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0. General

General				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(1)	Vol. 1, Level 1, 1.3.1 Name and address of applicant, pg 5 Vol. 3, B.1.1.1, pg 1-2	DAS: please change the Central address and contact person Dow AgroSciences, European Development Center 2nd Floor Milton Park Abingdon OX14RN – OXON United Kingdom [redacted] Regulatory Team Leader, Europe Phone ++39 02 48224086 Fax ++29 02 48224384	The central address and contact person have been amended (see updated version of Vol.3(B1) dd. September 2006).	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated version of Vol. 3 (B.1) is not available for the moment.
1(2)	Vol. 1, Level 1, 1.4.2 Manufacturer of the plant protection product, pg 8 Vol. 3, B.1.2.2, pg 1-5	DAS: please change Dow AgroSciences B.V. to Dow AgroSciences Italia S.r.l	Name of manufacturer of plant protection product has been amended (see updated version of Vol.3(B1) dd. September 2006).	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated version of Vol. 3 (B.1) is not available for the moment.

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(3)	Vol. 4, C.1.3 composition of the formulation	AT: A detailed composition of GF-1062 is required, since it is described under B.2.2 as similar to GF-1317. If RMS confirm the analogousness (except the replaced co-formulant), this point is superfluous.	RMS confirms that the only difference in composition between GF-1062 and GF-1317 is the co-formulant that has been replaced.	Addressed RMS to consider in a revised DAR or corrigendum.
1(4)	Vol. 1; 2.1.1 Identity, pg 16 Vol. 1, Level 4, 4.1 Identity of the active substance, Impurity profile, pg 76 *"The notifier should provide a case and/or data to show that the increased levels of both impurities will not have a significant adverse effect on the toxicity of technical Myclobutanil."*	DAS: a position document for the impurities in myclobutanil batch, including an assessment on the QSAR analysis was provided to RMS (June, 2005). QSAR assessment: DEREK reported no alerts. TOPKAT noted skin sensitisation and ocular irritation for both impurities at different severity levels (**imp. 3** being more severe), though accuracy cannot be determined. DEREK included skin sensitisation/ocular irritancy endpoints. Excedance of **imp. 3** (with greater predicted severity level) above the acceptable maximum limits (8% or 1g/kg) would not cause concern for these 2 tox end-points with new source. TOPKAT assessment of **imp. 8** shows lower severity levels for eye irritation/sensitisation, though sensitivity of this prediction is not clear. However, based on available data, the increased levels of this impurity in the new source would not lead to a change in hazard potential for myclobutanil.	The company provided a QSAR analysis that was considered as acceptable by the RMS and the increased levels of impurities 3 and 8 in the manufactured batch were considered as not toxicologically significant. This evaluation is included in an addendum of confidential information (see addendum Vol.4 (C1-C2) dd. September 2006). Data requirement is considered to be fulfilled.	Data requirement (for formal reasons) The applicant should provide a case and/or data to show that the increased levels of both impurities (3 and 8) will not have a significant adverse effect on the toxicity of technical Myclobutanil [This should be regarded as a technical data requirement since the data have been already submitted to the RMS] See also comment 1(8) This point to be transferred to the tox section.

Identity (B.1, Annex C)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(5)	Vol. 1, list of end points, minimum purity, p. 39 in relation to Volume 4	EFSA: According to Directive 94/37/EC the ratio of the content of the isomers must be provided. It seems that this information is not reported in the DAR. Furthermore, is the assumption correct that both isomers have the same biological activity, due to the fact that nothing else is mentioned?	As in the production process of myclobutanil neither stereo-selective reaction types nor enantiomerically pure substances are used, the myclobutanil obtained is a racemic mixture, i.e. 50:50 mixture of the two possible optical isomers. The nofier stated that there is no difference in biological activity between the two isomers.	Open point RMS to amend the list of end points to clarify the ratio of both enantiomers (preferably in the box "minimum purity").

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(6)	Vol. 1, LOEP, surface tension	NL: The purity of the a.s. from which the surface tension has been measured is only 92.1 %. This is no purified (>98%) material and doesn't meet even the specification for technical a.s. (92.5).	In Commision Directive 96/46/EEC, no requirement with respect to purity is set for testing surface tension. Moreover, in EEC A5, it is stated that the described methods are applicable to most substances "without any restriction with respect to their degree of purity". See also point 1(16).	See open point in comment 1(16).

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(7)	Vol. 3, IIA 2.8, partition coefficient	DE: The study indicating a log Pow of 2.56 was actually not accepted by the RMS. Since the log Pow appears to be close to 3 and a BCF study for section 5 might be triggered by this value, the requirement for a new log Pow study should be discussed in order to determine a reliable value. The (other) log Kow of 2.89 was derived by estimation (McFarlane, 2005). However, with the KOWWIN program (v1.67; © 2000 U.S. EPA), a log Pow of 3.5 can be calculated and, moreover, the program's database indicates an experimental log Pow of 2.94 (reference: BioByte, 1995).	Taking into account the fact that the two estimated log Pow values (i.e. 3.5, as mentioned by DE and 2.89) significantly differ from each other and are around the trigger value of 3, the RMS considers that it is up to the meeting in ecotoxicology to decide whether a BCF study is required. The estimated value of the log Pow, mentioned by DE, has been included in an addendum to Vol.3 (B2) dd. September 2006.	Addressed for section 1 The issue on whether or not a BCF study has to be provided must be deceided by the section on ecotoxicology.
1(8)	Vol 1, level 4, 4.1 identity of the active isomer	UK: The concerns surrounding impurities 3 & 8 are valid since they are present at higher amounts in the technical specification than in the tox batches. The technical specification cannot be modified to reduce the levels as they are seen at these levels in the production control data. Consequently further data on the tox properties of these impurities may be required.	See point 1(4).	See data requirement in comment 1(4)
1(9)	Vol 1, level 4, 4.2, physical and chemical properties of the active substance	UK: Spectra for impurity 14 would definitely required prior to Annex I listing if as suggested by the RMS it is deemed to be of toxicological significance	See point 1(15).	See data requirement in comment 1(15)

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(10)	Vol 3, B.2.2.19, shelf life at ambient temperature	UK: The storage stability could be dealt with at MS level, but as the notifier plans to submit in the near future it is best to evaluate it as part of the process to produce a more complete package and remove the need for MS's to evaluate data for the representative formulation.	RMS takes note of this comment. The shelf life study, of which the final report we await by October 2006 (see point 1(20)), will be evaluated at EU level.	See data requirement in comment 1(20)
1(11)	Vol 3, B.2.2.29, emulsifiability, stability and re-emulsifiability	UK: Additional emulsion stability data are unlikely to differ from those evaluated already and so are not critical to the Annex I listing of the active substance. As they are being submitted in the near future an evaluation prior to the vote on the listing would be prudent to minimise data gaps.	As the required additional data are expected to be submitted with the shelf life study by October 2006, it should be possible to do an evaluation of those data still prior to the vote on listing. See also point 1(10).	See data requirement in comment 1(20) It should be noted that the question whether something is crucial or not for listing in annex I is not subject of the risk assessment at this stage. This is rather subject of risk management.
1(12)	Vol 3, B.2.2.29, emulsifiability, stability and re-emulsifiability	UK: Persistent foam can be dealt with on a member state level if required as the differences between the two types of water are unlikely to have significant impact on the level of foam. However we note this is to be included in the shelflife study.	This comment resembles the conclusion drawn by the RMS and reported in the DAR dd. June 2005. The required additional data on persistent foaming will be submitted with the shelf life study report, which is expected by October 2006. See point 1(20).	See data requirement 1(20)

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(13)	Vol 3, B.2.2.32, pourability	UK: The pourability residue is >5%, but has been deemed acceptable by the RMS. Why is this so? Further data on the residue in the sales pack following the rinsing procedure on the label should be requested. This could be addressed at MS level if required.	RMS notes that neither in Directive 94/37/EC, nor in the „Manual on development and use of FAO and WHO specifications for pesticides (1st edition, rev. March 2006)“, a maximum level of 5% is mentioned. Besides, the residue was also determined in a stability test, which has already been reported under point B.2.2.16 of the DAR dd. June 2005 (IIIA 2.7.1; Speak & Kendall, 2004). The residue before storage was found to be 4.7%. The rinsed residue was determined to be 0.1%. The pourability of the EW formulation will also be investigated in the shelf-life study, which is expected by October 2006 (see point 1(20)).	Open point The criteria for accepting data on pourability should be discussed generally in a meeting of expert. Sse also comment 1(19)
1(14)	Vol 4, C.1.2.2, identity of isomers, impurities and additives	UK: The RMS has quoted the notifier's statement "no impurities of particular toxicological or environmental concern were observed". Does this cover the potential for the formation of nitrosamines during step 3 of the reaction?	RMS considers impurity 14 to be of toxicological relevance. No other relevant impurities are reported or detected in the batch analysis study. Moreover, RMS considers the formation of nitrosamines unlikely to occur, since no alerting substances or reaction types are used in the manufacturing process of Myclobutanil.	Addressed

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(15)	Vol. 1, Level 4, 4.2 Physical and chemical properties of the as, Spectra of impurities, pg 76 *"Notifier should provide spectra of relevant impurity 14"* Vol. 3 B.2.1.10, pg 2-5	DAS A spectra report was submitted to the RMS (August, 2005). The mass spectrum, carbon and proton NMR spectra and the IR spectrum of impurity 14 were consistent with the structure. The UV/Vis spectra were obtained in acidic, neutral, and basic media; wavelength maxima, band widths and extinction coefficients were calculated. The water content of the sample was found to be 0.3% using Karl Fischer coulometric titration.	The requested spectra were submitted by August 2005 and are considered acceptable (see addendum Vol.3(B2) dd. September 2006); data requirement is considered to be fulfilled.	Data requirement (for formal reasons) The applicant should provide spectra for relevant impurity 14. [This should be regarded as a technical data requirement since the data have been already submitted to the RMS] See also comment 1(9)
1(16)	Vol. 3, B.2.1.23 surface tension, p. 2-9	EFSA: Being aware that in EEC A5 is stated that the described methods are applicable to most substances "without any restriction in respect to their degree of purity", it should be confirmed that a possible influence of the impurities was considered by the interpretation of the measured value.	As the purity of the test substance (i.e. 92.1%) is only slightly below the min. specified purity of the technical a.s. (i.e. 92.5%), the RMS considers the measured value to be representative for the technical a.s. as specified. Moreover, the conclusion on surface activity is very unlikely to change if a.s. of higher purity would be investigated, since there is a relative big difference between the trigger value (i.e. 60mN/m) and the measured value.	Open point The acceptance of the study for the determination of the surface tension of myclobutanil should be discussed in a meeting of experts. See also comment 1(6).

Physical and chemical properties of the active substance (B.2.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(17)	Vol. 3, B.2.2.16 shelf life, p. 2-15f	EFSA: Taken into account that the RMS has identified one relevant impurity, it should be clarified whether or not data are available to demonstrate that the relevant impurity in the technical material are not increasing in the formulation upon storage.	Statement of notifier: *"NMP is present as an impurity in myclobutanil crude and active ingredient. It is not actually produced by any side chemistry in the process, but is only present in the product in small amounts due to the fact that it is the solvent employed in the coupling reaction. The NMP solvent is removed by vacuum distillation and small amounts remain with the product due to the physical difficulty of completely removing the NMP by distillation. Since the NMP impurity is not actually formed in the process due to any side chemistry, it is not possible for the levels of NMP to increase during storage of the active ingredient or any formulations."* It is proposed that this issue will be discussed in an expert meeting (see point 1(18)).	Open point RMS to include the additional information concerning content of the relevant impurity in the formulation in an addendum or revised DAR. The point is addressed, however, this additional information should be transferred into an addendum to the DAR, because of its importance. See also comments 1(18) and 1(22)

Physical, chemical and technical properties of the formulation (B.2.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(18)	Vol. 3, B.2.2.19 shelf life	AT: It should be discussed in an expert meeting, whether the content of the relevant impurity should be determined in the formulation, since it is described as result of incomplete removal of a solvent in the production process of the a.s. and the increase during storage seems unlikely.	RMS agrees that the need for determination of the relevant impurity in the formulation should be discussed in an expert meeting.	See open point in comment 1(17).
1(19)	Vol. 3, B.2.2.32 pourability	AT: The value for the residue should be max. 5%. The value for rinsed residue is missing.	RMS notes that according to Directive 94/37/EC and the „Manual on development and use of FAO and WHO specifications for pesticides (1st edition, rev. March 2006)“, the determination of the rinsed residue is not required for EW formulations. See also point 1(13).	See open point in comment 1(13)
1(20)	Vol. 1; 2.1.2 Physical and chemical properties, pg 16 Vol. 3, B.2.2.19, pg 2-17	DAS: the shelf-life study is on going, the final report will be submitted by **October 2006**.	RMS awaits the final report.	Data requirement A shelf life study must be provided. See also comments 1(10), 1(11) and 1(11). [This should be regarded as a technical data requirement since the data have been already submitted to the RMS (November 2006]

Further information (B.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(21)	Vol. 3, B 3.6 references relied on, p. 3-13f	EFSA: It seems that none of the mentioned studies is quoted in chapter 3. Furthermore, why are only references for two annex points given? Where is the other information coming from?	The studies that are mentioned in the list of references relied on, are actually quoted under points B.3.5.1.3 and B.3.5.2, respectively, in the original DAR dd. June 2005. The other information is coming from the Tier documents MII and MIII of the dossier (MSDS was included).	Addressed RMS to consider in a revised DAR or corrigendum. EFSA would like to apologise that the references have been overlooked

Classification and labelling Further information (B.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)

For comments on classification and labelling see the relevant sections.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(22)	Vol. 3, B.5.1.4 analytical method, relevant impurity in the formulation	AT: see number 1(18)	If it is considered necessary that the relevant impurity can be determined in the formulation (see point 1(18)), a properly validated analytical method will be required.	See open point in comment 1(17)
1(23)	Vol. 3, B.5.3.2 analytical method, residue in water	AT: A linearity range of 0.15 to 12.5 µg/L seems unreliable to cover a range of fortification levels of 0.05 to 50.0 µg/L. The numbers of samples for each fortification level are not in accordance with guidance document 825/00.	The linearity range of 0.15 to 12.5 µg/L represents the actual concentrations of the standard solutions that were analysed by HPLC-MS-MS to obtain the calibration curve. The concentrations of the samples that were used for recovery	Addressed

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			determinations were in the range of 0.05 to 50.0 µg/L. However, it should be noted that, prior to HPLC-MS-MS analysis, these samples were still evaporated to dryness and redissolved and thus concentrated (by a factor 10). Hence, the fortified samples were actually analysed by HPLC-MS-MS at concentration levels in the range of 0.5 to 500 µg Myclobutanil / L solvent, which is in line with the linearity range. Sample concentrations exceeding that linearity range were diluted appropriately to obtain responses within the range of the calibration curve. With respect to the recovery data, the provided validation data for each water type separately does, indeed, not comply with current guidelines as described in SANCO/825/00 (less than 5 replicates per fortification level). Nevertheless, we consider that the overall data suffice to demonstrate acceptability of the method for water analysis of different types. More than the required two spiking levels have been investigated, resulting in a total number of samples per water type of more than 10. Moreover, for each type of water, at least 3 recovery determinations were made at LOQ level, allowing a meaningful determination of mean and RSD.	
1(24)	Vol. 3, B.5.3.3 analytical method, residue in air	AT: The breakthrough behaviour is not reported.	A new method for the determination of residues in air has been submitted. See point 1(32)	See data requirement in comment 1(32)
1(25)	Vol. 1, LOEP, AM	NL: Please also indicate the presence of confirmation methods and/or ILV where applicable	The LoEP has been amended accordingly.	Addressed

