities, as shown by table B.7.2.4 of the DAR, folpet is the only possible indicator, since other (possible) intermediate/s are rapidly transformed into natural compounds in muscle and milk. The need for a residue definition in animal commodities should be discussed during the next expert meeting.	EPCO 24 (11.05. – 13.05.2005): Open point fulfilled. RMS to amend the list of end points. (See new open point 3.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	continued Open point 3.3: MS to discuss the residue definition for animal commodities, including the need for it, in an expert meeting. (see reporting table 3(13))	are not of toxicological significance and should not be included in the residue definition for risk assessment expression. The definition of the residue in animal commodities is therefore folpet alone. This conclusion is consistent with the conclusion of the RMS.		
	New open point 3.5: RMS to revise the list of end points according the amendments proposed by EPCO 24.			EPCO 24 (11.05. – 13.05.2005): Open point still open.

List of representative uses evaluated

Crop	Member state or country	Product name	F, G or I[a]	Pests or group of pests controlled	Formulation		Application			Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of a.s.	method kind	growth stage	number[b] (max.)	kg a.s./hL (max.)	water L/ha	kg a.s./ha (max.)		
Winter wheat	South EU	'Folpan' 80 WDG	F	*Septoria* Brown rust	WG	800 g/kg	Foliar spray; down-ward	Up to Z65	2	0.375	200	0.75	42	
Tomatoes	South EU	'Folpan' 80 WDG	F	various[c]	WG	800 g/kg	Foliar spray; down-ward	From beginning of fruit set	4	0.125	1000	1.25	7	
	South EU	'Folpan' 80 WDG	G	various[c]	WG	800 g/kg	Foliar spray; down-ward	From beginning of fruit set	3	0.16	1000 - 1300	1.6	7	
Grapes	North and south EU	'Folpan' 80 WDG	F	various[d]	WG	800 g/kg	Airblast foliar spray; upwards / sideways	Shoot emergence to veraison	10	0.75	200 - 400	1.5	28	

[a] F= field; G = greenhouse.
[b] Sprays on all crops are applied typically at intervals of 7 to 28 days.
[c] *Alternaria solanum, Cladospora, Colletotrichum, Septoria, Botrytis*
[d] Black rot, *Botrytis cinerea phomosis*. *Plasmopara viticola*.

REPORT OF EPCO EXPERT MEETING 25

FOLPET

Rapporteur Member State: Italy

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

2. Documents submitted for meeting:

Date	Supplier	File Name
28 April 2005	RMS/Italy	Folpet Addendum phys chem 2005-04-28
28 April 2005	RMS/Italy	Folpet Addendum phys chem confidential 2005-04-28 cover
28 April 2005	RMS/Italy	Folpet_evaluation table rev.0-1 physchem 2005-04-28
28 April 2005	RMS/Italy	Folpet list of endpoints physchem 2005-04-28
17 November 2004	RMS/Italy	Folpet consultation report (17-11-2004)
22 December 2004	RMS/Italy	Folpet reporting table rev1-1 (22-12-2004)
08 April 2005	RMS/Italy	Folpet supported uses (08-04-2005)

3. Documents tabled at the meeting:

Date	Supplier	File Name

The conclusions of the meeting were as follows:

4. **Data on preparations:** folpan 80 WDG.

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

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

7. Reference List

Areas of concern: data gap for the enforcement methods; specification see captan

Appendix 1: EPCO discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

1. Physical and Chemical Properties

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	General new open point:		EPCO 25(24.-26.05.2005): RMS to present the evaluation of the new submitted information presented in the addendum to the dossier and all information in an addendum to the DAR.
	Second general point:		EPCO 25(24.-26.05.2005): RMS to clarify whether the document or addendum to the dossier (tabled at the meeting) was written by the RMS or the notifier. Furthermore, it should be distinguished between confidential and non confidential information.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.1: RMS to clarify whether [redacted] has to be regarded as a relevant impurity or not. (see reporting table 1(1))	RMS: [redacted] is not considered to be a significant impurity in folpet technical (no toxicological relevance and found below 1 g/Kg) E.P. list amended The ecotoxicological concerns haven't been discussed. Thus the ecotoxicology section has to confirm this impurity.	EPCO 25(24.-26.05.2005): Open point closed. Message to toxicology and ecotoxicology section to confirm that [redacted] has not to be regarded as a relevant impurity.
	Open point 1.2: RMS to amend the list of endpoints regarding the declared content of the folpet in the FAO specification and to clarify the amended value for the minimum purity. According to the FAO specification the given value should be read as 880 g/kg ± 20 g/kg. The minimum purity should be given without a range. (see reporting table 1(5))	EP list amended. The meeting agreed on this.	EPCO 25(24.-26.05.2005): Open point fulfilled.
1.1	Notifier to provide data concerning the boiling point and temperature of decomposition,	Data requirement addressed. EP list amended.	EPCO 25(24.-26.05.2005): Data requirement: still open for technical reasons. See general points

