PEER REVIEW REPORT ON **FOLPET** 20.03.2006

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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: ***1*** Open points: ***-*** Data gaps: ***3***
	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.		Oct. 05 Addenda to the DAR (vol.3 and vol.4) have been prepared and already sent to the EPCO-Team (BVL) by 21/06/05.	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
	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.		Oct. 05 The document tabled at the meeting was written by the RMS, without distinguish between confidential and non-confidential information, due to our mistake. See general open point 1.12.	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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.
	Message from EPCO 25 to toxicology and ecotoxicology section to confirm that [redacted] has not to be regarded as a relevant impurity.			

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	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 Oct. 05 Data included in the addendum to vol.3. See new general open points	EPCO 25(24.-26.05.2005): Data requirement: still open for technical reasons. See general points Evaluation Meeting (06.-09.02.2006): Data requirement fulfilled.

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	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.

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	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 Oct. 05 Noted	EPCO 25(24.-26.05.2005): Open point closed. Data gap 1.6 identified. New open point 1.14. New open point 1.15. Data gap 1.7 identified.
1.6	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.		Oct. 05 Noted - Will be addressed when the definition of the residue is finalised.	EPCO 25(24.-26.05.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap still open

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	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.		Oct. 05 The following modifications in the ILV (Williams) have been made 1) for all crops (oily and non-oily) the final solvent for GC/ECD determination was changed from hexane to 2% di(ethylene-glycol)-diethylether in hexane (to reduce folpet degradation). In this context, the modification belong to both the Schleisinger and Nishioka methods. 2) Among non-oily crops (onion, apples, cantaloupe, cranberries, cucumbers, grapes, lettuce, strawberries and tomatoes), an additional purification step, based on a C18 solid phase extraction following the florisil clean-up, has been applied only to onion, a matrix not considered by the Scheisinger method. 3) For oily crops (avocado), two additional purification steps were included following the GPC clean-up. This modification belong only to the Nishioka method.	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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.		Oct. 05 The two laboratories are completely independent according to the information presented in the study reports. The study of Byast was carried out by Oxford Analytical Limited in the UK and the study of Simek was conducted by Anadiag in France. Therefore, the method of Simek may be considered to be an ILV of the Byast method.	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
1.7	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.		Oct. 05 A confirmatory method for folpet in grapes and tomatoes has been sent to the RMS (20/09/05). Data will be evaluated. The request for phthalimide will be addressed by the notifier when the definition of the residue is finalised.	EPCO 25(24.-26.05.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap still open.
	Open point 1.6: The need for further information regarding the flowability should be discussed in an expert meeting.	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,	Apr. 05 The conclusions are acceptable, but the data on the flowability will be discussed in an expert meeting Oct. 05 Noted	EPCO 25(24.-26.05.2005): Open point closed. New open point 1.16.

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	(see reporting table 1(11)) *continued* Open point 1.6: The need for further information regarding the flowability should be discussed in an expert meeting. (see reporting table 1(11))	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.		
	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.		Oct. 05 Noted	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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 Oct. 05 Noted – EP list amended	EPCO 25(24.-26.05.2005): Open point still open. RMS to amend the list of end points. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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 Oct. 05 Noted – EP list amended	EPCO 25(24.-26.05.2005): Open point still open. Depends on the final proposal by the 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. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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.
	Message from EPCO 25 to fate and behaviour section to confirm the DT_{90} value in surface water of below 1 day.			

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	Message from EPCO 21 to EPCO 25: EPCO 21 confirms that the DT_{50} in surface water is less than 3 days. See open point 4.16.			
	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.

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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 Oct. 05 Data included in the addendum to vol.4. See general open points	EPCO 25(24.-26.05.2005): Data requirement is still open for formal reasons. The information has to be presented in an addendum. See also general points Evaluation Meeting (06.-09.02.2006): Data requirement fulfilled.
	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.

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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 Oct. 05 Noted	EPCO 25(24.-26.05.2005): Data requirement closed. Message to toxicology and ecotoxicology experts: 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. Data gap 1.8 identified.
	Message from EPCO 25 to toxicology and ecotoxicology experts: Has [redacted] to be regarded as a relevant impurity?			Evaluation Meeting (06.-09.02.2006): ongoing

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	Message from EPCO 25 to toxicology experts: To confirm that [redacted] has not to be regarded as a relevant impurity in the technical material of folpet.			Evaluation Meeting (06.-09.02.2006): ongoing
1.8	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.		Oct. 05 Noted	EPCO 25(24.-26.05.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap still open.

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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 Oct. 05 Data will be evaluated when available	EPCO 25(24.-26.05.2005): Data requirement still open. Evaluation Meeting (06.-09.02.2006): Data requirement still open.