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(26)	Vol. 3, B.5.1.2, AM for the determination of significant and/or relevant impurities…….. See also C.1.2.4	NL: It is not allowed to calculate the LOQ. The LOQ is considered to be the lowest level at which acceptable validation data are obtained. The LOQ should be ≤ 0.1% for significant impurities.	RMS notes that according to Directive 96/46/EC (Annex I, point 4.1.3) determination of LOQ is not a validation requirement for impurity methods. It can thus be questioned whether the requirement in Guidance document SANCO/3030/99 that "LOQ must be reported and should be < 0.1%" is enforceable (Guidance document cannot overrule the Directive). According to the same Guidance document, accuracy of impurity methods should be addressed by determining recoveries at „levels appropriate to the material specification". We therefore believe that for most significant impurities the available validation data are sufficient to conclude that the methods are suitable for enforcement of the resp. specification limits, since at least one of the tested fortification levels was lower than the specification limit and the mean recovery/RSD at this level was acceptable.	Addressed
1(27)	Vol. 3, B.5.1.2, AM for the determination of significant and/or relevant impurities…….. See also C.1.2.4	NL: Not only the mean recovery data should be given but also the individual data or the range	A recovery range for each impurity determination has been included in the updated versions (dd. September 2006) of Vol.4(C1-C2) and Vol.3(B5).	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated versions of Vol. 4 (C1-C2) and Vol. 3 (B.5) are not available for the moment.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(28)	Vol.3, B.5.1.3, AM for the determination of the active substance in ppp	NL: The AM should be fully validated for the 20 EW formulation.	See point 1(33)	See open points in comment 1(33)
1(29)	Vol.3, B.5.3.1, soil	NL: The source of the soil used for the validation should also be mentioned	The source of the control soil samples used for validation was Crimplesham field station located in the UK. This information has been included in the updated version of Vol.3(B5) dd. September 2006.	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated version of Vol. 3 (B.5) is not available for the moment.
1(30)	Vol 4, C.1.2.4, methods of analysis for the determination of impurities	UK: The precision values from the method validation data for several of the impurities (1-7 & 14) are greater than prescribed in the guidelines. Therefore the method cannot be considered fully validated as stated.	The notifier submitted following justification (June 2005): *"The SANCO/3030/99 document specifies that the Horwitz test does not always apply. The Horwitz equation applicability to low levels at 0.1% or less is not straightforward as minor differences between first and second significant figures, although not different in practical, will make the Horwitz test fail. In addition, the SANCO/3030/99 document specifies a minimum of 5 samples. The data generated over two separate days will introduce more variability. In practical cases there is no difference between e.g. 0.020%, 0.019% and 0.022%. They all are 0.02%."* *"Furthermore, if we apply the test on one set and remove the day-day variability, the Horwitz test passes."* The latter was demonstrated for one impurity, but appears not applicable to all impurities. However, it should be noted that in	Open point The acceptability of the analytical method for the determiantion of impurities in the technical material should be discussed in a meeting of experts.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			those cases, the Horwitz values are exceeded only slightly. The RMS considers this justification acceptable.	
1(31)	Vol. 1, 2.2.1 Analytical Methods for analysis of active substance, pg. 19 *"for relevant impurity 14 the proposed LOQ of 0.036% remains to be validated.."* Vol. 1, List of end points, Impurities in technical as, pg 44 Vol. 1, Level 4, 4.5 Methods of analysis, pg 76 Vol. 3 B.5.1.2 Method for impurities, Conclusions, pg 5-4	DAS: the validation report for impurity 14 was sent to the RMS (August, 2005). Results for precision/recovery were acceptable. Testing at the level of 0.036% impurity 14, resulted in an acceptable recovery of 89% and acceptable precision by utilizing the horwitz equation.	The additional validation data, submitted by the notifier in August 2005, are considered acceptable by RMS and are included in the updated versions (dd. September 2006) of Vol.4(C1-C2) and Vol.3(B5). Data requirement is considered to be fulfilled.	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated version of Vol. 3 (B.5) is not available for the moment.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(32)	Vol. 1, 2.2.3 Analytical Method - Air, pg 19 Vol. 1, List of end points, Analytical methods for residues, Air, pg 44 "*additional validation data required*" Vol. 1, Level 4, 4.5 Methods of analysis, pg 76 Vol. 3 B.5.5.3 Analytical methods (residue) for soil, water and air, Air pg 5-16	DAS: A new method, "Method Validation Study for the Determination of Myclobutanil in Air" was developed in 2005 to replace the original method outlined in the dossier and was sent to the RMS (August, 2005).	RMS considers the new analytical method, submitted by the notifier in August 2005, suitable for the determination of residues of Myclobutanil in air. (See updated version of Vol.3(B5) dd. September 2006); data requirement is considered to be fulfilled.	Data requirement (for formal reasons) The applicant should provide additional validation data for the air method. [This should be regarded as a technical data requirement since the data have been already submitted to the RMS] See also comment 1(24)
1(33)	Vol. 3 B.5.1.3 Method for myclobutanil in Systhane 20EW, pg 5-4 / 5-5 *Method TM 96-176-02 (GC-FID on DB-1, internal standard octacosane in ethyl acetate), which was the basis for method DAS-AM-04-042, has been used in the storage stability studies with Systhane 20EW. Validation report for this method was not available for submission.*	DAS: a justification was submitted to the RMS (June, 2005): within the validated method DAS-AM-04-042 for Systhane 24EC pentadecane was used as the internal standard. When pentadecane was used with Systhane 20 EW it became an interference issue and octacosane was used in its place. Octacosane was analyzed using the conditions from DAS-AM-04-042 and compared with Systhane 20 EW and no interferences were observed. The linearity within DAS-AM-04-042 also bracketed the proper range for Systhane 20 EW. Therefore DAS-AM-04-042 can be used as a validated method for Systhane 20 EW only using octacosane instead of pentadecane as the	RMS considers the justification as submitted by the notifier acceptable. However, this point still might be discussed in an expert meeting.	Open point The acceptability of the analytical method used in storage stability studies with Synthane 20EW should be discussed in a meeting of experts. See also comment 1(28)

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		internal standard. The available Chromatograms of Systhane 20 EW formulation blank, a myclobutanil technical, and an internal standard of octacosane show no interferences and were analyzed using the gas chromatographic conditions within DAS-AM-04-042		
1(34)	Vol. 3, B.5.2.1 plant origin, p. 5-7	EFSA: The RMS should clarify the acceptability of the multi-method, since the reported LOQ is too high according to the criteria of SANCO/825/00 and Annex VI.	RMS agrees that the multi-method cannot be accepted, due to a too high LOQ according to SANCO/825/00 (a maximum LOQ of 0.1 mg/kg is allowed when MRL > 0.1 mg/kg). However, additional validation data for this method are not considered necessary, since the German multi-method (L.00.00-34, extended version of DFG S19) appears to be a good alternative. Myclobutanil is listed in the annex to the description of that method and has been validated properly for foodstuff matrices with high water content. A LOQ of 0.05 mg/kg is reported, which is in accordance with SANCO/825/00 rev. 7. The information and amendments outlined here above are included in the updated version of Vol.3(B5) dd. September 2006.	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated versions of Vol. 4 (C1-C2) and Vol. 3 (B.5) are not available for the moment.

Methods of analysis (B.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
1(35)	Vol. 3, B 5.6 references relied on, p. 5-18f	EFSA: It should be noted that the methods for the determination of residues in food of animal origin should not be listed here, since no MRLs are proposed and therefore an important parameter is missing to assess the methods. Consequently it is not possible to rely on them.	RMS agrees. In the updated version of Vol.3(B5) dd. September 2006, these references are no longer included in the list of references relied upon.	Addressed RMS to consider in a revised DAR or corrigendum. It should be noted that the mentioned updated versions of Vol. 3 (B.5) is not available for the moment.

Comments received on reporting table, section Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
1(4), 1(8)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted
1(7)	RMS	A new log Pow test will be conducted using the shake flask method. Information on phase separation shall be included in the study report. Report will be available by the end of February 2007.	Noted
1(7)	NOT	**DAS:** following recent discussion with RMS expert it was concluded that a reliable experimental logP value for myclobutanil can come from a new new „*shake flask*“ (GLP) study under current registration conditions (i.e. according to EEC A8), including the relevant details over 'information on phase separation'. DAS will run that study and the he final report will be available by **end of February 2007**.	Noted
1 (8)	UK	The response is acceptable.	Noted
1(9), 1(15)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted
1(9)	UK	The response is acceptable.	Noted

Comments received on reporting table, section Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
1(10), 1(11), 1(12), 1(20)	NOT	**Data Requirement:** *A shelf life study must be provided.* **DAS:** the final report **is available**, and was sent following request to RMS.	Noted and mentioned in the reporting table
1 (10)	UK	The response is acceptable.	Noted
1 (11)	UK	The response is acceptable.	Noted
1(12)	RMS	In the additional shelf life study report, received in November 2006, persistent foaming properties were again determined in CIPAC water C, instead of in the required standard water D (cfr. FAO/WHO manual). The notifier announced that testing of the initial (before storage) persistent foaming properties will be repeated in CIPAC water D; report will be available by the end of January 2007. However, the initial conclusion, i.e. that this issue can be dealt with on MS level if deemed required, remains as an adequate solution.	Noted
1 (12)	UK	The response is acceptable.	Noted
1 (13)	UK	The proposed discussion on acceptability criteria is welcomed.	Noted
1 (14)	UK	The response is acceptable.	Noted
1 (16)	UK	Agree with the comments of the RMS that a higher purity is unlikely to change to the surface tension such that the active substance is no longer considered surface active. A discussion of this issue in an expert meeting as proposed would however by useful.	Noted
1 (19)	UK	Comments re poured residue echo those of the UK. However test 148.1 does not determine rinsed residue, only poured residue.	Noted
1(20)	RMS	RMS received the announced shelf life study (November 2006).	Noted and mentioned in the reporting table
1(24), 1(32)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted and mentioned in the reporting table

Comments received on reporting table, section Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1- B.5)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
1 (30)	UK	The proposed discussion on the acceptability of the method is welcomed.	Noted

2. Mammalian toxicology

Acute toxicity (B.6.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(1)	General comment	EFSA: the declared minimum purity of myclobutanil is 925 g/kg. Many of the key toxicological studies were conducted with different purities (81.1%, 84.5%, 90.4%, etc). The relevance of the outcomes of the studies on the overall risk assessment has to be commented by the RMS. Furthermore, the applicant mentions (see comments on the draft assessment report) a "new package of acute toxicity studies conducted with myclobutanil technical grade from the actual registered source". It should be clarified whether the new studies are available and whether the tox data presented in the DAR are applicable also to the new source	In the dossier, a proposed minimum purity of 925 g/kg was accepted taking into account the GLP batch analysis and the purity range of toxicology batches. In this dossier, some studies such as acute toxicity studies, reproduction and developmental studies, and some genotoxicity studies, were performed with pilot plant batches with a purity of 84%. Some chronic studies were performed with a compound of higher purity (90-92%) coming from the final manufacturing process. The purity differed between the two processes as a result of an additional purification step in the final manufacturing process. The company provided recently a new package of acute toxicity studies in response to Brazilian authorities using a compound of 99.7% produced by KemFine. Except purity, no other information is provided about the origin of the compound. Therefore, before to take the results of this package into account, further information should be provided in order to assess the equivalence of the two sources of technical materials. RMS proposes at this stage, not to take this new package into account as the results of acute toxicity obtained with this new source present a lesser hazard compared to the reference source. A high increase in purity (from 84% up to 99.7%) could affect the complete toxicology profile of the	Data requirement (for formal reasons) Applicant to submit the new acute toxicity package. [This should be regarded as a technical data requirement since the data have already been submitted to the RMS.] Open point: RMS to assess and confirm the equivalence of the tox tested batches to the proposed technical specification.

<table>
<tr><th colspan="5">Acute toxicity (B.6.2)</th></tr>
<tr><td>No.</td><td>Column 1
Reference to DAR (vol., point, page)</td><td>Column 2
Comments from Member States or applicant</td><td>Column 3
Evaluation by (RMS) rapporteur and
- if available - (Co-RMS) Co-rapporteur</td><td>Column 4
Data requirement or Open point (if data point not addressed or fulfilled)</td></tr>
<tr><td></td><td></td><td></td><td>active ingredient and acute toxicity studies are not sufficient to address the hazard of myclobutanil taking into account the reproduction/developmental toxicity profile of this compound.
Further assessment of equivalence is considered necessary before to amend the proposed classsification.</td><td></td></tr>
<tr><td>2(2)</td><td>Vol 3, B.6.2.5, Eye irritation</td><td>UK: Classification as eye irritant is not considered appropriate. Vascularisation of the cornea was seen in only 1 out of 9 animals at day 21 in the study of Krzywicki and Bonin, 1984.</td><td>R36 irritating to eyes is applied when ocular lesions persist for more than 21 days. Such lesions are considered as irreversible. The number of rabbits that need to be affected is not reported in Dir classification and labeling of dangerous substances.</td><td>Open point
The need of classification R36 “Irritating to eyes” to be discussed in an experts’ meeting</td></tr>
<tr><td>2(3)</td><td>Vol. 1, 2.3.1 Classification and Labeling, Table 2.3.1-1 Summary of acute toxicity of myclobutanil pg 20-21 – Classification

Vol. 3 B.6.2.7 Summary of Acute toxicity, pg 6-17</td><td>DAS: Based on a requirement of the Brazilian Authorities, a new package of acute toxicity studies have recently been conducted with myclobutanil technical grade from the actual registered source.
A summary of the new data are presented below. Based on these data using current test guidelines, myclobutanil should not be classified for acute toxicity.
Therefore, the proposed classification for myclobutanil should be amended to reflect the new data generated.
<table><tr><td>Route/</td><td>Species/ strain</td><td>Result</td><td>EC</td><td>Ref.</td></tr></table></td><td>See comment reported in point 2(1).</td><td>See open point in 2.1</td></tr>
</table>

Acute toxicity (B.6.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		method (sex) class. Oral/gavage/ Up-Down Method — Rat/F344 (F) — LD_{50} = 3129 mg/kg bw/day — None — Moore, 2005 Dermal/topical — Rat/F344 (M/F) — LD_{50} = > 5000 mg/kg bw/day — None — Moore, 2005 Dermal/topical — Rabbit/NZW (M/F) — Slight irritation — None — Moore, 2005 Eye/instillation — Rabbit/NZW (M) — Mild irritation — None — Merkel 2005 Dermal/LLNA — Mouse/ Balb C (F) — Non-sensitiser — None — Woolhiser.2005		
2(4)	Vol. 1, Level 4, 4.6 Toxicology and metabolism, pg 77 *"Systhane 20 EW inhalation study"*	DAS: It has been clarified with the RMS that the previously submitted study at National Level is the same acute inhalation toxicity study on Systhane 2EC, which was submitted with this dossier.	Agreement.	Addressed