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	respectively. (see reporting table 1(6))	The meeting accepted this.	
	Open point 1.3: RMS to indicate in the list of endpoints that the density was determined. (see reporting table 1(7))	EP list amended The meeting accepted this.	EPCO 25(24.-26.05.2005): Open point closed.
	Open point 1.4: RMS to include the list of "representative uses evaluated" in the list of endpoints. (see reporting table 1(8))	EP list amended The meeting accepted this.	EPCO 25(24.-26.05.2005): Open point closed.
1.2	Notifier to submit the position paper: “Folpet. Position Paper on Residue Analytical Methods (May 2004)”. (see reporting table 1(9))	Data requirement addressed. Meeting accepted this.	EPCO 25(24.-26.05.2005): Data requirement fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.5: The need for a confirmatory method for food of plant origin should be discussed in an expert meeting (see reporting table 1(9))	EFSA informed that the residue definition for food of plant origin has been changed. Now it is folpet and phthalimide. The LOQ is 0.2 mg/kg for this metabolite. This is too high and thus no acceptable analytical method is mentioned for this metabolite. There is an HPLC/UV method mentioned on p. 36 of the DAR. But it is not validated and thus has to be deleted from the list of end points. RMS to delete the HPLC/UV method from the list of end point. Clarification is needed regarding the given conclusion on p. 36 (bottom) and 37 of the DAR.: It is unclear whether the indicated changes belong to both methods (Schleisinger and Nishioka) or only to the study of Nishioka. In case that the modifications belong also to the "original" method of Schleisinger a new ILV would be necessary. The method from Byast has no ILV. This might be covered by Simak. Meeting didn't accept this without further clarification even when 6 years have been between these studies. Addendum p. 8: an argumentation is given that no further confirmatory methods are needed. The RMS disagreed with this conclusion. The meeting is of the same opinion. The guideline has been discussed. Which and how many matrices have to be analysed was unclear according to the wording in the guidance. Some MS require all matrices, other MS are regarding these two sufficient. The meeting did regard two as sufficient in this case.	<u>EPCO 25(24.-26.05.2005):</u> Open point closed. New data gap identified: Notifier to provide an analytical method for food of plant origin (high water content and dry matrices) for phthalimide including ILV. New open point: RMS to check whether the indicated modification in the ILV belongs also to the Schleisinger method or only to the Nishioka method. New open point: RMS to clarify the independency of the two laboratories from the study of Byast and Simek. New data gap identified: Notifier to present a confirmatory analytical method for food of plant origin for folpet (matrices with high water content) and phthalimide (high water content and dry material matrices).

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.6: The need for further information regarding the flow ability should be discussed in an expert meeting. (see reporting table 1(11))	The conclusions are acceptable, but the data on the flow ability will be discussed in an expert meeting. According to the FAO criteria the value is not acceptable. Notifier gave an argumentation. However, taking the given explanation into account as well as the packaging size, the meeting agreed that there is no need for further data at the moment. Some MS argued that in case the packaging of the preparation might be change in future then a concern might be coming up.	<u>EPCO 25(24.-26.05.2005):</u> Open point closed. New open point: EFSA to indicate in the conclusion: The data with respect to flowability are out of the acceptable FAO criteria. The data of flowability may need to be reconsidered if new packaging types are requested.
	Open point 1.7: RMS to amend the list of endpoints regarding the applicability of CIPAC method(s), if appropriate. (see reporting table 1(13))	EP list amended. This hasn't been accepted completely. To delete everything after "… dispersible granules."	<u>EPCO 25(24.-26.05.2005):</u> Open point still open. RMS to amend the list of endpoints.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.8: RMS to amend the list of endpoints regarding the analytical method for food of animal origin with a phrase that an analytical method is not required since no MRLs are proposed. (see reporting table 1(16))	Depends on the final proposal by residue section.	<u>EPCO 25(24.-26.05.2005):</u> Open point still open. Depends on the final proposal by residue section. Provided that the residue definition includes Phthalimide only and MRL(s) will be proposed an analytical method incl. ILV is required according to Directive 96/46/EC.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.9: The need for an analytical method for the determination of residues in surface water should be discussed in an expert meeting. Depending on the outcome of the fate and behaviour meeting, it could be that no analytical method for the determination of residues of folpet in surface water is required. Open point relates to open point 4.16 (comment 4(46) in the reporting table) (see reporting table 1(18))	RMS agreed for a discussion in an expert meeting, because if DT90 <1 day, no methods are required. The meeting accepted this. Ecotoxicology section has just confirmed that only folpet is relevant. Note to fate and behaviour section to confirm the DT_{90} value in surface water of below 1 day.	<u>EPCO 25(24.-26.05.2005):</u> Open point closed. Message to fate and behaviour section to confirm the DT_{90} value in surface water of below 1 day.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	Open point 1.10: RMS to amend the list of endpoints to clarify that an analytical method for body fluids (blood) is not required since folpet is not classified as toxic or highly toxic. (see reporting table 1(21))	Done by the RMS. The meeting accepted this.	EPCO 25(24.-26.05.2005): Open point closed.
1.3	Notifier to submit data regarding the purity and source (commercially available or not) of the starting material. (see reporting table 1(23))	Data requirement addressed.	EPCO 25(24.-26.05.2005): Data requirement is still open for technical reason. The information has to be presented in an addendum. See also general points
	Open point 1.11: RMS to clarify the need to discuss the position paper on residue analytical methods under this topic. (see reporting table 1(24))	RMS clarify this as a mistake.	EPCO 25(24.-26.05.2005): Open point fulfilled.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
1.4	Notifier to justify the given specification for the impurities or submit a new one. (see reporting table 1(24))	Data requirement addressed. The impurity [redacted] is mentioned for captan as but not for folpet. Toxicology and ecotoxicology section: has this impurity to be regarded as a relevant impurity. Furthermore, the technical material contains [redacted] Therefore, the meeting wonder whether or not [redacted] has to be regarded as a relevant impurity, because it is classified as toxic (T) and Carc. Cat. 3. Note to tox experts: To confirm that the [redacted] has not be regarded as a relevant impurity in the technical material of folpet. The new specification was questioned. For most of the impurities the maximum content has been increased. Some of them are still not reliable and cannot be accepted without further clarification/justification. The impurities in question are in the rows 3 to 7 in the table presented on page 4 in the document Tier II, Annex II and III, Addendum to dossier confidential information, April 2005.	<u>EPCO 25(24.-26.05.2005):</u> Data requirement closed. Message to toxicology and ecotoxicology: Has [redacted] to be regarded as a relevant impurity. Message to toxicology experts: To confirm that [redacted] has not to be regarded as a relevant impurity in the technical material of folpet. New Data gap identified: Notifier to present justification for the values of the impurities in the newly presented justifications.