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1.9	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.		Oct. 05 Noted	EPCO 25(24.-26.05.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap closed, no MRLs are proposed.
	New open point 1.17 RMS to amend the list of end points according to the amendments proposed by EPCO 25.		Oct. 05 EP list amended	EPCO 25(24.-26.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

2. Mammalian toxicology

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	Section 2 Data requirements: ***4*** Open points: ***16***			Section 2 Data requirements: **-** Open points: ***1*** Data gaps: **-**
	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" suggests that an uncertainty exists regarding the carcinogenic potential of folpet. There is no such uncertainty with folpet. Robust chemical/physical	April 2005 (1) 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 appear only above a dose that causes chronic toxicity. (2) see above	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Classification: category 3, R 40 based on effects in the mouse study.

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	continued Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	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. 4. Folpet is not carcinogenic in rats or dogs; the gastrointestinal tumors (primarily in the duodenum)	(3) RMS supports the Notifier's response (see data presented in the addendum (table 10H)	

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	continued Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	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. (2) Denmark suggests classification for carcinogenicity, based on the increased incidences of adenomas and		

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	continued Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	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 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).		

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	continued Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	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). (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		

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	continued Open point 2.2: MS to discuss the carcinogenic properties at an expert meeting. (see reporting table 2(2))	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, 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		

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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 NOAEL of 450 ppm is supported.		
2.1	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 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.	April 2005 Summaries provided in the addendum	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

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	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)
2.2	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 developing young to folpet. Further reproductive or developmental toxicity testing of folpet should not be required.	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.

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	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)

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	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))	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 b.w. for the derivation of the ADI value.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. ADI: 0.1 mg/kg, SF 100, based on the1 year dog supported by the 2-year rat.
2.3	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.	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))	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 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		

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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))	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 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		

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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))	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. 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		

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		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 adverse effects. The weight of evidence shows that eye damage is restricted to surface areas (including the cornea) but that these insults do recover.		
	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))	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.		

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		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, 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.

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	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 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*.	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 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.	EPCO 23 (10 – 13.5.2005): Open point fulfilled.

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	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)) *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))	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 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	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 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.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. No genotoxic potential in vivo

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	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 the rat carcinogenicity study of Crown (1985) to be 500 ppm, based on	April 2005 RMS agrees	EPCO 23 (10 – 13.5.2005): Open point fulfilled. See open point 2.2

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	continued Open point 2.11: MS to confirm the NOAELs in the long term studies at an expert meeting. (see reporting table 2(22))	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.		

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	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. 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.	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. Oct.05 RMS: in a document sent in July 2005 to EFSA we confirmed the lack of toxicity of folpet metabolites. In addition, further data presented as position paper by notifier (sept 05) to the RMS demonstrate that parent compound and its main metabolite (Phthalimide) do not show developmental toxicity. This document reinforces the opinion of the RMS that Folpet MUST NOT be labelled R63	EPCO 23 (10 – 13.5.2005): Open point still open Evaluation Meeting (06.-09.02.2006): RMS to summarise the rabbit developmental study assessed in the JMPR evaluation (2004). Open point still open.

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		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. 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		

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	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))	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] 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 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] 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		

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	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))	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 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		

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	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))	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 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.		

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	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))	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 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.	April 2005 RMS agrees with the Notifier‘s conclusions.	EPCO 23 (10 – 13.5.2005): Open point fulfilled. Phthalimide and phtalic acid are present in the in vivo studies. The ADI for folpet cover the metabolites.

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	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 radioactivity), with a higher rate of excretion at lower doses.	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.

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2.4	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 accepts a 1% absorption rate while this issue is further evaluated by EU scientists.	April 2005 See above	EPCO 23 (10 – 13.5.2005): Data requirement fulfilled.

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	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 Oct. 2005 Calculations of operator exposure using a 10% dermal absorption value show exposure levels below the AOEL for all intended uses when operators wear protective clothing (see Addendum). Two new assessments of exposure in greenhouses (tomatoes) are provided in the Addendum. The first estimate, based on surrogate exposure data (IVA, 1996), show exposure levels below the AOEL (from 29% to 33% of the AOEL) when protective gloves, cotton overalls and impermeable (chemical proof) coveralls is worn during mixing/loading and application. The exposure study did not measure exposure for operators wearing protective gloves only The second assessment (based on EUROPOEM with BBA data), show acceptable exposure for operators wearing protective gloves when handling the concentrate and during application (83% of the AOEL).	EPCO 23 (10 – 13.5.2005): Open point still open A new estimation on operator exposure has to be submitted for all uses. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	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 Oct. 05 New calculations of bystander exposure using a 10% dermal absorption value show that exposure of bystanders is below the AOEL (1,6% of the AOEL).	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 Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	Open point 2.16: MS to discuss available residue decline data with respect to worker exposure at an expert meeting.	A new risk assessment to workers using decline data is summarised in 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.	April 2005 RMS agrees Oct. 05 Calculations of worker exposure using a 10% dermal absorption value show that, based on dislodgeable residue data following repeated applications (available for captan), the estimated exposure for workers re-entering grape and tomato crops treated with 'Folpan 80 WDG' is 133% and 68% of the AOEL, respectively. Therefore, it is necessary for workers to wear protective gloves for harvesting operations in treated grapes.	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 Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
	Message from EPCO 21 to tox section (EPCO 23): It cannot be excluded that traces of thiophosgene occur in the air.			Evaluation Meeting (06.-09.02.2006): Noted Closed.