Acute toxicity (B.6.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(5)	Vol. 3, B.6.11.3 Acute inhalation toxicity in rats *"The company should provide this study"* Conclusion, pg 6-82	DAS: it was clarified with the RMS that the previously submitted study at National Level is the same acute inhalation toxicity study on Systhane 2EC, which was submitted with this dossier. **Systhane 20 EW should not be classified R20**: harmful by inhalation. Based on the DPD (1999/45/EC), there is one substance in both of these formulations (cyclohexanone) which is classified R20. Cyclohexanone is present in GF-1137 preparation at 20% (w/w), and most likely causes the inhalation toxicity. The overall LC_{50} for the combined male/female data was ≥ 5.0 mg of RH-53,866 2EC per L of air. In Systhane 20EW (the representative formulation), cyclohexanone is present at only 10% (w/w). The overall toxicity of Systhane 20EW is expected to be notably less than for GF-1137, in particular the inhalation toxicity effects. Also, based on 91/414/EC criteria, Systhane 20EW does not meet the requirement criteria for an inhalation toxicity study (Column 3).	Agreement	Addressed
2(6)	Vol. 3, B.6.11.3 Acute inhalation toxicity in rats Materials and Methods, pg 6-82	DAS: "Systhane 20 EW" should read **Systhane 2 EC**	Agreement	Addressed

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(7)	Vol. 3, B.6.3.2.2 90-day study dog	NL: The effects on the liver cannot be regarded as 'just' adaptive. The high increase in liver weight (varies from 9%-52%) in combination with the histopathology (centrilobular/midzonal hepatocyte hypertrophy) is definitely an adverse effect. For the females, the NOAEL is 200 ppm (7.88 mg/kg bw/d) and for the males 10 ppm (0.34 mg/kg bw/d).	No agreement. Hepatcellular hypertrophy (and its corresponding increased liver weight/size) may be indicative of adaptation which, by itself, is not necessarily adverse. Such effects should be considered as adverse if associated with other more severe changes such as alterations in relevant clinical chemistry parameters and or/histopathology. Blood chemistry levels are usually considered as adverse when at least two liver parameters have a dose-dependent, biologically significant change. Histopathology: adverse lesions such as hyperplasia, degeneration, or necrosis should be assessed based on incidence and severity**.** (HED Guidance Document G0201 on hepatocellular hypertrophy, 2002) In this dog study, SAP is not increased 2-fold at 800ppm; the values are within the control ranges of typical measurement in beagle dog; therefore this increase is considered as statistically significant but without biological significance. No other blood chemistry parameter was affected and no histopathological adverse lesions were reported in this study.	Open point The relevance of liver effects in the 90-day and 1-year studies in dog to be discussed in an experts' meeting

Short-term toxicity (B.6.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(8)	Vol. 3, B.6.3.2.3 1-year study dog	NL: The high increase in liver weight of 27% at 400 ppm in combination with the histopathology (hypertrophy) in 2 animals is an adverse effect. The NOAEL for this study is 100 ppm (3 mg/kg bw/d).	No agreement. See point 2(7) In this study, clear histopatholodical adverse effects (hepatitis acute/multifocal and ballooned hepatocytes) are reported only at top dose. Slight hematological effects were seen at top dose as well as spleen hemosiderosis.	See open point in 2(7)
2(9)	Vol. 3, B.6.3.3.3 Percutaneous 28-day toxicity rat	NL: The Material and Methods paragraph is very concise. It is stated that the substance was applied unocclusively to the skin. However, some kind of protection should have been used, otherwise the animals will lick of the substance.	Indeed, RMS forgot to add that rats had a cardboard collar.	Addressed
2(10)	Vol. 3, B.6.3.2.2, Oral 90-day toxicity (dog) and B.6.3.2.3, Oral 1-year toxicity (dog)	DE: Remark: The liver is clearly the target organ. Therefore, the NOAEL in the 90-day study in dogs is seen at 10 ppm based on concomitant relative liver weight increase and hepatocyte hypertrophy at 200 ppm. Similar effects were noted in the 1-yr study at 400 ppm with the next lower dose of 100 ppm being a clear NOAEL. Thus, 100 ppm (ca 3 mg/kg bw/d) can be considered an overall NOAEL for subchronic toxicity in dogs. Liver effects in dogs should be discussed on an EPCO meeting.	See comment on point 2(7)	See open point in 2(7)

Genotoxicity (B.6.4)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(11)	Vol. 3, B.6.4.1.2 In vitro mammalian cell gene mutation studies Table B.6.4.1.2-1, pg 6-33	DAS: Typo: Table numbering is repeated for the 2 tables on this page	Agreement	Addressed

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(12)	Vol. 3, B.6.6 Reproductive toxicity	NL: In the past, myclobutanil was evaluated for a national request for authorisation. In this evaluation, R62 was also proposed and for teratogenicity the proposal was R61.	No comments	Open point Reproductive and developmental toxicity to be discussed in an experts' meeting
2(13)	Vol. 3, B.6.6, Reproduction toxicity (Classification and labelling)	DE: Remark: Myclobutanil caused clear reproductive effects and had an impact on male sex organs in the 2-gen study in rats but these findings were confined to the top dose level of 80 mg/kg bw/d, i.e., a dose in the systemically toxic range. Additional classification and labelling with R62 is not considered necessary and the already allocated risk phrase R63 seems to be more appropriate.	Systemic toxicity was low at the top dose. No information is provided in the dossier concerning myclobutanil potency to inhibit 14 α lanosterol demethylase and aromatase activities. However, according to the open literature it is reported that: Imidazoles and triazoles antifungal activity is based on inhibition of fungal CYP51 (lanosterol 14 α demethylase), and CYP19 (aromatase). Sterol 14 α demethylase is crucial for the production of meiosis activating sterols (MAS), which recently were shown to modulate germ cell development in both sexes of mammals.	See open point in 2(12)

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			Aromatase is responsible for the physiologic balance of androgens and estrogens. At high doses, azole fungicides and other azole compounds affect reproduction organs, fertility and development in several species, effects which could be explained by inhibition of 14 sterol α demethylase and/or aromatase (See Zarn et al., Environ. Health Perspect. 2003, 111, 255-261). Therefore, RMS considers that the reproductive effects seen at top dose are not consecutive to a systemic toxic effect, which is low in this study, but results from the intrinsic properties of the compound.	
2(14)	Vol. 1, 2.3.1 Reproductive toxicity and teratogenicity, Proposal for R62, pg 25 Vol. 1, List of end points Impact on Human and Animal Health, Reproductive Toxicity pg 61-62 Vol. 3, B.4.1, Table B.4.1-1, pg 4-2 Vol. 3, B.6.6.1.1 Two generation reproductive	DAS: There is no clear evidence that the testicular atrophy observed only in aged rats (first noted at 12 months in the 2-year rat carcinogenicity study) and P2 males (following 27 weeks exposure in the 2-generation reproduction study) caused impaired fertility. Effects observed in the top dose group of the 2-generation study included reduction in the number of viable foetuses and numbers of females delivering, and an increased number of pups born dead. These effects are most likely the result of post-implantation loss and/or perinatal death, rather than a consequence of impaired fertility. This information would suggest that the effects observed in the 2-generation study were due to developmental toxicity and not impaired fertility. The relevance to humans of this species-specific	In the 2 year carcinogenicity rat study, testes atrophy was reported after 12 month exposure affecting 15% of the animals at 400/560/800 ppm , 22% after 17 month exposure, and 54% of the animals at the end of the study in comparison to 12% of the male control rats at the end of the study. In the 2 generation rat study, at the top dose of 1000 ppm (70-76 mg/kg bw/d) in P2, testicular lesions affected 11 rats versus 3 in control group, epididymal lesions affected 12 rats versus 2 in control group and prostate atrophy was seen in 11 rats versus 2 in control group. RMS agrees with the notifier that increased post implantation loss is not related to fertility. Adverse effects on mating performance were reported at 1000 ppm in the 2 generation rat	See open point in 2(12)

<table>
<tr><th colspan="5">Reproductive toxicity (B.6.6)</th></tr>
<tr><td>No.</td><td>Column 1
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Comments from Member States or applicant</td><td>Column 3
Evaluation by (RMS) rapporteur and
- if available - (Co-RMS) Co-rapporteur</td><td>Column 4
Data requirement or Open point (if data point not addressed or fulfilled)</td></tr>
<tr><td></td><td>toxicity in the rat
Conclusion, pg 6-53

Vol. 3, B.6.6.3 Summary of reproductive toxicity and teratogenicity, pg 6-58</td><td>testicular atrophy remains unclear and R62 classification is unwarranted.</td><td>study: in the P1/F1a and P2/F2a matings only 20/25 delivered litters and in P2/F2b mating only 17/25 females delivered litters and there was a slight prolongation of mating time.
Further discussion could be necessary at EPCO meeting.</td><td></td></tr>
<tr><td>2(15)</td><td>Vol. 1, 2.3.1 Reproductive toxicity and teratogenicity, skeletal observations: 7th cervical ribs, pg 26
“More information from the Company could clarify this point”

Vol. 1, List of end points Impact on Human and Animal Health, Reproductive Toxicity pg 61-62

Vol. 3, B.6.6.2.1 Teratogenicity test by the oral route in the rat

Foetal morphological observations;</td><td>DAS: as agreed with the RMS, the notifier reviewed the available data and issued the report “Re-analysis of selected skeletal findings from a teratology study with RH-53,866 (myclobutanil) in Rats” that was sent to the RMS (December, 2005).
Re-evaluation of the skeletal specimens showed a small, biologically significant (not statistically) increase in incidence of 7th cervical ribs at a high dose (469 mg/kg bw/day) only. Total incidence of 4 foetuses in 3 litters is minimal, occurring at a maternally toxic dose, which also showed a significant increase in resorbed implantations and reduced viability. Incidences of 14th rudimentary rib were also only increased in this high dose group, affecting a total of 6 foetuses in 6 litters (litter effect statistically significant). Given marginal nature of these supernumerary rib increases, lack of any corresponding pattern of foetal malformation, and presence of maternal toxicity during the critical period for supernumerary rib induction, these skeletal alterations represent foetotoxicity, not teratogenicity, associated with maternal toxicity.</td><td>A Re-analysis of selected skeletal findings from a teratology study with RH-53,866 (myclobutanil) in rats (Carney et al., 2005) was provided to the RMS. This study will be summarized in the addendum.
All fetal skeletal specimens from the original study were retrieved from long-term storage, and those specimens with an observation of 7th cervical rib and/or 14th rudimentary rib were re-evaluated based on lentgh . As per standard procedure in the laboratory, supernumerary rib with a length which was less than twice its width was considered normal, whereas larger ribs, defined as having a length equal to or more than twice their width, remained classified as 7th cervical or 14th rudimentary ribs.
Incidence of 7th cervical rib and 14th rudimentary rib as re-evaluated according to the length criteria is reported in this table:
<table>
<tr><td>Dose mg/kg bw/d</td><td>0</td><td>468.9</td></tr>
<tr><td>N° fetuses / litters examined</td><td>223/22</td><td>201/22</td></tr>
<tr><td>7th cervical ribs</td><td>0/0</td><td>4/3</td></tr>
</table></td><td>See open point in 2(12)</td></tr>
</table>

Reproductive toxicity (B.6.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	Conclusion, pg 6-55 Vol. 3, B.6.6.3 Summary of reproductive toxicity and teratogenicity, pg 6-58	This finding itself does not warrant classification, and should not be included in the R63 definition for myclobutanil.	14^{th} rudimentary ribs 1/1 6/6* 3%/27% *statistically different from controls RMS concluded that as maternal toxicity was apparent at top dose, it can be considered that these effects are secondary to maternal toxicity.	
2(16)	Vol. 3, B.6.6.2.2 Teratogenicity test by the oral route in the rabbit Methodology – study acceptance, pg 6-58	DAS: Please delete the statement: "The study is accepted if the results of the range-finding study reported in the JMPR 1992 could be provided." This study has been provided in June 2005, as acknowledged by RMS at the beginning of the paragraph of pg 6-58.	Agreement	Addressed

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(17)	Vol. 1, 2.3.1 Toxicity studies on metabolites and supplementary studies, pg 27 and Table 2.3.1-7 pg 28 Triazolylalanine (TA), *"…classification for developmental effect as cat. 3 R63 is therefore*	DAS: TA is not a toxicologically relevant metabolite and thus would not be classified in category 3 (R63). *"Developmental toxicity of TA (Clapp et al., 1983)"*, assessed according to regulatory guidelines, showed a number of skeletal variations in foetuses at the highest dose level at higher incidence than in controls on a foetal basis. The findings occurred in the absence of maternal toxicity. A relationship to treatment is possible, but findings are considered to	It was not clear why these studies were included in the dossier. TA is a metabolite occurring in wheat grain which is not an intended use. RMS considers that the effects seen in fetuses are indicative of foetotoxicity: the effects occurred at doses where no maternal toxicity was seen. Moreover, foetuses did not show	Open point The issue of triazole metablite is going to be discussed in a dedicated experts' meeting. Conclusions to be awaited.