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
1.5	Data to confirm the identity of the impurities revealed by chemical analysis must be provided to address the requirement of the Directive on the specificity of the method(s). (see reporting table 1(25))	RMS confirmed that the notifier will submit further data.	EPCO 25(24.-26.05.2005): Data requirement is still open.
		Residue definition for food of animal origin did change. Phthalimide expressed as folpet Probably MRLs have to be calculated. For this there are no analytical methods presented at all Data requirement:	EPCO 25(24.-26.05.2005): New data gap: Notifier to provide an analytical method for the determination of phthalimide of food of animal origin including the ILV according to Directive 96/46/EC provided that MRLs will be proposed. See also open point 1.8

No.	Subject	Discussion EPCO Expert Meeting	Conclusions EPCO Expert Meeting
	List of end points	- RMS to delete the HPLC/UV method from the list of end point. (see open point 5.1) - UV/VIS box: in the unit, "L" is missing. - Purity in the temperature of decomposition is missing. - Template of EPCO manual E4 should be used. - Analytical methods for residues: only validated methods have to be mentioned. - EEC number is probably incorrect. Post note meeting: The correct no. is 205-088-6. The given number is the ECB index number.	EPCO 25(24.-26.05.2005): RMS to amend the list of end points

Appendix 2: Evaluation table

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

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Section 1 Data requirements: ***5*** Open points: ***11***			Section 1 Data requirements: ***3*** Open points: ***8*** Data gaps: ***4***
	General new open point 1.12: RMS to present the evaluation of the new submitted information presented in the addendum to the dossier and all information in an addendum to the DAR. This open point was proposed at EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.
	General new open point 1.13: RMS to clarify whether the document or addendum to the dossier (tabled at the meeting) was written by the RMS or the notifier. Furthermore, it should be distinguished between confidential and non confidential information. This open point was proposed at EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Open point 1.1: RMS to clarify whether [redacted] has to be regarded as a relevant impurity or not. (see reporting table 1(1))	The metabolic pathway of [redacted] is expected to be very similar to folpet and the occurrence of [redacted] is below 0.1%, [redacted] is not considered to be a significant impurity in folpet technical. See text in Addendum under point IIA, 1.10.	Apr. 05 [redacted] is not considered to be a significant impurity in folpet technical (no toxicological relevance and found below 1 g/Kg) E.P. list amended	EPCO 25(24.-26.05.2005): Open point closed. Message to toxicology and ecotoxicology section to confirm that [redacted] has not to be regarded as a relevant impurity.
	Open point 1.2: RMS to amend the list of endpoints regarding the declared content of the folpet in the FAO specification and to clarify the amended value for the minimum purity. According to the FAO specification the given value should be read as 880 g/kg ± 20 g/kg. The minimum purity should be given without a range. (see reporting table 1(5))	FAO specification changed to 880 g/kg ±20 g And Minimum purity specification changed to 940 g/kg	Apr. 05 Noted – EP list amended	EPCO 25(24.-26.05.2005): Open point fulfilled.
1.1	Notifier to provide data concerning the boiling point and temperature of decomposition, respectively. (see reporting table 1(6))	New data submitted in the new Addendum under Point IIA 2.1.3. **Conclusion**: The test substance decomposed above its melting point starting at 184°C.	Apr. 05 Data requirement addressed EP list amended	EPCO 25(24.-26.05.2005): Data requirement: still open for technical reasons. See general points

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Open point 1.3: RMS to indicate in the list of endpoints that the density was determined. (see reporting table 1(7))	Since density and relative density, D^{20}_4, are numerically identical, the end point table does not need to be changed.	Apr. 05 Noted - EP list amended	EPCO 25(24.-26.05.2005): Open point closed.
	Open point 1.4: RMS to include the list of "representative uses evaluated" in the list of endpoints. (see reporting table 1(8))		Apr. 05 Noted - EP list amended	EPCO 25(24.-26.05.2005): Open point closed.
1.2	Notifier to submit the position paper: “Folpet. Position Paper on Residue Analytical Methods (May 2004)”. (see reporting table 1(9))	Summarised in the new Addendum. The position paper is summarised in the new Addendum under Point IIA, 4.2.1.	Apr. 05 Data requirement addressed	EPCO 25(24.-26.05.2005): Data requirement fulfilled.
	Open point 1.5: The need for a confirmatory method for food of plant origin should be discussed in an expert meeting (see reporting table 1(9))	The notifier concludes that no additional data are necessary to fulfil the Annex point requirement. The position paper detailing this argument is summarised in the new Addendum under Point IIA, 4.2.1.	Apr. 05 We disagree with the notifier conclusions and agree with the EFSA conclusions	EPCO 25(24.-26.05.2005): Open point closed. New data gap identified (1.6) New open point (1.14) New open point (1.15) New data gap identified (1.7)