section 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
	Message from EPCO 25 to experts of toxicology and ecotoxicology section: To confirm that [redacted] has not to be regarded as a relevant impurity. See open point 1.1.			Evaluation Meeting (06.-09.02.2006): This issue is still open
	Message from EPCO 25 to experts of toxicology and ecotoxicology section: Has [redacted] to be regarded as a relevant impurity. See data requirement 1.4.			Evaluation Meeting (06.-09.02.2006): It is classified T + and is thus considered as a relevant impurity. Closed
	Message from EPCO 25 to toxicology experts: To confirm that [redacted] has not to be regarded as a relevant impurity in the technical material of folpet. sSee data requirement 1.4.			Evaluation Meeting (06.-09.02.2006): It is classified T and is thus considered as a relevant impurity. Closed

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
	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.

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
3.1	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.
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

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
3.3	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. Oct. 05 Data requirement still open.	EPCO 24 (11.05. – 13.05.2005): Results of studies have to be awaited. Data requirement still open. Evaluation Meeting (06.-09.02.2006): The data requirement is obsolete (see new open point 3.4).

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
	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. (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.	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	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))	**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.	animal commodities should be discussed during the next expert meeting. 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 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.		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.	EPCO 24 (11.05. – 13.05.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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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 requirements: **-** Open points: **-** Data gaps: ***2***
	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 Oct. 05 Notifier has provided revised FOCUS gw modelling and list of endpoints has been 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

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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.			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.
	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.		Oct. 05 Phthalimide is not increasing in the sediment at the end of the study. List of endpoints amended.	EPCO 21 (11. – 14.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
	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.

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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	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.

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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))	readily released from the sediment, except as carbon dioxide or methane. 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.		
	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	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. Data gap 4.5 identified: 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.

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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
		0.8 and 28.2 days, only.		
4.5	Calculation of PEC sw with consideration of drainage needs to be done. This data gap was identified at EPCO 21.		Oct. 05 Notifier has provided an assessment which demonstrated that drainage is not an exposure route of concernbased on FOCUS SW scheme. This assessment is summarised in a DAR Addendum (Oct. 2005).	EPCO 21 (11. – 14.04.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap open for formal reasons.
	Message from EPCO 21 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.

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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.

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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 Oct. 05 List of endpoints amended.	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). Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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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).

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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 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.		Oct. 05 New mean DT50 values have been calculated by the Notifier. These have been used in new groundwater modelling. List of endpoints has been amended.	EPCO 21 (11. – 14.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
	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.

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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
	Message from 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 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*		EPCO 21 (11. – 14.04.2005): Open point fulfilled. The experts agreed to disregard Koc values from two LUFA but use Koc values

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	continued 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))	*using the FOCUS groundwater scenarios* and a pragmatic approach for use of the data advanced.	Oct. 05 List of endpoints amended.	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 the study report: *Folpet. Degradability in the water/sediment system. (Crowe, A. 1999; IIA, 7.2.1.3.2/01)* see page 33.	Oct. 05 The goodness of fitting for the calculated water/sediment DT50 values are not provided in the water/sediment study. However, given the clearly very fast degradation of folpet and its metabolites in the water/sediment systems it is considered that goodness of fitting values are not needed.	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.

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	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 4.6 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.

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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. This data gap was identified at EPCO 21.		Oct. 05 Notifier has provided new FOCUS groundwater modelling incorporating the required changes. This is evaluated in a DAR Addendum (Sept. 2005). List of endpoints has been amended. PECgw are <0.001 µg/L. Hence, low risk to groundwater.	EPCO 21 (11. – 14.04.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): It will be indicated in the conclusion that the input parameters have been checked by the RMS and EFSA Data gap open for formal reasons.
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 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.

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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 DT_{50} in surface water is less than 3 days.			
	Message from EPCO 25 to the fate experts: To confirm the DT90 value in surface water of below 1 day. See open point 1.9.			