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
	proposed." Vol. 3, B.6.8.1.2 Triazolylalanine Developmental rat study, conclusions, pg 6-69 Vol. 3, B.6.8.3, Summary of Toxicity studies, pg 6-71	be of no biological significance, not to be adverse and represent typical aspects of normal development because: • The low number of changes involved (including both more and less ossification) • The lack of impact on the foetus, given the changes are part of normal development • The increased incidences of isolated skeletal variations are seen at high dose levels only There is no evidence for a concommitant effect (i.e. decrease) on pup weight	reduced body weight confirming that the effect could not be considered as a developmental delay. In this study, only the foetal incidence was provided and not the litter incidence.	
2(18)	Vol. 1, 2.3.1 Toxicity studies on metabolites and supplementary studies, pg 29 Triazolylalanine (TA), *"triazolylalanine should be considered as relevant metabolite from a toxicological point of view…"* Vol. 1,List of end points Impact on Human and Animal Health, Other toxicological studies Triazolylalanine (TA),pg 62	DAS: We do not consider TA to be a relevant metabolite of myclobutanil as its toxicity is significantly lower than the active substance itself. It is agreed that the conservative NOEL for developmental toxicity effects is 100 mg/kg bw/day. This is higher than the NOAEL (31 mg/kg bw/day) for developmental toxicity of myclobutanil, and the adverse end-points were less critical (e.g. delayed ossification for TA at 1000 mg/kg bw/day versus reduced viability and increased resorptions for myclobutanil from 93.8 mg/kg bw/day). Therefore, it is considered that TA is not a relevant metabolite of myclobutanil. **See also comment (4)**	The reason why these studies were provided to the RMS is not clear as the use of myclobutanil in wheat grain is not supported and this metabolite was just identified in wheat grain. Wording "relevant" could be considered as inappropriate in this context as TA is a plant metabolite. However, this plant metabolite is toxic due to skeletal effects reported in the developmental rat study at doses of 300 mg/kg bw/d. Myclobutanil, skeletal effects were observed at 468 mg/kg bw/d.	See 2(17)

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(19)	Vol. 3, B.6.8.1.1 RH9090, RH 9089 and 2 impurities Conclusion, pg 6-61	DAS: RH-9090 and RH-9089 are both plant metabolites, and not substances of their own right. Therefore, they do not come under consideration by the Dangerous Substances Directive (67/548/EEC), and would not warrant classification.	RMS agrees with notifier that metabolites are not substances that will be included in Annex I of the Directive. The aim of this proposal is more related to a problem of risk assessment in the context of residues taking into account that consumer will come in contact with these substances. RMS considers this classification should more be considered as an alert but this alert will indeed not be apparent on classification/labelling of the active ingredient.	Addressed
2(20)	Vol. 3, B.6.8.3 Summary of toxicity studies on metabolites and supplementary studies Triazolylalanine, pg 6-72 Vol. 3, B.6.10 Summary of mammalian toxicology and proposed ADI, AOEL and drinking water limit Triazolylalanine and triazolyl acetic acid: Triazolylalanine, pg 6-78	DAS: We do not consider TA to be a relevant metabolite of myclobutanil as its toxicity is significantly lower than the active substance itself. It is agreed that the conservative NOEL for developmental toxicity effects is 100 mg/kg bw/day. This is higher than the NOAEL (31 mg/kg bw/day) for developmental toxicity of myclobutanil, and the adverse end-points were less critical (e.g. delayed ossification for TA at 1000 mg/kg bw/day versus reduced viability and increased resorptions for myclobutanil from 93.8 mg/kg bw/day). Therefore, it is considered that TA is not a relevant metabolite of myclobutanil. See **Comments (4) and (5)**	See response to point 2(18).	See 2(17)

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(21)	Vol. 1, lev. 4, point 4.1	EFSA agrees with the RMS's data requirement on the impurity profile with regard to the impurities 3 and 8.	No comments	Point transferred from section 1: Data requirement (for formal reasons) The applicant should provide a case and/or data to show that the increased levels of both impurities (3 and 8) will not have a significant adverse effect on the toxicity of technical Myclobutanil [This should be regarded as a technical data requirement since the data have been already submitted to the RMS] See 1(4). Open point: The relevance of impurities 3 and 8 to be discussed in an experts' meeting .
2(22)	Vol. 3, B.6.8.3 Summary of toxicity studies on metabolites	EFSA: According to the residue scientific check (see comment 9), metabolites RH9090 and its glucoside should be included in the residue definition. Their toxicological relevance for the consumers should be addressed (the only available information show that the acute oral toxicity of metabolite RH 9090 is comparable to that of myclobutanil).	RH-9090 (M4) and RH-9083 (M3) are major metabolites identified in the rat. Further studies are therefore not required.	Open point The relevance of metabolites RH-9090 (M4) and RH-9083 (M3) to be discussed in a meeting of experts.

Other toxicological studies & Medical data (B.6.8-B.6.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(23)	Vol. 3, B.6.9.1 Report on medical surveillance on manufacturing plant personnel	EFSA: information provided are poor, only 15 workers considered. Considering that the substance is used since a long time and that ECB classified it already in 1997, it cannot be considered sufficient.	No comments	Data requirement Applicant to provide further information on health effects/surveillance programmes in manufacturing plant personnel In the comments to the reporting table the applicant announced that a report covering medical surveillance in a manufacturing plant in Italy (2000-20005) was sent to the RMS.

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(24)	Vol. 3, B.6.10.4, AOEL	DK disagrees with the proposed AOEL. We propose to base the AOEL on the NOAEL from the long-term rat study where effects are seen on the testes at 9.8 mg/kg/d already after 1 year. And as the effects are serious we propose to use a SF of 300. I.e. the AOEL will be 0.03 mg/kg bw/d.	RMS disagrees: testes effect seen after 1 year affected 15% of the rats at a dose of 39.21 mg/kg bw /d. At the lower dose of 9.84 mg/kg bw/d, after 1 year, 1/20 animal was affected.	Open point AOEL to be discussed in an experts' meeting

<table>
<tr><th colspan="5">Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)</th></tr>
<tr><td>No.</td><td>Column 1
Reference to DAR (vol., point, page)</td><td>Column 2
Comments from Member States or applicant</td><td>Column 3
Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur</td><td>Column 4
Data requirement or Open point (if data point not addressed or fulfilled)</td></tr>
<tr><td>2(25)</td><td>Vol. 3, B.6.10.4
AOEL</td><td>NL: If the NOAEL in the dog studies will be reconsidered based on the NL comments (see comments 1 and 2), the “overall” NOAEL of the dog studies will be 3 mg/kg bw/d. The AOEL will then be 0.03 mg/kg bw/d.</td><td>See comment on point 2(7) and 2(8)</td><td>See open point in comment 2(24)</td></tr>
<tr><td>2(26)</td><td>Vol. 3, B.6.10.4, AOEL</td><td>DE: Proposal: A lower AOEL of 0.03 mg/kg bw/d is proposed that should be derived from the suggested overall NOAEL for subchronic toxicity in dogs (see comment above). Discussion on an EPCO meeting is recommended.</td><td>See comment on point 2(7) and 2(8)</td><td>See open point in comment 2(24)</td></tr>
<tr><td>2(27)</td><td>Vol 3, B.6.10.3, Derivation of the ARfD</td><td>UK: The effects observed in the multigeneration study (including increased numbers of stillborn and decreased numbers of females delivering) are considered potentially relevant to acute exposure, and thus the UK considers that the ArfD should be derived using the NOAEL from this study.

With a proposed ARfD of 0.16 mg/kg bw, there is a margin of 200 on the NOAEL for developmental effects. This should give an adequate margin.</td><td>The proposal made in the DAR takes into account the spacing of the doses. Therefore, RMS considers that the ARfD should be derived using the NOAEL from the developmental rat study:
<table><tr><td>Study</td><td>NOAEL</td><td>LOAEL</td></tr><tr><td>Multigen rat</td><td>16 mg/kg bw/d</td><td>71 mg/kg bw/d</td></tr><tr><td>Develop rat</td><td>31 mg/kg bw/d</td><td>93 mg/kg bw/d</td></tr><tr><td>Develop rabbit</td><td>60 mg/kg bw/d</td><td>200 mg/kg bw/d</td></tr></table></td><td>Open point
The ArfD to be discussed in an experts’ meeting</td></tr>
<tr><td>2(28)</td><td>Vol 3, B.6.10.3, Derivation of the AOEL</td><td>UK: Due to the magnitude of the liver weight effects in females at 400 ppm in the 1 year dog study, combined with the increased SAP activity and histopathology, the UK considers that this study derives a NOAEL of 100 ppm. This is lower than that obtained in the rat multigeneration study, and should be used in the derivation of the AOEL.</td><td>See comment on point 2(7)</td><td>See 2(7) and 2(24)</td></tr>
</table>

Summary of mammalian toxicology and setting of ADI, AOEL and ARfD (B.6.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(29)	Vol. 1, 2.3.5 Drinking Water Limit, pg 30 Vol. 3, B.6.10.5 Maximum acceptable concentration in drinking water, pg 6-80	DAS: In accordance with the Annex VI Uniform Principles to 91/414/EEC (C. Decision Making, point 2.5.1.2), it is required to demonstrate that the safe level of the active substance in drinking water is greater than the drinking water limit of 0.1 g/L. An extensive toxicological data base was used to set the ADI. In accordance with the International Programme of Chemical Safety (IPCS) criteria (WHO, 1994) and the EU Drinking Water Directive (98/83/EC, 1998), on the basis that exposure through drinking water should not account for more than 10% of the ADI (0.025 mg/kg bw/day), assuming an average consumption of 2 L of water/person/day and a body weight of 70 kg, **a drinking water limit for myclobutanil would be 87.5 µg/L.**	No comments	Addressed. EFSA agrees that the trigger currently used for the level of the a.s. in drinking water is 0.1 µg/L, according to 91/414/EEC

Toxicity of the product(s) (B.6.11)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(30)	Vol. 1, 2.1.4., Classification and labelling	DE: Remark For the classification and labelling of the preparation the needed classification and labelling of the co-formulants (Risk phrases R65 and R66) should also be considered into account.		Open point RMS to provide details on the existing classification of co-formulants and their impact on the classification of the preparation

Dermal absorption (B.6.12)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(31)	Vol. 3, B.6.12, dermal absorption	DK finds that the estimated dermal absorption is too low. In table B.6.12.1-4 is stated that the absorption is the sum of urine and faeces excretion and taken into account the excretion after i.v. application. But the figures in the table are only based on urinary excretion and the amount in the skin is not included. In the other study the exposure for the concentrate is even higher. We propose to discuss the absorption in an expert meeting.	There is an error in the title of the table: the title in the table should be modified as following: % excreted dose (urine).	Open point Dermal absorption to be discussed in an experts' meeting.
2(32)	Vol. 3, B.6.12.1 Dermal absorption (Didonato and Steigerwalt, 1986)	NL: We do not understand the correction for urinary excretion after i.v. exposure. In Table B.6.12.1-2 the recovery after 7 days is reported. The absorbed dose is 28.8% for the concentrate and 47.7% for the dilution, based on the excretion in urine, urine funnel wash, feces, cage wash and ring washes. This is correct. In Table B.6.12.1-4 the absorbed dose is estimated based only on excretion in urine (although in the table it is suggested that also feces was included, but this is not correct). However, the amount excreted in feces should be included! Furthermore, the validity of the i.v. data should be questioned, given the recovery of 124%. Therefore, we propose to use 28.8% and 47.7% for dermal absorption of the concentrate and dilution, respectively.	The aim of this table is to clarify how the absolute bioavailability of myclobutanil is calculated. For that, urinary excretion alone is reported in the table after dermal exposure and iv administration (there is an error in the title: % excreted dose (S urine+ feces) should be corrected as % excreted dose (urine alone). The recovery of the 3 studies was high: RMS considers that the validity of the complete study could then be questioned if the recovery value of 124% is rejected for the iv study. RMS disagrees with this approach.	See open point in comment 2(31)

Dermal absorption (B.6.12)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(33)	Vol. 3, B.6.12, Dermal absorption	DE: Remark: It is not considered appropriate to calculate dermal absorption on a comparison of only urinary excretion following i.v. and dermal administration. Based on the 2nd *in vivo* study (DiDonato and Hazelton, 1991), absorption values of 53% concentrate and up to 36% (dilution) may be assumed but the outcome of the *in vitro* studies that are under way should be awaited.	Urinary excretion after dermal and iv exposure for estimation of absolute bioavailability is a well accepted approach for estimation of bioavailability.	See open point in comment 2(31)
2(34)	Vol 3, B.6.12.1, Dermal absorption *in vivo* in rat	UK: In the absence of comparative *in vitro* dermal absorption data, we propose adopting a worst case approach, with dermal absorption values of 50% for the concentrate and dilution. For the study of DiDonato and Steigerwalt, 1986, the UK considers it more appropriate to derive dermal absorption values based on absorption rather than comparative dermal bioavailability. Therefore, based on levels of radioactivity in urine, funnel wash, faeces and cagewash, dermal absorption values of 26.9% and 44.2% are proposed for the concentrate and dilution respectively. It is noted that levels of radioactivity in the carcass were not determined. The study of DiDonato and Hazelton, 1991, indicates carcass levels of 7.1% for the concentrate and 1.7% for the dilution, giving corrected values of 34% for the concentrate and 45.9% for the dilution respectively. For the study of DiDonato and Hazelton, 1991, based on levels of radioactivity in urine, funnel wash, faeces, cagewash, skin and carcass at 24 hours,	There is no reason to consider that estimation of dermal absorption based on bioavailability as not appropriate; this type of approach is well accepted for oral absorption estimation/calculation.	See open point in comment 2(31)

Dermal absorption (B.6.12)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		with urine levels over 7 days (as while urinary and faecal excretion continues over day 7-14, the increased excretion is comparable to loss of radioactivity from the carcass), dermal absorption values of 53.5% for the concentrate and 29.8% for the dilution are proposed.		
2(35)	Vol. 1, 2.3.6 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it, pg 30-31	DAS: as agreed with the RMS, a new *in vitro* dermal absorption study has been conducted with Systhane 20 EW (submitted to RMS, August, 2005). Refined dermal absorption values of 5% for the formulation and 22% for the spray dilution are recommended. Based on these new data, a revised dermal absorption assessment and the revised risk assessment for operator, bystander and re-entry worker as been submitted to RMS (August, 2005)	The new in vitro dermal absorption study will be summarized in the addendum.	Data requirement (for formal reasons) Applicant to submit the new *in vitro* dermal study. [This should be regarded as a technical data requirement since the study has already been submitted.] See open point 2(31)
2(36)	Vol 1, List of end points Impact on Human and Animal Health Dermal Absorption pg 62	DAS: the endpoints for dermal absorption and the output of the Operator Exposure modelling should be amended according to the revised calculation, **see comment (7)**	Endpoints will be amended after EPCO meeting.	Addressed
2(37)	Vol. 3, B.6.12 Dermal absorption	EFSA: both *in vivo* studies show some drawbacks. In the DAR, a new ongoing *in vitro* study is mentioned. It should be clarified whether it is available.	The new in vitro study will be summarized in the addendum.	See data requirement 2(35)

Toxicity of non-active substances (B.6.13)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(38)	Vol 1, List of end points Impact on Human and Animal Health Adsorption, distribution, extraction and metabolism Toxicologically significant compounds pg 61 *"Parent compound and metabolites"*	DAS: this should say 'Parent compound only': Metabolites RH-9090 and RH-9089 have comparable acute oral toxicity to myclobutanil, and have been fully evaluated in the toxicology package for myclobutanil as they are both major rat metabolites. They do no represent a toxicological concern, and do not form part of the residue definition for human health assessment and monitoring. TA is less toxic than myclobutanil and is therefore toxicologically non-significant. Please see **comment (5)**.	We agree with the notifier that Metabolites RH-9090 and RH-9089 have comparable acute oral toxicity to myclobutanil, and have been fully evaluated in the toxicology package for myclobutanil as they are both major rat metabolites. Therefore, they should be included in the listing of endpoints in the box related to toxicologically significant compounds.	See 2(22)

Exposure data (B.6.14)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(39)	Vol. 3, B 6.15.1, operator exposure	DK: We would like to see the exposure recalculated with the lower AOEL we have proposed.	New calculations will be provided after the EPCO meeting using the different agreed endpoints.	Re-calculation of the operator, worker and bystander exposure needed according to the outcome of the experts' meeting.
2(40)	Vol. 3, B.6.15 Exposure data	NL: A NOAEL for local effects after dermal exposure was derived (10 mg/kg bw/d). The external dermal exposure does not exceed this local NOAEL, but this was not evaluated in B.6.15.	The usual EU approach is to use the systemic AOEL	Addressed.