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
1.6	New data gap: Notifier to provide an analytical method for food of plant origin (high water content and dry matrices) for phthalimide including ILV. See open point 1.5. This data gap was identified at EPCO 25.			EPCO 25(24.-26.05.2005): Data gap identified.
	New open point 1.14: RMS to check whether the indicated modification in the ILV belongs also to the Schleisinger method or only to the Nishioka method. See open point 1.5. This open point was proposed at EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.
	New open point 1.15: RMS to clarify the independency of the two laboratories from the study of Byast and Simek. See open point 1.5. This open point was proposed at EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
1.7	New data gap: Notifier to present a confirmatory analytical method for food of plant origin for folpet (matrices with high water content) and phthalimide (high water content and dry material matrices). See open point 1.5. This data gap was identified at EPCO 25.			EPCO 25(24.-26.05.2005): Data gap identified.
	Open point 1.6: The need for further information regarding the flowability should be discussed in an expert meeting. (see reporting table 1(11))	The results indicate that any agglomerates that formed were friable enough to be broken by dropping the sieve a distance of 1 cm. The applicant contends that the flowability parameter has little practical importance in this case. When used, water dispersible granules are mixed with and dispersed in water. The important technical parameters for this procedure are suspensibility, dispersibility and wet sieve. The results of these tests were all acceptable. Argument added to new addendum under Point IIIA, 2.8.8.1. This conclusion is consistent with the conclusion of the RMS.	Apr. 05 The conclusions are acceptable, but the data on the flowability will be discussed in an expert meeting	EPCO 25(24.-26.05.2005): Open point closed. New open point (1.16)

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	New open point 1.16: EFSA to indicate in the conclusion: The data with respect to flowability are out of the acceptable FAO criteria. The data of flowability may need to be reconsidered if new packaging types are requested. See open point 1.6. This open point was proposed at EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.
	Open point 1.7: RMS to amend the list of endpoints regarding the applicability of CIPAC method(s), if appropriate. (see reporting table 1(13))		Apr. 05 Noted- EP list amended	EPCO 25(24.-26.05.2005): Open point still open. RMS to amend the list of endpoints.
	Open point 1.8: RMS to amend the list of endpoints regarding the analytical method for food of animal origin with a phrase that an analytical method is not required since no MRLs are proposed. (see reporting table 1(16))		Apr. 05 Noted- EP list amended	EPCO 25(24.-26.05.2005): Open point still open. Depends on the final proposal by residue section. Provided that the residue definition includes Phthalimide only and MRL(s) will be proposed an analytical method incl. ILV is required according to Directive 96/46/EC.

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Open point 1.9: The need for an analytical method for the determination of residues in surface water should be discussed in an expert meeting. Depending on the outcome of the fate and behaviour meeting, it could be that no analytical method for the determination of residues of folpet in surface water is required. Open point relates to open point 4.16 (comment 4(46) in the reporting table) (see reporting table 1(18))	It is a reasonable assumption that the method presented, which is extremely sensitive for drinking water (LOQ = 0.02 µg/L) with a highly specific detection technique (UV photodiode array), will be directly applicable to surface water at relevant concentrations. It is concluded that the requirement of an analytical method for surface water may be waived under these circumstances (as stated by the reviewer from Germany "A method for residues in surface water is not required because of the low stability of Folpet (DT_{90} < 1 day)"). Newly calculated hydrolysis DT_{90} values for folpet are confirmed to less than 3 hours under worst case conditions.	Apr. 05 We disagree with the first conclusion provided by the notifier: surface water is a more complex matrix than drinking water. We agree for a discussion in an expert meeting, because if DT90 < 1 day, no methods are required.	EPCO 25(24.-26.05.2005): Open point closed. Message to fate and behaviour section to confirm the DT_{90} value in surface water of below 1 day.
	Open point 1.10: RMS to amend the list of endpoints to clarify that an analytical method for body fluids (blood) is not required since folpet is not classified as toxic or highly toxic. (see reporting table 1(21))		Apr. 05 Noted - EP list amended	EPCO 25(24.-26.05.2005): Open point closed.

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
1.3	Notifier to submit data regarding the purity and source (commercially available or not) of the starting material. (see reporting table 1(23))	This information is added to the new Addendum under Point IIA, 1.8.	Apr. 05 Data requirement addressed	EPCO 25(24.-26.05.2005): Data requirement is still open for technical reason. The information has to be presented in an addendum. See also general points
	Open point 1.11: RMS to clarify the need to discuss the position paper on residue analytical methods under this topic. (see reporting table 1(24))	RMS action	Apr. 05 No need to discuss the position paper under this topic. The comment to point 1 (24) in the Reporting Table was erroneously inserted for a printing mistake.	EPCO 25(24.-26.05.2005): Open point fulfilled.
1.4	Notifier to justify the given specification for the impurities or submit a new one. (see reporting table 1(24))	New specification presented in the new Addendum under Point IIA, 1.11. This information is Confidential and not for disclosure.	Apr. 05 Data requirement addressed	EPCO 25(24.-26.05.2005): Data requirement closed. Message to toxicology and ecotoxicology: Has [redacted] to be regarded as a relevant impurity. Message to toxicology experts: To confirm that [redacted] has not to be regarded as a relevant impurity in the technical material of folpet. New Data gap identified (1.8)

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
1.8	New data gap: Notifier to present justification for the values of the impurities in the newly presented justifications. See data requirement 1.5. This data gap was identified at EPCO 25.			EPCO 25(24.-26.05.2005): Data gap identified.
1.5	Data to confirm the identity of the impurities revealed by chemical analysis must be provided to address the requirement of the Directive on the specificity of the method(s). (see reporting table 1(25))	Specificity of the impurity methods has been adequately addressed in the dossier. Specificity was confirmed by comparison of chromatograms of certified analytical standards and blank solvent. Absence of interfering peaks is taken as confirmation of specificity. Regarding identity of the impurities, this has been confirmed by the use of certified reference standards in the validation procedures. There is no sound scientific basis on which to reject this argument. Confirmation of the identity of the impurities is inherent in the proven specificity of the method. The Directive does not directly require any further confirmation of the identity of the impurities. This conclusion is consistent with the conclusion of the RMS.	Apr. 05 Data required A new study, required to confirm the identity of the impurities, will be submitted by the notifier	EPCO 25(24.-26.05.2005): Data requirement is still open.

section 1 - Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis (B.1-B.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
1.9	New data gap: Residue definition: Notifier to provide an analytical method for the determination of phthalimide of food of animal origin including the ILV according to Directive 96/46/EC provided that MRLs will be proposed. See also open point 1.8. This data gap was identified at EPCO 25.			EPCO 25(24.-26.05.2005): Data gap identified.
	New open point 1.17 RMS to amend the list of end points according to the amendments proposed by EPCO 25.			EPCO 25(24.-26.05.2005): Open point still open.