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	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.

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	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.		Oct. 05 List of endpoints amended.	EPCO 21 (11. – 14.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	Section 5 Data requirements: ***5*** Open points: ***12***			Section 5 Data requirements: ***-*** Open points: ***2*** Data gaps: ***2***
	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. 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:	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.

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	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))		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.		Oct. 05 RMS (September 2005): Applications to winter wheat are only on late growth stages (which are unpalatable). Hence, low risk to herbivorous birds and mammals.	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.

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	New open point 5.14: 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.		Oct. 05 Notifier submitted recalculated TERs using default RUD and NOEL of 78.3 mg/kg bw/d. TER for cereal use is >5. For grapes and tomato TERs are 2.9 and 3.4, i.e. <5. Higher tier risk assessment has been submitted (Ref: Gerlach, 2005) based on published ecology information. Risk assessment evaluated in Addendum to DAR (Sept 2005) . Choice of key species (yellow wagtail for tomato; yellowhammer and cirl bunting for grapes) and refinements considered to be reasonable. Refined TERs range from 11.3 to 13.3, i.e. >5. Taking refined assessment together with fact that no effects in avian reproduction studies at highest treatment level of 1000 ppm, risk is considered to be acceptable	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): 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.		Oct. 05 RMS (September 2005): RMS has reviewed the endpoint and proposes to remain with original value (548.6 mg/kg bw/d). This issue is considered in a DAR Addendum (Sept 2005).	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point still open.

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	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.		Oct. 05 This will be corrected.	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Will be done by EFSA Open point closed.
	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))		List of endpoints amended	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.
	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.

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	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 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	EPCO 22 (11.04.-15.04.2005): Data requirement fulfilled.

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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 number 18202060. Date: 27 January 2004. (Company file R-16401). (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 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.

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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.

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	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 end points.

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	New open point 5.17: The tested dose rate of the field studies should be added in the list of end points. See open point 5.5. This open point was proposed at EPCO 22.		Oct. 05 List of endpoints has been amended.	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
	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.

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	Open point 5.7: MS to discuss the risk to non target plants in an expert meeting. (see reporting table 5(14))	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.
	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 5.6 identified.

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	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 proposed at EPCO 22.		Oct 05 Notifier has submitted a justification that endpoints from the 28 d semi-static study on rainbow trout should not be used to derive TERs. Study should be used to indicate no build-up of effects from multiple applications. TERs should be based on *acute* static studies. RMS agrees with Notifier (issue addressed in a DAR addendum, Oct. 2005)	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point still open.
	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.		Oct. 05 Endpoint for brown trout (*Salmo trutta*) already included in list of endpoints. Latin name added for clarification.	EPCO 22 (11.04.-15.04.2005): Open point still open. Evaluation Meeting (06.-09.02.2006): Open point fulfilled.
5.6	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.		Oct. 05 Risk assessment should be based on acute risk to fish. 21 day semi-static study on *D. magna* is regarded as supplementary information. To provide reassurance, Notifier proposes to conduct the study for submission at Member State level.	EPCO 22 (11.04.-15.04.2005): Data gap identified. Evaluation Meeting (06.-09.02.2006): Data gap still open.

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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 5.10: 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 evaluate the study by Nengel 1996c on bees in an addendum and revise the risk assessment for bees accordingly. (see reporting table 5(44))	For information, this study on Folpan 80 WDG shows a low toxicity to bees (acute oral and contact LD50 of >179 and >160 µg a.s./bee, respectively).	The missing summary has been reported in the addendum. There were no significant mortalities at any dosage 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	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))		See point 5.6	EPCO 22 (11.04.-15.04.2005): Open point fulfilled.

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M 1	Message from EPCO 21 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.			EPCO 22 (11.04.-15.04.2005): The metabolites are not regarded as relevant.
M 2	Message from EPCO 25 to experts of the toxicology and ecotoxicology section: To confirm that [redacted] has not to be regarded as a relevant impurity. See open point 1.1.			Evaluation Meeting (06.-09.02.2006): No information was provided, therefore a data gap is proposed.
5.6	New Data gap Information on the ecotoxicological relevance of [redacted] is required. See M 2			Evaluation Meeting (06.-09.02.2006): Data gap still open

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M 3	Message from EPCO 25 to toxicology and ecotoxicology experts: Has [redacted] to be regarded as a relevant impurity? See data requirement 1.4.			Evaluation Meeting (06.-09.02.2006): No information was provided, therefore a data gap is proposed.
5.7	New Data gap Information on the ecotoxicological relevance of [redacted] is required. See M 3			Evaluation Meeting (06.-09.02.2006): Data gap still open