Exposure data (B.6.14)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(41)	Vol. 3, B.6.15.1, Estimation of operator exposure (Table B.6.15.1-1)	UK: The spray volumes on which the exposure estimates are based (100 – 1200 l/ha for grapevine and 200 – 2000 l/ha for apple) differ from those presented in the GAP table (1000 l/ha for grapevine and 1000 – 1500 l/ha for apple). Similarly, the pack size of 1.5 litres reported in this table differs from the packaging options of 0.25, 0.5, 1, 2, 3 and 5 litre containers described in the DAR.	In the operator exposure assessment, the company provided the data reported in table B.6.15.1-1. However, pack sizes of 1l and 5L were used in the calculations. New estimations will be performed after EPCO meeting taking into account the different agreed values.	Open point Input parameters for exposure assessment to be confirmed in an experts' meeting.
2(42)	Vol. 3, B.6.15.1, Estimation of operator exposure (Tables B.6.15.1-2 and B.6.15.1-3)	UK: The German Model estimates for broadcast air-assisted sprayers reported in this table assume a work rate of 15 ha/day and an operator body weight of 60 kg rather than the standard values of 8 ha/day and 70 kg, respectively, in this model.	New estimations will be performed after EPCO meeting.	See open point in comment 2(41)
2(43)	Vol. 3, B.6.15.3, Estimation of bystander exposure	UK: The bystander exposure calculation is based on a spray concentration which differs from that described in the GAP table and also uses data relating to the use of field crop (boom) sprayers (Lloyd and Bell 1983) rather than the equivalent data relating to the use of broadcast air-assisted sprayers (Lloyd *et al* 1987). Also, for assessing the risk to bystanders, a body weight assumption of 60 kg is more appropriate than the value of 70 kg used in this calculation.	Bystander exposure estimation is a semi quantitative assessment. Up to now, there is no agreed database that could be used for such an estimation.	Open point Bystander exposure to be discussed in an experts' meeting

Exposure data (B.6.14)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
2(44)	Vol. 3, B.6.15.4, Estimation of worker exposure	UK: The worker exposure calculation is based on the application rate of 0.048 kg a.s./ha for grapevine and does not consider the higher application rate of 0.090 kg a.s./ha for apple. Also, as the supported uses on grapevine and apple involve a total of 4 applications at 10 day intervals, the assessment should address the likelihood of a build up of foliar residues from multiple applications and the resulting risk to workers.	Such an assessment could indeed be very interesting but RMS has no models to do that and still believes that worker exposure assessment is a semi quantitative approach and no official recommendations exist until now.	Open point Worker exposure to be discussed in an experts' meeting
2(45)	Vol. 3, B.6.15 Exposure data	EFSA notes that in case dermal absorption values are revised, a re-calculation of the operator, worker and bystander exposure has to be provided.	Indeed.	See 2(39)
2(46)	Vol. 3, B.6.15.1 Estimation of operator exposure	EFSA: Work rate considered is15 hectares per day. It's not clear whether this value was applied to both German and UK POEM scenario. In this case, the operator exposure calculated with the German model would be overestimated, since the default treated area for high crop is 8 ha.	15 hectares were used in both models as proposed by the notifier. New estimations will be performed after EPCO meeting taking into account the different agreed values.	See 2(41)
2(47)	Vol. 3, B.6.15.1 Estimation of operator exposure	EFSA: in the table B.6.15.1-1, the pack size indicated is 1.5 L, which is not in accordance neither with what is reported in the B3 nor with the calculation appendix. RMS to clarify	Agreement: in the table B.6.15.1-1, the pack size indicated is 1.5 L, and this value was not used for estimation of operator exposure. In the calculations, pack sizes of 1L and 5L were used.	See 2(41)
2(48)	Vol. 3, B.6.15.1 Estimation of operator exposure	EFSA notes that a body weight of 60 kg is considered for both UK POEM and German model (the default considered in the German model is 70 kg).	Agreement. New estimations will be performed after EPCO meeting taking into account the different agreed values.	See 2(41)

Comments received on reporting table, section Mammalian Toxicology (B.6)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
2(1), 2(3)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted.
2(1)	UK	The submitted toxicity studies were performed with material of lower purity, and can therefore be considered as 'worst case' with regard to identifying the toxicity of the impurities. However it may be necessary to correct the reference values if they are derived from studies performed using material of significantly lower purity.	Noted. The issue will be discussed in a meeting of experts.
2(2)	UK	Although R36 classification is triggered according to the guidance, the low incidence and severity of the lesions at 21 days may indicate that this is not appropriate.	Noted.
2(7)	UK	Interpretation of the increased liver weight should be guided by the recent JMPR guidance document.	Noted. The issue will be discussed in an experts' meeting.
2(8)	UK	See 2(7)	Noted. The issue will be discussed in an experts' meeting.
2(10)	UK	See 2(7)	Noted. The issue will be discussed in an experts' meeting.
2(21)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted
2(23)	NOT	**Data requirement:** *Applicant to provide further information on health effects/surveillance programmes in manufacturing plant personnel* **DAS:** a report covering medical surveillance data available from the manufacturing/formulation of myclobutanil at Mozzanica, Italy over the time span 2000-2005 **is available,** and was sent to RMS.	Noted. Point copied into the reporting table.

Comments received on reporting table, section Mammalian Toxicology (B.6)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
2(34)	UK	New dermal absorption values should be calculated, based on the new comparative *in vitro* studies.	Noted.
2(35), 2(31)	NOT	Technical Data Requirement – Data already submitted to the RMS	Noted.

3. Residues

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(1)	Vol. 3, B.7.1.1, metabolism in grape	NL: Table B.7.1.1-1: how can the accountability be given when the TRR values were not provided for the different matrices? Were the tabulated values for the unextracted residues calculated values instead of measured values? If there is no reliable data on accountability, is this study then acceptable?	This study was performed in laboratory and was therefore not representative of the supported uses. These data have to be considered as indicative. -The total radioactive residues values were not provided for the different matrices. -The tabulated values for the unextracted residues were measured values by radio combustion analysis.	Refer to open point in 3(9) RMS agreed that the study is not acceptable and has to be deleted from list of studies relied upon
3(2)	Vol. 3, B.7.1.1, metabolism in grape	NL: First study, Nelson, 1984a: is the study with root treatment (growth in treated nutrient solution) representative for the proposed use (spray treatment)?	No, this study gave only qualitative information on the metabolism of Myclobutanil in grape plants following root uptakes for 7 and 16 days.	Refer to open point in 3(9) RMS agreed that the study is not acceptable and has to be deleted from list of studies relied upon
3(3)	Vol. 3, B.7.1.2, metabolism in apple	NL: Table B.7.1.2-1: (1) The TRR in the methanol extract of the pomace is missing from this table. (2) Were the unextractable residues not determined?	(1) : Pomace was extracted with refluxing methanol and the methanolic extract was reduced to dryness and was taken up in 100 mL water. The aqueous sample was partitioned and the distribution of metabolites was determined using the same procedure as described for juice, i.e., the diluted juice was extracted with chloroform and the resulting aqueous fraction was further extracted with n-butanol. The chloroform, butanol and remaining aqueous fractions were radioassayed. Extracted pomace was radioassayed to determine the extraction efficiency but the values were not given in the report. (2) : The unextractable residues were not	Open point RMS to present clarification on apple metabolism given in column 3 in an addendum

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			determined in the study.	
3(4)	Vol. 3, B.7.1.2, metabolism in apple	NL: The extractability figures for pomace in the text may not be correct (based on radioactivity level in chloroform extract, but should be based on radioactivity level in methanol extracts).	RMS agrees with that remark.	Refer to open point in 3(12) RMS to provide correction of the respective information in a revised DAR/corrigendum or in the announced addendum on the apple metabolism study, respectively
3(5)	Vol. 3, B.7.1.3, metabolism in wheat	NL: Table B.7.1.3-1: how can the accountability be given when the TRR values were not provided for the different matrices? Were the tabulated values for the unextracted residues calculated values instead of measured values? If there is no reliable data on accountability, is this study then acceptable?	This study was performed in laboratory and was therefore not representative of the supported uses. These data have to be considered as indicative. -The total radioactive residues values were not provided for the different matrices. -The remaining plant material was combusted to determine the amount of the non extractable residues.	Open point RMS to clarify whether the study is reliable and acceptable for evaluation of the residue behaviour of myclobutanil Open point was re-phrased based on a comment received by RMS: The study 'Laboratory metabolism studies of 14C RH-3866 in wheat' by Nelson, S.S. (1984) is considered as not acceptable for evaluation by RMS. This should be highlighted in a revised DAR/addendum/corrigendum as appropriate, and the list of references relied upon in the DAR as well the list of information, tests and studies considered relied upon should be amended accordingly. See also comment in 3(13)

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(6)	Vol. 3, B.7.1.3, metabolism in wheat	NL: Table B.7.1.3-1: The TRR in the methanol extracts is missing from this table.	RMS agrees.	Open point RMS to provide the missing TRR values for the wheat metabolism study in an addendum
3(7)	Vol 3, B.7.1.3, metabolism, distribution and expression of residues of myclobutanil in wheat	UK: The wheat metabolism study shows a different picture for the fruit crops which may have potential implications for future uses of the Myclobutanil. The presence of small molecular metabolites Triazole Acetic acid and Triazole Alanine is common with other triazole compounds. The RMS's conclusion that formation of these molecules occurs *via.* metabolism in the plant appears valid and is supported by reference to the soil metabolism study.	RMS notes the remark.	Open point As recently concerns have been raised on the toxicological relevance of the triazole derivate metabolites (teratogenic and/or embryotoxic resp.) these aspect needs prudent consideration even if the use on cereals is currently not notified as a representative use (but may be in future on MS level) As this metabolites are not specific to myclobutanil but to all triazole pesticides, a general solution with support of the toxicology meeting could be discussed in an experts' meeting See also comment in 3(28), 3(29)
3(8)	Vol. 1, List of end points, summary of representative uses	EFSA: For confirmation: is it correct that the representative use for NEU is in table and wine grapes.	RMS confirms that the representative use for Northern Europe is table/wine grapes.	Addressed
3(9)	Vol. 3, B.7.1.1 Grapes metabolism study: Nelson S.S., 1984(a)	EFSA: (1) This metabolism study investigating the uptake via roots is not relevant for the representative use (foliar application). Moreover, the information	The reference *Laboratory Metabolism Studies of ^{14}C RH-3866 in Grapes –Report TR 310-84-15 (Nelson S.S., 1984a)* will be deleted in the list of studies relied on (Addendum-September 2006-	Open point Updated list of studies relied upon to be provided as a clear indication of which of the available studies are considered

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		provided in this study is of limited value as it is not clear which parts of the grape seedlings have been analysed and the concentration of myclobutanil equiv. in mg/kg is not provided. Consequently, the reference should be deleted in the list of studies relied on. The metabolism study in grapes has the same reference (Nelson S.S., 1984a). If the study for grapes is deleted as it is not relevant for the supported use, no further changes are necessary in Annex B. In order to distinguish the two studies, the reference has to be changed in Annex A of the DAR to Nelson S.S. 1984b.	Myclobutanil-VOL3(B7).doc.).	acceptable and reliable for evaluation of the residue behaviour of myclobutanil See also comment in 3(1), 3(2)
3(10)	Vol.3, General comment for all metabolism studies	EFSA: Please provide information on the radioactive purity and the specific activity of the test substance.	The radioactive purities and the specific activities of the test substance are presented in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc	Open point Information on the radioactive purity and the specific activity of the test substance to be provided in an addendum
3(11)	Vol. 3, B.7.1.1 Grapes metabolism study: Nelson S.S., 1984(b)	EFSA: (1) The RMS mentioned that the extraction pathway for whole grapes was missing. To our understanding, the grapes were first separated into juice and pomace, and then extracted separately. On the basis of the weight of the juice and pomace fractions the identified compounds were recalculated to whole grapes. (2) The concentration and percentage of residual radioactivity (non extractable residues) for juice and whole grapes should be provided in order to decide whether further attempts to release the	(1) : RMS agrees. (2) : -From the results obtained from the individual fractions, the nature and the magnitude of the metabolites in whole grapes was determined. Therefore, no extraction procedure was applied to the whole grapes and no residual radioactive residues were determined. -Juice was partitioned successively against chloroform followed by 1-butanol to provide the organo and aqueous soluble partitioned phases. No residual radioactive fraction resulted from this	Open point RMS to present clarification on grape metabolism following a foliar treatment given in column 3 in an addendum

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		radioactivity and characterise/identify the components are required. (3) The total radioactive residue concentrations are provided for wet and dried pomace, but it is not clear whether the values for the methanol extraction phase and the subsequent partition in hexane and chloroform are related to wet or dry pomace. (Most likely the values are for wet pomace, please confirm) The same applies for the identified metabolites. Are they calculated for wet or dry pomace?	partitioning procedure. -According to guidance doc., if the non – extractable residues are less than 0.05 mg/kg or 25 % of the TRR and a significant proportion of the total residues has been identified, then no further work is required. Uncharacterized radioactivity in juice was present in the aqueous fraction and was impossible to isolate because of the low activity and the amount of material remaining from the juice. (3) : TLC analysis for isolation/characterization of the metabolites were performed on the chloroform extracts and the aqueous fractions of wet pomace.	
3(12)	Vol. 3, B.7.1.2 Metabolism study in apples , Nelson S.S., Streelman DR, 1984c	EFSA: (1) Apple pomace was first extracted with methanol. Please provide the myclobutanil equiv. concentration and the TRR% for this fraction (before the partitioning). (2) Please provide the information on the residual radioactive residues in the last row of the table on page 7-6. According to the second paragraph on page 7-7, more than 52% and 73% of TRR could be extracted. As the trigger values for characterisation/identification of metabolites might be exceeded, the notifier should provide information on attempts to release, characterise and identify the non extractable residues.	(1) : No rate of extractability with methanol was given for pomace and the residual radioactive residues were not radioassayed. (2) This information was presented in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Open point RMS to give clarification on apple metabolism study with regard to extractability and attempts to release, characterise and identify the non extractable residues in an addendum See also comment in 3(4)
3(13)	Vol. 3, B.7.1.3 Metabolism study in wheat (Nelson S.S. 1984a)	ESFA: (1) How many days after the last application was the sampling? Is there an explanation for the different myclobutanil concentrations in straw under field	1) Outdoor conditions : -Phenyl-^{14}C labelling form : PHI value : 41 days -Triazole- ^{14}C labelling form : PHI value : 68 days Greenhouse conditions :	Open point RMS to present clarification on wheat metabolism study given in column 3 in an addendum

Metabolism in plants (B.7.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		and greenhouse conditions? (Maybe different PHI?) (2) What was the residual radioactive residue concentration in grain (field and greenhouse conditions, phenyl label) and straw (field and greenhouse condition, triazole and phenyl label, respectively). (3) EFSA shares the view of the RMS that the cleavage of the molecule in wheat is likely. The argument provided by the notifier that in case of cleavage of the molecule metabolites containing only the phenyl ring moiety would arise is true, but as about 50 % of extracted TRR in grain were not identified and probably about 50% of TRR were not extractable it cannot be excluded that phenyl-metabolites are present in these fractions.	-Phenyl-^{14}C labelling form : PHI value : 43 days RMS agrees that further clarifictaion should be brought regarding the residue level of 68.57 mg/kg recovered in the phenyl labelled treated wheat straw under greenhouse conditions. 2) -The extraction procedure for the phenyl labelled field treated grain was not provided in the study. -The analysis of extraction and metabolites'identification in the phenyl labelled greenhouse treated grain were not performed. -For the phenyl ring labelled greenhouse treated straw, the blender extraction phase and the Soxhlet extraction phase amounted respectively 86.3 % of TRR and 15.3 % of TRR and the residual radioactive residues fraction was not recovered. -The extraction procedure for the triazole labelled treated field straw as not provided. (3) RMS agrees with the remark of EFSA. This point should be clarified by the notifier at MS level if wheat becomes an intended use.	Upon receipt of RMS comment the open point was closed. The study 'Laboratory metabolism studies of 14C RH-3866 in wheat' by Nelson, S.S. (1984) is considered as not acceptable for evaluation by RMS. Refer to open point in 3(5)