Report of PRAPeR Expert MEETING 39

FOLPET

Rapporteur Member State: IT

Specific comments on the active substance in the section

2. Mammalian Toxicology

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

1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

2. Documents submitted for meeting:

Date	Supplier	File Name
Nov 2007	IT	Folpet JMPR eval DRAFT final_ed_2007.pdf
Nov 2007	IT	Folpet addendum Vol3 B6 ARfD (Nov 2007).doc
Nov 2007	IT	Folpet addendum Vol3 B6 ARfD (Nov 2007).pdf
24.04.2006	EFSA	praper_concl_sr70_folpet_rev3_en.pdf

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** xxx

5. **Classification and labelling:** xxx

6. **Recommended restrictions/conditions for use:** xxx

7. **Reference List:** xxx

Areas of concern: xxx

Appendix 1: Discussion table: CAPTAN

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet

2. Mammalian toxicology

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Italy, as Rapporteur Member State, requested a revision of the Acute Reference Dose of the active substances captan and folpet. Both substances were included in Annex I. **<u>Folpet</u>** During the experts' meeting (May 2005) it was considered that the developmental toxic effects might be relevant for the acute exposure. The final proposal from the meeting was an ARfD of 0.1 mg/kg bw based on a NOAEL 10 mg/kg bw/day (developmental study in rabbit, summarised in the DAR – LOAEL 40 mg/kg bw/day, endpoint: skeletal abnormalities), SF 100. It was noted that JMPR (2004) set a value of 0.2 mg/kg bw based on a different developmental study in rabbit (Feussner 1984) not evaluated by the RMS in the DAR, requested during the peer review process, but not presented in the final addendum. Recently the applicant submitted three new studies: a developmental study with phthalimide and two new studies to investigate the effects of folpet and phthalimide on microrganisms representative of the rabbit gut. <u>Discussion on toxicological relevance of phtalimide</u> IT then presented the information that was provided in addenda to the DARs of captan	

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		and folpet submitted to EFSA. Overall, the information presented there would give a different picture on the substance. Concerning the toxicological relevance of a the folpet metabolite phtalimide the experts discussed whether or not its properties were covered by the parent compound. A possible classification of the parent compound as Repr. Cat. 3 R63 was still an open issue while Carc. Cat. 3 R40 was already agreed for folpet. It was pointed out by EFSA that non-relevance of phtalimide would mean that its toxicity profile is of less concern than that of the parent compound folpet. The RMS pointed out that in regard to teratogenicity the metabolite was clearly of less concern based on the data available. Some experts reported that in regard to carcinogenicity there was an NTP study and some mechanistic data on phtalimide available, suggesting a non-relevance of this metabolite. In the subsequent discussion it was noted that the metabolite was in the residue definition and it was difficult to say whether it was of a lower toxicity profile than the parent compound or not. The RMS admitted that there was no full data set adding, however, that was also not necessary to assess the toxicity of the metabolite. To clarify the issue, the experts considered helpful to know the amount of the metabolite in the residue (in comparison to the parent compound). In some cases only phtalamide was found as a residue. There were indications that the metabolite was not of higher concern than the parent compound; however, the submitted data package was likely incomplete. Furthermore, since the experts had not been able to fully access the relevant information provided by the RMS, it was decided to postpone the discussion on the metabolites of folpet/captan to the next meeting. **It was agreed that the RMS provides further information on the following**	

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		endpoints on the metabolite phtalimide: Acute toxicity, genotoxicity, carcinogenicity, relevance of dog study and developmental effects in comparison to the parent compound. <u>Discussion on the setting of the ARfD of Folpet</u> The RMS (IT) introduced the addendum "Folpet - Position paper relating to non-setting and ARfD". The experts discussed the developmental data provided. It was agreed that the rabbit was the more sensitive species. The ARfD of 0.1 mg/kg bw was based on the data obtained in a first rabbit developmental study but now there was another rabbit study on the table (in the addendum) that has not been evaluated previously. The experts discussed the new information and agreed to a maternal NOAEL of 10 mg/kg bw/d and to a developmental NOAEL of 20 mg/kg bw/d. The Chair pointed out that the question was whether the effects observed would trigger and ARfD or not. It was noted that there were no teratogenic effects observed. Some inconsistencies are observed in the bodyweight; overall it was proposed to set the NOAEL at 20 mg/kg bw/d based on the occurrence of hydrocephalus. Considering a safety factor of 100 that would result in and ARfD of 0.2 mg/kg bw. The experts agreed to that.	

REPORT OF PRAPeR EXPERT MEETING 40

FOLPET

Rapporteur Member State: IT

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
Nov 2007	IT	Folpet addendum Vol3 B6 ARfD (Nov 2007).doc
Nov 2007	IT	Folpet addendum Vol3 B6 ARfD (Nov 2007).pdf
Nov 2007	IT	Folpet addendum Vol3 B7 (Nov 2007).doc
Nov 2007	IT	Folpet addendum Vol3 B7 (Nov 2007).pdf
11.07.2006	EFSA	praper_concl_sr70_folpet_rev3_en.pdf

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** Not relevant

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

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

7. **Reference List:** Not relevant

Areas of concern: Not relevant

Appendix 1: Discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet ()

3. Residues

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Review of the EFSA conclusions published in July 2006 with regard to the proposed ArfD value and the proposed residue definitions.	The EFSA conclusions on captan and folpet were published in July 2006. The applicant contested however the EFSA conclusion, in particular the toxicological end points and the residue definitions set for these substances. New data have been provided by the applicant and post-inclusion addenda were provided by the RMS. In order to address the issues raised by the applicant, the following four questions concerning captan and folpet were submitted by the residue section to the mammalian toxicology section: - Does the mammalian toxicology meeting confirm the ARfD adopted in the EFSA conclusion on 24th April 2006 or adopt another value? - Does the mammalian toxicology meeting still confirm that the ARfD applies to the general population? - In case the mammalian toxicology meeting considers that the ARfD applies to women of child-bearing age only, does the active substance exhibit at higher dose another acute toxicological effect which would be relevant for the general population, including infants and toddlers, and what would be the ARfD related to this effect ? - Does the mammalian toxicology meeting consider that captan metabolites (THPI, 3-OH THPI and 5-OH THPI) and folpet metabolite (phthalimide) participate to the effects selected for setting reference values (ADI and ARfD) of the respective parent compounds? Following these questions, the mamalian toxicology meeting decided to revise the ARfD values and the ARfD values of the JMPR have been adopted by the meeting (0.2 mg/kg bw/d for folpet and 0.3 mg/kg bw/d for captan). These end points are considered to be applicable to the total population. Concerning the metabolites the mamalian toxicology meeting didn't reach a conclusion yet because some data were not fully reported in the addenda. The discussion in the tox section concerning these metabolites has been	The new ARfD values proposed by the mammalian toxicology section will not affect the overall outcome of the residue risk assessment. Concerning the residue definitions the residue section awaits the outcome of the mammalian toxicology section on the relevance of the metabolites.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		postponed to a next meeting (probably in April 2008). When using the new ARfD values in the risk assessment, the uses supported in the the framework of the peer review still lead to an exceedances of the ARfD for toddlers. Therefore the new ARfD values don't influence the outcome of the previous assessment. In addition the meeting disagrees with the fact that the mamalian toxicology section didn't restrict the proposed ARfD values to the appropriate subpopulation and that it didn't consider the need for an alternative reference dose for the rest of the population. The approach followed by the mamalian toxicology meeting results in a risk assessment comparing an ARfD to the exposure of the wrong subpopulation.	

Report of PRAPeR Expert MEETING 44

FOLPET

Rapporteur Member State: IT

Specific comments on the active substance in the section

2. Mammalian Toxicology

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

1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

2. Documents submitted for meeting:

Date	Supplier	File Name
Nov 2007	IT	Folpet addendum Vol3 B6 ARfD (Nov 2007).doc
March 2008	IT	Folpet addendum Vol 3 B6 B7 (Mar 2008).doc
Nov 2007	IT	Folpet addendum Vol3 B7 (Nov 2007).doc
07.03.2006	IT	Folpet evaluation table rev2-1 (07-03-2006).doc
2007	IT	Folpet JMPR evaluation DRAFT (2007).pdf
April 2006	EFSA	praper_concl_sr70_folpet_rev3_public_en.pdf
10.05.2005	EFSA	Report EPCO 23 – 05 Folpet.doc
13.12.2007	EFSA	Report PRAPeR_39_06_folpet.doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** no need to discuss

5. **Classification and labelling:** no need to discuss

6. **Recommended restrictions/conditions for use:** no need to discuss

7. **Reference List:** no need to discuss

Areas of concern: no need to discuss

Appendix 1: Discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

2. Mammalian toxicology

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Folpet is included in Annex I to the Directive 91/414. After the inclusion, the RMS Italy asked for a revision of the toxicological profile of phthalimide, based on the availability of new toxicological studies. <u>Discussion on the toxicological relevance of metabolite of folpet PHTHALIMIDE</u> The RMS presented extensively the information on the toxicological properties of folpet and its metabolites which had been laid down in detail in the addendum to Volume 3, Annex B, submitted in March 2008. Phthalimide is a main metabolite of folpet. The parent compound has been proposed for classification as a carcinogen and a reprotoxic agent and the metabolite should be considered to have the same toxicity profile unless the contrary is proven. Folpet and the metabolite phthalimide are currently in the residue definition. The proposal of the RMS is to remove the metabolite from the residue definition since the data indicated that phthalimide has a lower toxicity profile. The toxicological information on folpet and phthalimide were compared: • Acute oral toxicity: Folpet LD50>5 g/kg Phthalimide LD50>5 g/kg • Genotoxicity Folpet is mutagenic *in vitro* Phthalimide is not mutagenic *in vitro* • Carcinogenicity	

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Folpet induces gastrointestinal tumours in mice, primarily in the duodenum (due to local chronic irritation) Phthalimide was not tested for carcinogenicity; however the absence of treatment-related systemic tumours would indicate that folpet products of degradation are not carcinogenic. • Developmental toxicity Folpet induces secondary developmental delays in rabbit foetuses in presence of maternal toxicity. Relevant NOAEL 10 mg/kg bw/day. Phthalimide is not teratogenic in rabbit, nor does induce maternal toxicity at equivalent folpet doses (based on a ratio of about 2:1 folpet:phthalimide). Relevant NOAEL 30 mg/kg bw/day (equivalent to 60 mg/kg bw/day folpet) As for the products of degradation of phthalimide (phthalamic acid and phthalic acid) it is assumed that have also lower toxicity than folpet since they represent detoxification products of phthalimide . There is also mechanistic information available that the part of the molecule responsible for the toxic effects of concern is thiophosgene that is formed immediately after administration of folpet. Phthalimide does no not contain the moiety trichloromethyltio (TCMT) that is responsible for both pesticidal activity and mammalian toxicity of folpet. The TCMT moiety reacts with thiol groups resulting in protein denaturation and captan degradation, whose product is thiophosgene, responsible for degradation of thiols and other functional groups. The weight of evidence indicates that folpet induces gastrointestinal tumours in mice by a non genotoxic mechanism involving citotoxicity and consequent cell hyperplasia, responsible of the cascade of events leading to cancer, but for which a threshold is recognized. **The experts agreed that the results of the existing studies demonstrate less toxicity of phthalimide compared with Folpet. Also mechanistic data indicate that phthalimide does not have the potential to induce critical effects (carcinogenic, reprotoxic effects).**	

Appendix 2: Evaluation table

No amendment of the evaluation table necessary or foreseen at this stage.