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(14)	Vol. 3, B.7.2.1, metabolism in lactating cow	NL: Test substances: why is the value for logPow given? To which compound does the value of 2.55	According to the template provided by EFSA, the partition coefficient water/octanol of thetest	Addressed logPow to be corrected in an revised

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		pertain?	substance must be given. The value of 2.55 at 22°C related to the purified active substance was not acceptable (cf. chapter VOL3(B2)-point B.2.1-13) The value of 3.5 for myclobutanil is now proposed. No data for log Po/w on the metabolites RH-9090 and RH-9089 were given.	DAR/corrigendum
3(15)	Vol. 3, B.7.2.1, metabolism in lactating cow	NL: In the study conclusion it is stated that myclobutanil was extensively oxidised into RH-9090, and that RH-9090 was further oxidised into RH-9089. Since however the cows were dosed with a mixture of 14C radiolabeled parent compound, 14C-RH-9090 and 14C-RH9089, in a ratio of 32:58:10, which evidence is there that RH-9090 and RH-9089 are indeed degradation products formed in the lactating cow?	RMS agrees that it should have been more appropriate to use the parent compound as the main test substance to describe clearly the metabolic pathway in lactating cows. However, since no parent was recovered in any of the matrices, there is evidence that RH-9090 and RH-9089 are degradation products of myclobutanil in the lactating cows.	Refer to open point in 3(23)
3(16)	Vol. 3, B.7.2.2, metabolism in laying hens	NL: Table 7.2.2-3 and text below table: what is meant by "Undissociated lactone/RH-9090/RH-9089"?	The Ethyl acetate extract was resolved by HPLC into fractions with retention times matching with the reference compounds parent, RH-0294 (diol), RH-9090, RH-9089 and the hydroxy-lactone. The highest percent of radioactive residues were found in the RH-9090, RH-9089 and the hydroxy-lactone area for liver and kidney (85 % of TRR and 84 % of TRR, respectively).	Open point RMS to present clarification on metabolism in laying hens given in column 3 in an addendum
3(17)	Vol. 3, B.7.2.3, metabolism in pigs	NL: Appendix A, metabolic pathway in plants and animals: Figure 3, the drawn structure of M2 (isomer) (metabolite in rat) is unclear. Is the structure identical to 4-hydroxy-3-lactone found in cow and hen?	The structure of M2 lactone recovered in the rat metabolism is similar to the 4-OH-3 lactone recovered in the liver and kidney of ruminants.	Addressed

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(18)	Vol. 3, B.7.1-B.7.3	NL: At several places it is stated that RH-9090 (alcohol) is reduced to RH-9089 (ketone). This step is an oxidation, not a reduction.	RMS confirms that this step is an oxidation.	Addressed to be corrected in an revised DAR/corrigendum
3(19)	Vol 3, B.7.1.3 Metabolism study in cows (Jacobson A.H. 1986b)	EFSA: (1) For compounds with multiple ring structures usually separate metabolism studies reflecting labelling of each ring is required, unless the cleavage of the ring systems can be excluded. In addition, the metabolism study should be performed not with a mixture of active ingredients and plant metabolites. Only the parent should be fed. Did the notifier provide a rationale for this study design deviating from the general approach? Due to this study design for example it would not be possible to identify metabolites containing the triazol ring after cleavage as the precursor molecule (parent compound) was only labelled in the phenyl ring. (2) The log Pow provided in the list of end points for the parent compound is different (2.89). Are there log Pow values available for the metabolites? (3) Calculation of the dietary burden: see comment no. (13) (4) Please provide detailed information on the extraction pathway and the subsequent partitioning in solvents systems. Did the identified metabolites occur in the water or in the organic phase? (5) In table B.7.2.1-3 the RMS reported the percentage of the total radioactive residues. Can	Clarifications are given in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Open point Clarifiying information on the metabolism study in cows addressing comments 3(19)-1 to 3(19)-7 to be presented in an addendum

Metabolism in livestock (B.7.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		you please report also the concentration of myclobutanil equiv. in mg/kg. (6) What are residues of myclobutanil related metabolites in muscle? (7) In the conclusion the RMS mentions that carboxylic acid RH-294 was formed after hydroxylation of RH.9090. According to the metabolic pathway in figure 2 RH-294 is a diol and not a carboxylic acid.		
3(20)	Vol. 3, B.7.1.4 Metabolism in hens, Table 7.2.2-3	EFSA: (1) Please provide detailed information on extraction pathway (which solvents were used, which extracts were used for further partitioning?). (2) In table B.7.2.2-3 metabolites were identified as lactone metabolite and undissociated lactone/RH9090/RH9089. Please specify what exactly is meant.	Clarifications are given in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Open point Clarifiying information on the metabolism study in hens to be presented in an addendum

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(21)	Vol. 1, 2.4.1, Definition of residues	AT: No residue definition for food of animal origin has been proposed by the RMS, since the intake based on residues found in possible feed according to the intended uses is not regarded relevant. Nevertheless, metabolism studies on laying hen and lactating cows have been provided and evaluated.	Based on the available metabolism data for ruminants and poultry in DAR, the residue definition for monitoring is proposed as follows : *ruminants : - parent for muscle and fat - metabolite RH-9090 expressed as myclobutanil for milk, liver and kidney.	Open point Proposed residue definition for food of animal origin and consideration of whether or not MRLs might be needed to be presented in an addendum Justification for the resepective proposals should be given, taking into

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		After a possible annex 1 inclusion of this substance, additional uses may be supported by the notifier; a proposal for the residue definition of animal origin is therefore very helpful to be peer reviewed.	*poultry : - metabolite RH-9090 expressed as myclobutanil for eggs - parent for the other matrices. No MRLs are required. The residue definition for the risk assessment should be myclobutanil +RH-9090 expressed as myclobutanil for all the livestock matrices.	account open point in 3(24) in terms of MRL proposlas and comments in 3(25) and 3(30) in terms of relevance of metbolites (potential of toxicity and/or fat solubility) See comments in 3(25) and 3(30)
3(22)	Vol. 3, B.7.3.1, residue definition plants	NL: Based on the metabolism studies, a conversion factor may be proposed to include the metabolite RH-9090 in the residue definition for risk assessment (7-9% TRR free and 5-6% TRR as glucoside in grape; 11.5% TRR free and 20.9-23.4% TRR as glucoside in apple). Is the non-inclusion based on the results of the field residue trials?	The metabolite RH-9090 was found in the rat metabolism along with the parent compound. Moreover, the oral acute toxicity (LD50) of RH-9090 in mice was found in a range of 300-1000 mg/kg. This metabolite is therefore as toxicologically relevant as the parent compound and it is therefore justified to include this metabolite in the residue definition for risk assessment.	Open point RMS to elaborate on the changed proposal for the residues definition for risk assessment (myclobutanil + RH 9090) in an addendum; consideration should be also given to a potential inclusion of RH-9089 depending on its toxicological relevance See also comments in 3(26), 3(27), 3(29)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(23)	Vol. 3, B.7.3.2, residue definition animal products	NL: See comment 8: which evidence is there that RH-9090 and RH-9089 are indeed degradation products formed in the lactating cow?	RMS agrees that considering the mixture of labelled compounds used as the test substance in the study and the fact that the parent compound was labelled only on the phenyl ring moiety, no definitive degradation pathway of myclobutanil in ruminants can be established.	Open point RMS to elaborate on the question of whether the available metabolism study in cows can be used to derive a metabolic pathway and to confidently propse a residue definition in ruminants, resepectively, in an addendum See also comment in 3(15) and 3(48)
3(24)	Vol. 3, B.7.3.2, residue definition animal products	NL: Last paragraph: in the metabolism study at the 1X dose level, total radioactive residues in liver and milk were >0.01 mg/kg (0.11 and 0.029 mg eq./kg respectively).	See point 3(21).	Open point RMS to verify the residue levels occurring in liver and milk of cows at the 1x dose rate in order to decide on necessity of MRL proposals May be incorporated into the considerations requested in Open point at 3(21).

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(25)	B.7.3.2 p.7-28	DE: a residue definition should be proposed for myclobutanil The metabolite RH-9090 was found in rat metabolism along with the parent compound . It cannot be excluded that observed effects (R 63) have been caused by this compound. Moreover acute toxicty (LD50) of R-9090 in mice rwas found in a range of 300-1000 mg/kg (Xn/R22). It is proposed thtat the residue definition of Myclobutanil in food of animal origin should include the metabolite R-9090	See point 3(21).	Refer to open point in 3(21)
3(26)	Vol 3, B.7.3.1, residue definition in plants	UK: Agree with tox assessment that RH-9090 should be included in the residue definition as it is potentially significant in apples, and was also observed in the grape metabolism study. The inclusion of RH-9089 would depend upon its toxicity as it was only observed at relatively low levels in the apple and grape metabolism studies (<4%).	Considering the toxicological relevance of the metabolite RH-9090 and its non negligible amount recovered in the whole fruit of apples and grapes, this metabolite should be included in the residue efinition for risk assessment only. The metabolite RH-9089 is as toxicologically relevant as the metabolite RH-9090. However, RH-9089 was observed at relatively low levels in the apple and grape metabolism studies and thefore, RMS considers that it is not worth including it in the residue definition for risk assessment.	Refer to open point in 3(22)
3(27)	Vol 3, B.7.3.1, residue definition in plants	UK: If RH-9089 is included in the residue definition then all of the trials would need to be repeated or samples re-analysed for this metabolite. Samples were analysed for parent & RH-9090 and so residue levels should be adjusted in the DAR to be reported as the sum of parent and its metabolite. Subsequent MRL calculations and risk	The metabolite RH-9089 has not to be included in the residue definition both for monitoring and risk assessment for the different reasons discussed under point 3(26). The metabolite RH-9090 has to be included only in the residue definition for risk assessment as it has a similar level of toxicology as the parent.	(1) Concerning RH -9089: Refer to open point in 3(22) (2) Open point Inlcusion of RH-9090 in the residue definition for risk assessment triggeres reevaluation of residue data relevant

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		assessments should be repeated taking into account the revised residue levels.	Myclobutanil remains the most valid indicator for monitoring in apples and grapes.	for consumer intake assessment and assessment of livestock dietary burden (STMR, HR) Revised calculations to be presented in an addendum In that context it should be checked whether sufficient data on RH-9090 are available for risk assessment purposes (e.g. storage stability data, validated analytical data generation methods, processing data) To be reported in an addendum.
3(28)	Vol. 1, 2.4.1 Definition of the residues relevant to MRLs, Plant products, pg 31	DAS: TA metabolite should not be considered as toxicologically relevant (see comment **(5) of Section 2 Mammalian Toxicology)** and therefore should not be included in the residue definition for wheat (or any other plant). Wheat is not included in the List of uses supported for myclobutanil.	RMS notes the remark. This point should be discussed within the toxicology section.	Refer to open point in 3 (7)

Residue definition (B.7.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(29)	Vol 3, B.7.3 Residue definition for plant products	EFSA agrees with the proposed residue definition for monitoring for the uses in fruit, but disagrees with the proposal for risk assessment. According to the metabolism studies in apples ca 35 % of TRR were identified as RH-9090 and RH-9090 glucoside. For grapes the percentage was about 15%. If these metabolites are not taken into account, the consumer risk might be underestimated. The proposed residue definitions are only valid for fruit crops. According to the metabolism study in wheat additional metabolites might be included in the residue definition. However, for these metabolites the toxicological relevance has to be clarified.	-RMS agrees and the residue definition for risk assessment is proposed as myclobutanil and the metabolite RH-9090 expressed as myclobutanil equivalent. No revised chronic and acute dietary risk assessment was presented in the Addendum as the new residue definition for risk assessment will not change significantly the chronic and acute intakes. -The toxicological relevance of the triazole metabolites recovered in wheat grain has to be discussed in the mammalian tox. Section in order to propose a residue definition both for monitoring and risk assessment.	Refer to open point in 3(22) in terms of residue definition for fruit crops Refer to open point in 3 (7) in terms of residue definition for cereals
3(30)	Vol 3, B.7.4 Residue definition for animal products	EFSA: If residues above the trigger values of 0.1 mg/kg feed (DM) are expected a residue definition for animal products should be proposed. In addition it should be clarified whether the residues are water or fat soluble. The RMS states that myclobutanil residues should be considered as non liposoluble due to the log Pow of the parent compound. However, no information is available on the log Pow of the metabolites. In the cow metabolism study only metabolites were observed, no parent compound was not detected in any tissue of the cow and in milk.	-See point 3(21). -Indeed, no data on the partition coefficient n-octanol/water was provided for the relevant metabolites RH-9090, RH-0294. However, based on the available livestock feeding study in ruminants (point B.7.8.1 in DAR), it can be concluded that these metabolites were not liposoluble as for the different dosing levels, the residue levels of the parent compound, the alcohol metabolite RH-9090 and the diol RH-0294 were below the LOQ of the analytical method in milk and in all the edible tissues.	Refer to open point in 3(21)

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(31)	Vol. 3, B.7.6.1, residues in supervised trials in apples	NL: Several trials in apples with a spray concentration of 0.0045 kg a.s./hL were not accepted as the dose in terms of kg a.s./ha was <25% below the cGAP rate of 0.09 kg a.s./ha. However, the spray concentration was within 25% of that of cGAP (0.006 kg a.s./hl), and the trees were spayed to run-off. Are these trials not acceptable, since the key parameter determining the residue when orchards are sprayed is not the areal dose, but the spray concentration?	RMS agrees with that remark although considering the EU guideline, the dose in terms of kg a.s./ha is the key parameter for the acceptability of the residue values. Other trials (SE) with a spray concentration of 0.0045 kg a.s./hL should be accepted : -parent myclobutanil : 0.04-0.05-0.07-0.04-0.04 ppm -RH-9090 expressed as myclobutanil: <0.01-<0.01-<0.01-<0.01-<0.01 ppm.	Open point Results of trials additionally accepted as valid by RMS to be presented in an addendum Note: If higher residues occur at a later PHI than 14, these residues values have to be considered in the risk assessment. RMS to review residue data accordingly
3(32)	Vol. 3, B.7.6.1, residues in supervised trials	NL: Certain trials in grape used a spray concentration of 0.003 kg a.s./hL, which is >25% below that of cGAP (0.0048 kg a.s./hL), but these trials were accepted since the the dose in terms of kg a.s./ha was within 25% of that of cGAP. Is the key parameter determining the residue when orchards are sprayed not the spray concentration instead of the areal dose?	RMS agrees. However, the dose in terms of kg a.s./ha was within 25 % of that of the critical GAP and the corresponding trials are judged acceptable.	Addressed
3(33)	Vol. 3, B.7.6.1, residues in supervised trials in grapes	NL: Several trials in grape with a spray concentration within 25% of that of cGAP were not accepted as the dose in terms of kg a.s./ha was <25% below the cGAP rate of 0.048 kg a.s./ha. Are these trials not acceptable, since the key parameter determining the residue when orchards are sprayed is not the areal dose, but the spray concentration (when sprayed to run-off)?	RMS agrees. Other trials (SE) with a spray concentration of 0.00375 kg a.s./hL should be accepted : -parent myclobutanil : 0.03-0.03-0.04-0.03-0.02-0.03 ppm -RH-9090 expressed as myclobutanil: <0.01-<0.01-<0.01-<0.01-<0.01-<0.01 ppm.	Open point Results of trials additionally accepted as valid by RMS to be presented in an addendum Note: If higher residues occur at a later PHI than 14, these residues values have to be considered in the risk assessment. RMS to review residue data accordingly

Use pattern, critical GAP, residues trials (B.7.4 to B.7.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(34)	Vol. 3 B 7.6.2, Conclusions pg 7-33.	DAS: There is a typographical error in the STMR indicated for grape trials in the South (SZ). The document indicates that the STMR is 0.043 mg/kg. However, **the correct STMR should be 0.052 mg/kg**, based on the 14 trial results considered, which are 0.063-0.043-0.09-0.04-0.10-0.13-0.02-0.03-0.09-0.03-0.06-0.02-0.10-and- 0.02 mg/kg.	RMS agrees. The STMR value is 0.0515 mg/kg.	Addressed To be corrected in a revised DAR/corrigendum/addendum following an update of the selected residues values according to Open point in 3(31)
3(35)	Vol. 3 Table B7.7.2-1, pg 7-34.	DAS: in the title of the table the following phrase is included: "(Residues expressed as mg myclobutanil equivalents/kg)". The word "equivalents" should be removed from this phrase since it is only myclobutanil residues (not metabolites) that are reported here.	RMS agrees.	Addressed To be corrected in a revised DAR/corrigendum/addendum
3(36)	Vol. 3 Table B7.8.1-1, pg 7-37	DAS: the heading in column 1 should be changed from "Metabolites" to "Analytes". Myclobutanil is included as one of the analytes and should not be referred to as a metabolite.	RMS agrees.	Addressed To be corrected in a revised DAR/corrigendum/addendum

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(37)	Vol. 3, B.7.7.1, effect on nature of residues	NL: The conditions for hydrolysis described in Annex I of appendix E of the Lundehn document (90-120°C) are more severe than in the available hydrolysis study (50°C). The data on heat stability of pure myclobutanil obtained during boiling point determination are not relevant to address hydrolytic stability. Hydrolysis studies are required, performed according to the procedures in	RMS agrees.	Data requirement Studies simulating representative processing conditions to be sumitted by the applicant. This study should investigate the behaviour of the relevant residue (potenbtially including relevant metabolites) on crops to be processed.

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		Annex I of appendix E of the Lundehn document.		The notifier indicated that a study will be conducted and the final report will be available by June 2007 See also comment in 3(39) .
3(38)	Vol. 3, B.7.7.2, effect on magnitude of residues	NL: Transfer factors for wet apple pomace were 0.55 and 0.646 in the first two trials, but much higher (2.87 and 2.97) in the last two trials. How can the difference be explained? Why is it stated under "Conclusion" that the average transfer factor for wet apple pomace is 2.97? Are the results from the first two trials not valid?	The 3 first trials in Table B.7.7.2-1 (p.7-34) were considered as valid. The trial referenced AF/8164/DE/4- GHE-P-10967 should not be acceptable as the critical dose rate was a magnitude of 5 higher than the critical does rate in the use pattern. The conclusion under point B.7.7.2 will be amended in the Addendum-September 2006-Myclobutanil-VOL3 (B7).doc. However, there is no clarification to explain the discrepancy between the different calculated transfer factors.	Open point Addendum on transfer /processing factors is awaited. Note: The discrepancy observed in terms of the apple pomace processing factors is easily explained by the fact that the factors 0.55 and 0.646 refer to apple puree rather than to apple pomace. (refer to p.16 and p.29 of the report) Why is a residue study with a higher application rate not eligible to derive a processing factor? A sound argument should be provided for that decision. However, final conclusion on processing is pending the outcome of the study on the effects on the nature of residues (data requirement) See also comment in 3(40) and 3(52)
3(39)	Vol. 3, B.7.7.1 Effects on the nature of residues	EFSA: A study investigating the effects on the nature of residues has to be provided. The justification for not providing the study is not acceptable.	RMS agrees.	Refer to data requirement in 3(37)

Processing (B.7.7)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(40)	Vol. 3, B.7.7.2 Effects on the level of residues	EFSA: The study is of limited validity as no information on the nature of potential metabolites generated during processing is available. A final conclusion is pending the outcome of the study on the effects on the nature of residues. Is there a reason why in two of the processing studies the transfer factors for wet pomace was lower than 1 (indicating that the residues would be diluted). Please provide a statement on the acceptability of this studies?	See point 3(38).	Refer to open point in 3(38)

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(41)	Vol. 3, B.7.8, livestock feeding studies	NL: The intake for livestock is based on the maximum residue in wet apple pomace in the two processing trials at cGAP. However, is it not more appropriate to correct the highest residue, measured in apple fruit in all acceptable trials, by the average transfer factor for apple pomace? That would give a much higher value, based on residues data in apples from far more trials than two.	RMS agrees. The intake for livestock has been re-calculated considering the measured residue in apple fruit and the average transfer factor. This calculation is presented in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Open point Recalculation of livestock dietary burden under consideration of the relevant residues for risk assessment and valid processing factors to be presented in an addendum Upon that recalculation the comparison to the dose rates in feeding studies and an estimation of potential residues in food of animal origin to be redone See also comment in 3(42), 3(43), 3(49)

Livestock feeding (B.7.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(42)	Vol. 3, 7.8 Livestock feeding study	EFSA: 1) The calculation of the dietary burden for cattle should be based on the results of the residue trials in apples and the processing factor for apple pomace. In this case, the STMR of the apple trials (0.142 mg/kg) and the processing factor proposed by the RMS (2.97) gives 0.42 mg/kg in wet pomace. The dietary burden for beef cattle results in 0.55 mg/kg feed (DM) or 0.023 mg/kg bw. 2) From metabolism studies in cows it was concluded that one of the main metabolites in animal products was 4-hydroxy-3-lactone (46% and 22% in liver and kidney, resp.). In the feeding study this compound was not analysed. 3) What is carboxylic acid RH-0294? According to the metabolic pathway presented in Figure 2 (page 7-61) RH-294 is a diol, but does not contain a carboxylic group.	-The residue levels in milk reached a plateau after day 2 or 3 after first dosing. In this case, the highest residue measured in apple fruit was used and not the STMR value. Reference is made to open point 3(42) in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc. -RMS agrees. However, this metabolite was recovered in rat metabolism and is therefore out of any toxicological relevance. -RMS agrees.	1) refer to open point in 3(41) 2) Open point RMS to specify what “out of any toxicological relevance” means (as toxic as myclobutanil?) 3) Open point While in metabolism study the diol metabolite RH294 was identified as a major metabolite, in the feeding study the carboxylic acid RH294 was anaylsed for. RMS to give further clarification on that issue.
3(43)	Vol. 3, 7.8.1 Livestock feeding studies in lactating cows or goats	EFSA: Considering the revised dietary burden calculation with the STMR from apples and the average processing factor, the lower dose group in the feeding study 1.6 mg/kg bw/day represents a 3 fold dose rate. The statement in the conclusion should therefore be amended accordingly.	On the basis of the revised livestock intake calculation, the lower dose group in the feeding study (1.6 mg/kg diet) represents a 3 fold dose rate instead of 6 fold dose rate as mentioned in the conclusion under point B.7.8.1 in DAR (p.7-37).	Refer to open point in 3(41) Upon recalculation of livestock burden to be corrected accordingly

Succeeding/Rotational crops (B.7.9)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(44)	Vol. 3, B.7.9, rotational crop studies	NL: It is stated that studies on residues in rotational crops are not required based on the DT90 (field) and (lab) values ((>1 year and 637-1906 days respectively). These DT90 values however would trigger studies on residues in rotational crops.	RMS agrees. However, the planting of succeeding crops is not relevant in this case since both apples and grapes are long-lived crops that are not grown in rotation with other succeeding crops.	Open point Given the long-life of myclobutanil residues in soil it should be checked with F&B section whether generation of soil metabolites that have not been found in plant metabolism may occur (e.g. trialzoles), and thus a potential uptake/accumulation of this compounds in plants following a repeated application (year by year) of myclobutanil might be expected The statement in the DAR concerning the DT90 and non-requirement of studies is wrong and thus confusing and should be corrected in a revised DAR/corrigendum/addendum See also comment in 3(45)
3(45)	B.7.9 p 7-38; 2nd para	DE: the causality of this conclusion remains unclear The opposite conclusion results from a DT90 >1 year. Nevertheless a rotational crop study is not deemed necessary since both intended uses are long-lived crops	See point 3(45).	Refer to open point in 3(44)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(46)	Vol. 3, B.7.11.2, NESTI calculations	NL: Details on the calculations of STMR-P for all processed products would be helpful for transparency.	Reference is made to Table B.7.11.2. The STMR was calculated on the basis of the whole data base both for Northern and Southern Europe, respectively for grapes and apples. The detailed calculation is presented in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Open point RMS to present recalculation of NESTI under consideration of the relevant residues for risk assessment in an addendum The addendum should include details on the calculations of the HR-P/ STMR-P values used in the NESTI calculations. See also comment in 3(54) and 3(53)
3(47)	Vol. 3, B.7.14, storage stability	NL: Results for 24 months for almond hulls (parent + metabolite) are not acceptable since the residues were corrected for procedural recoveries which were <70%. This applies also to almond meat, metabolite only, after 24 months. It is considered to be more appropriate to assign a storage stability of 18 months in these cases.	The procedural recoveries for almond hulls at 24 months raised 67.1 % and 66.5 %, respectively for the parent and its metabolite RH-9090 (table B.7.14-4). These values are acceptable. Regarding the almond meat, RMS agrees that it is more appropriate to assign a storage stability of 18 months.	Open point Procedural recoveries have to be at least 70%. In the light of that information RMS to review and report acceptable storage stability data in an addendum
3(48)	Vol. 1, 2.4.1, definition of residues relevant to MRLs	NL: Which evidence is there that RH-9090 and RH-9089 are indeed degradation products formed in the lactating cow (see also comment 8 and 13)?	See comment under point 3(15).	Refer to open point in 3(23)
3(49)	Vol. 1, 2.4.1, definition of residues relevant to MRLs	NL: Revised intake calculations for livestock (see comment 20) might lead to a higher intake and necessitate comparison with higher dose groups from the feeding study.	See comment under point 3(41) and 3(43).	Refer to open point in 3(41)
3(50)	Vol. 1, List of Endpoints, storage stability	NL: Data from other commodities (almond, cucumber, tomato) may also be included.	These data will be included in the updated version of the LoEPs.	Addressed

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(51)	Vol. 1, List of Endpoints, critical residues data	NL: The STMRs for apple and grape are apparently based on the combined data set from Europe-N and Europe-S. The STMRs for the separate regions (vol. 3, B.7.6.1) are higher than the values in the Endpoints. Is it justified to combine the data from the N and S regions? In particular for grape the data sets seem to differ substantially.	Using the STMRs values calculated on the combined data sets from Northern and Southern Europe does not lead to significant change in the short term dietary intake.	Open point RMS to revise list of end points to reflect the resepective STMR and HR values for the individual updated [as proposed in open points in 3(31) & 3(33)] data sets for N-EU and S-EU. The more critical data set is the one for N-EU.
3(52)	Vol. 1, List of Endpoints, processing factors	NL: For apples transfer factors from all 4 trials for e.g. wet pomace were included, but in vol. 3, B.7.7.2, the conclusion only referred to the transfer factors from two studies (see also comment 19). How can this discrepancy be removed?	RMS agrees.The trial AF/8164/DE/4 GEHE-P-10967 was considered as not acceptable (dose rate 5 fold the critical GAP rate). The conclusion under point B.7.7.2 in DAR and the processing factors in the LoEPs should be amended. See Addendum-September 2006-Myclobutanil-VOL3(B7).doc. and updated LoEPs.	Refer to open point in 3(38)
3(53)	Vol 3, B.7.11, estimates of potential and actual exposure through diet	UK: Both chronic and acute risk assessments reveal no problems with the proposed MRL's, although this may change depending upon the outcome of the decision on the residue definition and subsequent amendment of the residue levels.	RMS notes the remark.	Open point RMS to present recalculation of chronic intakes under consideration of the relevant residues for risk assessment and revised residue endpoints in an addendum For NESTI calculation refer to open point in 3(46)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
3(54)	Vol. 3, B.7.11.2 Short term dietary intake risk assessment	EFSA: In general, the risk assessment for processed commodities like wine should be calculated with the STMR on grapes (0.12 mg/kg for NEU), multiplied with the average processing factor (0.128), respectively. The same calculation has to be performed for apple juice. However, the final result will not be influenced significantly.	RMS notes the remark.	Refer to open point in 3(46)
3(55)	Vol. 3, B7.16 References relied on	EFSA: The study Betteley, 1994 is not relevant and should be deleted from the list of studies relied on.	See Addendum-September 2006-Myclobutanil-VOL3(B7).doc.	Refer to open point in comment 3(9)

Comments received on reporting table, section Residues (B.7)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
3(5)	RMS	RMS considers that this study presents some important data gaps to support the evaluation of the residue behaviour of myclobutanil in wheat and has to be deleted from the list of studies relied upon.	It is understood that RMS considers the wheat metabolism study by Nelson, S.S. (1984) as not acceptable for evaluation. The reporting table was updated accordingly.
3(7)	UK	The proposal for a discussion is welcome as this is a series issue affecting many active substances which does not have a straight forward solution.	The triazole metabolites issue will be discussed in general in the January 2007 PRAPeR meeting. Apart from that, every concerned substance will need an individual consideration of the triazole metabolites levels generated.