REPORT OF PRAPeR EXPERT MEETING 45

FOLPET

Rapporteur Member State: IT

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
Dec 2007	EFSA	Folpet – information.doc
March 2008	IT	Folpet addendum Vol3 B6 B7 (Mar 2008).doc
Nov 2007	IT	Folpet addendum Vol3 B7 (Nov 2007).doc
07.03.2006	IT	Folpet evaluation table rev2-1 (07-03-2006).doc
April 2006	EFSA	praper_concl_sr70_folpet_rev3_public_en.pdf

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** none

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

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

7. **Reference List:** not discussed

Areas of concern: none

Appendix 1: Discussion table: FOLPET

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Folpet (Fu)

3. Residues

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
3.1	<u>EPCO 24 (11.05. – 13.05.2005):</u> The meeting confirmed that the specific hydrolysis studies are still required. Data requirement still open. <u>Evaluation Meeting (06.-09.02.2006):</u> Data requirement still open.	According to the RMS these studies were reported in an addendum to the dossier of February 2006. This addendum indicates that in processed commodities folpet is completely transformed to phthalimide and phthalic acid. Phtalic acid is not to be considered of any toxicological concern. However the document was not available to all experts in advance to the meeting and the data requirement therefore remains open.	Data requirement still open.
	New open point Residue definition to be rediscussed.	The applicant asks for phthalimide to be excluded from the residue definitions. Toxicological data have been provided to the toxicological section in order to demonstrate that the metabolite is not of toxicological significance. The toxicological section clearly concluded that the metabolite does not show the same toxicity profile as the parent compound and that no signs of toxicity have been identified for it. However, a complete toxicological data set for this metabolite was not available and the toxicological section was not able to derive toxicological end points. The toxicological meeting therefore decided that for the time being that the toxicological end points of the parent compound should be used also for the metabolite.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		Considering the opinion of the toxicological section, the residues meeting concludes that the metabolite needs to be retained in the residue definitions. The residue definitions are not modified. The meeting notes that the ARfD for folpet has been raised from 0.1 to 0.2 mg/kg bw/d.	

Appendix 2: Evaluation table

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Section 3 Data requirements: ***3*** Open points: ***3***			Section 3 Data requirements: ***1*** Open points: **-** Data gaps: **-**
	Open point 3.1: RMS to prepare an acute risk assessment in an addendum to be discussed in expert meeting. (see reporting table 3(3))	The notifier contends that an ARfD for folpet is not necessary. This is supported by a position paper summarised in the new addendum under Point IIA 5.10/01.	Using the UK model for the determination of the acute intake, the ARfD for table grape is exceeded by the 807 % in toddler and by the 167% in adults. Other values are 17.8% of the ARfD for tomatoes in adults and 82.2% of the ARfD for tomatoes in toddler. Oct. 05 List of representative use amended (See Addendum) since the Notifier advised the RMS that regarding use on grapes, only wine grapes are supported for the EU review and not table grapes. The existing GAP for grapes is unchanged but this relates to wine grapes only. (Uses on wheat and tomato are also supported by the Notifier)	EPCO 24 (11.05. – 13.05.2005): Acute risk assessment was presented by the RMS. Open point fulfilled.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
3.1	Notifier to provide hydrolysis studies in representative hydrolytic conditions. (see reporting table 3(5))	A position paper (Goodyear, 2004) is summarised in the new addendum under Point IIA 6.5.1/01. **Conclusion**: The position paper concludes that sufficient data already exist to predict the effect of processing hydrolysis on the nature of the residue and therefore new studies are not required.	Data discussed in the position paper do not fulfil the point. Specific studies are still required. Moreover we have been informed from the applicant that hydrolysis studies are on going and results will be available soon. Oct. 05 Data requirement still open.	EPCO 24 (11.05. – 13.05.2005): The meeting confirmed that the specific hydrolysis studies are still required. Data requirement still open. Evaluation Meeting (06.-09.02.2006): Data requirement still open. PRAPeR 45 (10 – 11 April 2008): Data requirement still open.

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
3.2	Notifier to provide a whole balance study for tomato washed, peeled and canned or used for juice, 3 follow-up studies in juice and canned tomato. (see reporting table 3(6))	The results of a new balance study and three follow-up studies (Pollmann, 2005) are summarised in the new addendum under Point IIA 6.5.2/07. **Conclusion**: The studies show that there is no concentration of folpet residues in tomato juice and canned tomato fruit (human edible commodities).	Studies have been revised. The conclusions of the main data submitter are accepted. Oct. 05 Following results of the last toxicological evaluations (see the Addendum "definition of the residue" of July 2005) the residue definition for folpet was changed going back to the parent compound alone, (residue definition for folpet=folpet). Data requirement is therefore fulfilled	EPCO 24 (11.05. – 13.05.2005): Studies need to be re-evaluated in the light of the new residue definition. Data requirement still open for formal reasons. Evaluation Meeting (06.-09.02.2006): According to the information present in the addendum, phtalimide was not analysed Data requirement closed

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
3.3	Notifier to provide 2 greenhouse residue trials for tomatoes. (see reporting table 3(7))	The results of the existing studies and arguments against the need for new studies are presented in the new addendum under Point IIA 6.3. **Conclusion:** The notifier contends that, since a EU MRL for folpet in tomatoes already exists, and since the existing value of 3 mg/kg is supported by the results of 10 trials carried out under worst-case conditions for residues, i.e. under greenhouse conditions, (of which 6 are validated by freezer storage study), it is not necessary to set a new MRL for folpet in tomato as part of the EU review of folpet. Therefore, it is concluded that as sufficient information is available, additional residue trials in greenhouse grown tomatoes are not required for the EU review of folpet.	Ten trials in greenhouse grown tomatoes treated according to the EU GAP were originally presented. In four trials, samples were stored for periods longer than the period tested in freezer storage stability studies and so were not accepted. According to the applicant, new freezer storage stability study in tomato fruit is underway to validate the residue studies in tomato which were not accepted, and results will be available at the beginning of 2006. The MRL for folpet in tomatoes of 3 mg/kg is therefore provisionally accepted, waiting for results of the above mentioned studies. <u>Oct. 05</u> Data requirement still open.	<u>EPCO 24 (11.05. – 13.05.2005):</u> Results of studies have to be awaited. Data requirement still open. <u>Evaluation Meeting (06.-09.02.2006):</u> The data requirement is obsolete (see new open point 3.4).

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	Open point 3.2: MS to discuss the residue definition for risk assessment in an expert meeting. RMS to prepare an assessment of the toxicological relevance of metabolites (including their contribution to the toxicological burden). (see reporting table 3(12))	A review of the toxicity of potential folpet metabolites is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/01. In addition a discussion paper by Gordon (2005) is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/02. **Conclusion**: The discussion paper expands on the discussion of the toxicological significance of the degradates of folpet and concludes, based on the DG SANCO Guideline for Metabolism and Distribution in Plants (European Commission 1997) that they are not of toxicological significance and should not be included in the residue definition for risk assessment expression. The definition of the residue in plants is therefore folpet alone. This conclusion is consistent with the conclusion of the RMS.	Assessment has been included in the addendum and is open for discussion. According to our opinion, folpet metabolites are of low toxicological significance compared to folpet. Residue definition for risk assessment should be therefore folpet alone. Oct. 05 Following results of the last toxicological evaluations (see the Addendum "definition of the residue" of July 2005) the residue definition for folpet was changed going back to the parent compound alone, (residue definition for folpet=folpet). The open point is therefore invalid. The amendment of the list of end-point no more required.	EPCO 24 (11.05. – 13.05.2005): Open point fulfilled. Due to the change in the residue definition a new open point was proposed: New open point 3.4: RMS to go back to the available data set and make new evaluation of the available data so that the MRL proposals and the risk assessment can be done on the basis of the new residue definitions. The new calculations should be summarised in an addendum. RMS to amend the list of end points. (See new open point 3.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	New open point 3.4: RMS to go back to the available data set and make new evaluation of the available data so that the MRL proposals and the risk assessment can be done on the basis of the new residue definitions. The new calculations should be summarised in an addendum. This open point was proposed at EPCO 24.		Oct. 05 Open point still open.	EPCO 24 (11.05. – 13.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): The raw data have been assessed by EFSA. The result is that the available data (supervised residue trials and processing studies) do not contain sufficient data on the presence of phtalimide in commodities. Consequently such studies should be carried out accordingly to the residue definition established in expert's meeting. Also the data requirement 3.3 needs to be considered as obsolete. Open point fulfilled.
	Open point 3.3: MS to discuss the residue definition for animal commodities, including the need for it, in an expert meeting.	A review of the toxicity of potential folpet metabolites is summarised in new addendum under Point IIA 6.7 and Point II 5.8.1/01. In addition a discussion paper by Gordon (2005) is summarised in new addendum under Point IIA 6.7 and	A discussion has been included in the addendum. For animal commodities, as shown by table B.7.2.4 of the DAR, folpet is the only possible indicator, since other (possible) intermediate/s are rapidly transformed into natural compounds in	EPCO 24 (11.05. – 13.05.2005): Open point fulfilled. RMS to amend the list of end points. (See new open point 3.5)

No.	Column A Conclusions of the EFSA Evaluation Meeting	Column B Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion	Column C Rapporteur Member State comments on main data submitter / applicant comments	Column D Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting
	(see reporting table 3(13)) *continued* Open point 3.3: MS to discuss the residue definition for animal commodities, including the need for it, in an expert meeting. (see reporting table 3(13))	Point II 5.8.1/02. **Conclusion**: The discussion paper expands on the discussion of the toxicological significance of the degradates of folpet and concludes, based on the DG SANCO Guideline for Metabolism and Distribution in Plants (European Commission 1997) that they are not of toxicological significance and should not be included in the residue definition for risk assessment expression. The definition of the residue in animal commodities is therefore folpet alone. This conclusion is consistent with the conclusion of the RMS.	muscle and milk. The need for a residue definition in animal commodities should be discussed during the next expert meeting. <u>Oct. 05</u> Following results of the last toxicological evaluations (see the Addendum "definition of the residue" of July 2005) the residue definition for folpet was changed going back to the parent compound alone, (residue definition for folpet=folpet). The amendment of the list of end-points no more required.	
	New open point 3.5: RMS to revise the list of end points according the amendments proposed by EPCO 24.		<u>Oct. 05</u> Following results of the last toxicological evaluations (see the Addendum "definition of the residue" of July 2005) the residue definition for folpet was changed going back to the parent compound alone, (residue definition for folpet=folpet). The open point is therefore invalid.	<u>EPCO 24 (11.05. – 13.05.2005):</u> Open point still open. <u>Evaluation Meeting (06.-09.02.2006):</u> Open point fulfilled.