Comments received on reporting table, section Residues (B.7)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
3(10)	RMS	The radioactive purities and the specific activities of the test substance were included in the Addendum-September 2006-Myclobutanil-VOL3(B7).doc	No such addendum has been received by EFSA yet. (December 2006) Open point remains open
3(13)	RMS	See point 3(5). This study cannot be considered as acceptable to describe completely the metabolism of myclobutanil in wheat and has to be deleted from the list of studies relied upon.	The reporting table was updated accordingly
3(15)//3(23)	RMS	The level of radioactive residues in muscle and fat was found to be below the LOQ (0.02 ppm) of the analytical method and no further metabolites identification was attempted. Identification of the metabolites was performed only in milk whey soluble fraction, liver and kidney in which no parent was recovered and the metabolite RH-9090 was metabolised into the 4,5-diol-RH-294, the ketone RH-9089 and the 4-HO-3 lactone metabolite. The metabolite RH-9090 can be considered as a valid indicator of the level of contamination of the edible matrices in ruminants to propose a residue definition for monitoring as RH9090 alone. Considering the oral acute toxicity (LD50) of the metabolites alcohol-RH-9090 and the ketone RH-9089 which is higher than for the parent compound, the residue definition for risk assessment should include both the 2 metabolites RH-9090 and RH-9089 for all the matrices. No residue definition is proposed for poultry matrices.	Noted Addendum is awaited.
3(22)	RMS	In plants : -DOR for monitoring : parent alone. -DOR for risk assessment : myclobutanil + RH-9090+ RH-9090 glucoside expressed as myclobutanil considering the toxicological relevance of the metabolite RH-9090 (acute oral toxicity higher than for the parent compound). The metabolite RH-9089 was recovered at a trace level (<0.01 mg/kg) and was not included in the DOR for risk assessment.	Noted Addendum is awaited.
3(24)	RMS	RMS disagrees with the comments from the Netherlands. The calculated dietary burden amounted to 0.291 and 0.89 mg/kg diet, respectively for dairy cattle and beef cattle. In table B.7.2.1-1, the lowest feeding level was 0.915 mg/kg diet corresponding to a 3 and 1 orders of magnitude higher than the calculated dietary burden respectively for dairy cattle and beef cattle. Considering these overdosing factors, the residue levels in milk ranged between 0.002-0.008 ppm and in liver	The reporting in the DAR is ambiguous and should be revised for the sake of clarity. The lowest feeding level of 0.915 mg/kg diet was reported

Comments received on reporting table, section Residues (B.7)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
		between 0.015-0.045 ppm based on the metabolism data.	as 0.3 N treatment group in the DAR. (p.7-12 to 7-14) It should be recalled by RMS when estimating residue levels in food of animal origin that the proposed animal residue definition for RA includes also the metabolite RH9090 (see comment/answer in 3(21)) Addendum is awaited.
3 (26)	UK	The response is acceptable.	Noted.
3(27)	UK	The response is acceptable.	Noted.
3(27)	RMS	RMS agrees to include the metabolite RH-9090 in the residue definition for the risk assessment in plants but this will not change significantly the consumer intake risk assessment and the livestock dietary burden since the residue levels of the metabolite RH-9090 in the trials on grapes and apples raised to around the LOQ of the analytical method (0.01 mg/kg). Processing data with RH-9090 are available. The analytical method to determine the parent and RH-9090 was considered as sufficiently validated and storage stability data for RH-9090 are available for almond meat and hulls, cucumbers and tomatoes.	Noted Addendum is awaited.
3(37), 3(39)	NOT	**Data requirement** *Studies simulating representative processing conditions to be submitted by the applicant. This study should investigate the behaviour of the relevant residue (potentially including relevant metabolites) on crops to be processed.* **DAS:** The study will be conducted and the final report will be available by **June 2007**	The reporting table was updated accordingly
3(38)	RMS	RMS checked again the processing data for apple wet pomace in the first 2 trials (DEU86F21221/241) in the report and confirms that the transfer factors proposed in the DAR	No such addendum has been received by EFSA yet.

Comments received on reporting table, section Residues (B.7)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
		concern the wet pomace and not the apple puree. RMS agrees that the trial performed at a higher rate of application (5 fold the critical GAP rate) has to be taken into account. Therefore, the mean transfer factor is 1.784 instead of 1.35 (Addendum-September 2006).	(December 2006) The analysis report of the laboratory on the determined residues in apple samples (study EU86F21221/241; p. 16 and p.29) clearly refers to 'Mus' meaning apple puree. It is advised to clarify any potential reporting error somewhere in a study summary with the notifier. Open point remains open
3(53)	UK	The response is acceptable.	Noted

4. Environmental fate and behaviour

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(1)	Vol. 1, list of endpoints, route of degradation in soil and Vol.3, B.8.1.1.1 Aerobic degradation in soil, Table B.8.1.1.1-5	AT: Did the metabolite Myclobutanil butyric acid exceed the 5 % level only once (76 d) or at several consecutive time points? If the metabolite accounts for more than 5 % in at least two sequential measurements its relevance must be assessed (according to Guidance Document on the assessment of the relevance of metabolites in Groundwater).	As mentioned in the DAR, in this study the radioactivity has been characterized for the only unknown peak at level >10% (10.2%) DT50 in several soils, Koc and PEC have been determined for the metabolite Myclobutanil butyric acid.	Addressed
4(2)	Vol. 1, list of endpoints, rate of degradation in soil, laboratory studies	AT: The DT50-values (DT50 = 5-42 d at 25°C) of the metabolite Myclobutanil butyric acid (max. 6 %, 76 d) determined by a separate study should be mentioned in the list of endpoints	The listing of endpoints has been amended.	Addresssed
4(3)	Vol.1, list of endpoints, route of degradation in soil – supplemental studies, soil photolysis and Vol. 3, B.8.1.1.3. soil photolysis	AT: The study showed many deviations from the current guidelines; especially the light intensity of 21 W/m^2 was too low and the range of the light source of 290 – 480 nm was too small. Can this study really be accepted as valid and is the photodegradation of the active substance really clarified with this study? If not, a new study has to be conducted/provided. The deviations should be mentioned in the list of endpoints.	The RMS has considered that sufficient information was available to show that photolysis is a minor route of degradation. Further study is not required.	Open point Meeting of experts to confirm that the available soil photolysis study is not reliable, then subsequently discuss if a new soil photolysis study should be required to complete the risk assessment for this substance, or not. The absence of significant absorption by myclobutanil above 290nm is important information for this discussion.

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(4)	Vol.3, B.8.1.3.1 Soil dissipating testing and Vol. 3, B.8.1.3.2. soil residue testing –soil accumulation testing and Appendix 1 – field studies	AT: Was the metabolite RH9090 (putative photolytic metabolite) the only metabolite investigated although the metabolites RH9089 and Myclobutanil butyric acid seemed to occurred in higher amounts than RH9090 during the studies in laboratory? Is there any explanation given for this selection?	The myclobutanil butyric acid has been determined at max level of 6% in a metabolism study of **2003**. Although this metabolite is not major it has been fully evaluated (DT50, Koc, PECgw calculations). The metabolite RH9089 is not major. The metabolite RH-9090 was recovered at level < 0.0 1 mg/kg in a field study performed in **1990**.	Addressed
4(5)	Vol 3. B.8.1.1.2 Anaerobic degradation in soil, pg 8-10 Vol 3. B.8.1.2.2 Anaerobic degradation, pg 8-13	DAS: the statement "no acceptable study" it is not appropriate: the study is simply not required.	We agree with the DAS statement. The study is simply not required. The listing of endpoints has been amended.	Addressed
4(6)	Vol. 3 B.8.1.3.1 Soil dissipation testing, pg 8-13	DAS: the soil dissipation data have been summarized separately in an appendix while it would be more consistent to include the DT50 values in the main body of the document as with the lab data.	No comment	Addressed
4(7)	Vol 1, list of endpoints, general	EFSA: Please add to the endpoints sheet the endpoints for the metabolite myclobutanil butyric acid (degradation rates, adsorption, groundwater PEC)	The listing of endpoints has been amended.	Addressed
4(8)	Vol 1, list of endpoints, Anaerobic degradation, p.45	EFSA: Please state 'no acceptable study, not required for the representative uses evaluated'	It is always assumed that the assessment is related to the representative uses evaluated.	Open point EFSA requests the endpoints should state: ,for the representative uses evaluated (summer application to fruit crops)'

Route and rate of degradation in soil (B.8.1)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(9)	Vol 1, list of endpoints, Rate of degradation in soil, method of calculation, p.45	EFSA: The appropriate information needs to be added to this box. I.e first order linear regression, or first order non-linear regression, field studies biphasic first order etc.	The listing of endpoints has been amended.	Open point Please clarify in the endpoints if the lab studies method of DT50 calculation were estimated by linear or non linear regression (first order).
4(10)	Vol 1, list of endpoints, Rate of degradation in lab soil, DT50 values, p.45	EFSA: Please also add the FOCUS normalised geomean value of 250 days that has been used in some (the most recent) FOCUS groundwater modelling as well as the arithmetic mean value that is currently listed, that has been used for the FOCUSsw modelling.	The listing of endpoints has been amended.	Addressed
4(11)	Vol 1, list of endpoints, Photochemical oxidative degradation in air, p.53	EFSA: Please state the OH concentration assumed for the calculation..	The listing of endpoints has been amended.	Addressed

Adsorption,desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(12)	Vol.1, list of endpoints, soil adsorption/desorption and Vol.3, B.8.2.1 Adsorption and desorption	AT: The Kd- and Koc-values of the metabolite Myclobutanil butyric acid should be mentioned in the endpoint list.	The listing of endpoints has been amended.	Addressed

Adsorption,desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(13)	Vol. 3, B.8.2.1, Adsorption and desorption	UK: We note that the adsorption of myclobutanil is postulated to correlate with both CEC and pH. We also note the RMS conclusion that refined PECgw calculations should take this into account. Currently the exposure assessments presented in the DAR appear to be based on the mean Koc value only. Given the relatively narrow range of Koc values, the UK would propose that the use of a mean Koc value is valid and the possible influence of soil pH and CEC does not need to be investigated further.	This information on the correlation of K with CEC and pH was mentioned in the study. However, afterwards we base the PEC assessment on the mean Koc. We agree with the UK comment.	Open point LoEP soil adsorption/desorption to be updated to state there is no clear pH dependence of soil adsorption. As the final RMS, UK and EFSA (see comment at line 4 (15)) conclusion is there is no clear evidence of pH dependance, RMS to to consider stating this position in a corrigendum or amended DAR.
4(14)	Vol. 1, B.2.5.2, Fate and Behaviour in soil, Lysimeter study, pg 33	DAS: this point was discussed with the RMS during the preparation of the DAR and the agreed conclusion was that a lysimeter study **is not necessary** and that this requirement was not to be included in the DAR as it is stated in Vol. 3, point 8.2.4. pg 8-18 of the DAR: "*We have considered that a lysimeter study would not be necessary: sufficient lab data to determine the PEC, several scenarios are acceptable"*	We agree with the DAS comment. The statement of pg 8-18 of the DAR is still valid; moreover the lysimeter study is not required in the level 4 of the DAR. The listing of endpoints has been amended.	Addressed RMS to consider in a corrigendum or amended DAR.
4(15)	Vol. 3. B.8.2.1, adsorption/desoprtion p. 8-16 Vol 1, list of endpoints, adsorption/desorption, p.46	EFSA: Based on such a small data set it is unlikely that the correlation identified for Kf with CEC and pH regarding parent myclobutanil is real. Also for a compound with a pKa of 2.3 there is no first principles reason to expect any correlation with soil pH. If as rapporteur you are convinced the correlations are real these should be taken into account for PEC groundwater (and possibly surface water) calculations at the first tier of assessment.	See comment made by UK - 4(13)	Covered by open point against point 4 (13) above.

Adsorption,desorption and mobility in soil (B.8.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(16)	Vol. 3. B.8.2.1, adsorption/desoprtion p. 8-17	EFSA: Study on soil batch equilibrium adsorption/desorption of myclobutanil butyric acid has the study author and date missing. Presumably this study was Smith J.K. 2004? Please clarify this.	Yes	Addressed RMS to consider in a corrigendum or amended DAR.

PEC in soil (B.8.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(17)	Vol. 3, B 8. 3, Predicted environmental concentration in soil (PECs); and Vol. 3, B. 8. 6. 1., Predicted environmental concentration in groundwater (PECgw)	PL: For the calculation of PEC_S the highest soil DT_{50} value was used, while for the calculation of PEC_{GW} the mean values (two times lower) were used. Could you please explain the reasons for such choice (as it seems to be inconsistent).	The PEC soil are generally based on the worst case DT50. The modeling softwares to calculate PECgw require using mean DT50.	Addressed
4(18)	Volume 3 B.8.3 Predicted environmental concentration in soil (PECs) pg 8-19	DAS: The initial PECs values reported in the DAR are slightly lower to those calculated by DAS (0.126 and 0.236 mg/kg *vs.* 0.128 and 0.240 mg/kg for vines and apples, respectively). DAS believes this to be an error because the RMS subsequently used 0.128 and 0240 mg/kg as the initial PECs values in the accumulation PEC table and calculation. Also, DAS considers that it is more consistent to use the mean lab DT50 for the TWA calculations, rather than the worst case.	The differences in the PEC have no impact on the risk assessment for soil organisms.	Addressed

PEC in soil (B.8.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(19)	Vol 3, B.8.3, PECsoil p 8-19-20 Vol, List of endpoints PECsoil p 47-48	EFSA: The EFSA can agree to the use of the longest single first order laboratory DT50 for myclobutanil of 574 days to calculate an accumulated PEC in soil. However field data would probably provide a more realistic estimate. For the available field data to be used as the basis for PEC soil calculation, a new kinetic assessment of the field studies that accurately estimated the biphasic DT90 (which is currently not available) would be required.	Worst case PECsoil considering accumulation of the a.s. during several years were used in the risk assessment. We consider that other calculations are not necessary.	Addressed

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(20)	Vol. 1, Level 2, 2.1.4. , Classification and Labelling, Table 2.1.4-1	NL: The environmental safety phrases S60 and S61 are assigned to formulated products and not to the active substances	We take note	Addressed RMS to consider in a corrigendum or amended DAR.
4(21)	Vol.1, Level 2, 2.5.3 Fate and behaviour in water, Impact on water treatment procedures	NL: The active substance is myclobutanil in stead of the metconazole mentioned here.	No comment	Addressed RMS to consider in a corrigendum or amended DAR.
4(22)	Vol. 3, B.8.4.1 Hydrolysis rate of relevant metabolites , degradation and reaction products	NL: The information in the table on page 8-22 is correct, but the format is rather unusual.	No comment	Addressed
4(23)	Vol. 1, 2.5.3 Fate and behaviour in water impact on water treatment procedures, pg 34	DAS: typo: change metconazole to myclobutanil	No comment	Addressed RMS to consider in a corrigendum or amended DAR.

Fate and behaviour in water and impact on water treatment procedures (B.8.4-B.8.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(24)	Vol. 3. B.8.4.4, Water sediment study p. 8-23-26 Vol 1, list of endpoints, Route and rate of degradation in water, p.48	EFSA: Two sediment water systems were studied. Only a degradation endpoint (whole system) for 1 system is reported in the endpoints. Values for both systems should be reported (Even if for the second system just a graphical estimate is reported, although first order non linear regression can be made to provide a reasonable fit (first order DT50 805 days r^2=0.786) if samples at day 1 and 2 are treated as outliers). Also if a long value (805 / 838 days) is not included in the endpoints it is unclear where the value used in FOCUS sw modelling (626 days, presumably the arithmetic mean of 415&838 days) comes from. Arguably a less precautionary geomean value of 578 days (from 415 & 805 days) could have been used for FOCUSsw modelling (surrogate sediment input value).	The second study has not been included in the listing of endpoints due to low R2. However, the DT50 of 626, 578 or 415 days are in the same order of magnitude and would give similar PECsed results	Open point RMS to add the second longer whole system single first order DT50 of 838 days to the endpoints sheet with an indication that the value is an uncertain estimate extrapolated significantly beyond the end of the study

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(25)	Vol. 3, B.8.6.2 PECsw – FOCUS	DK: What is the purpose of presenting PECsw where only drift is considered?	We did not blindly trust the FOCUS PEC modeling results. Therefore the simple drift calculations assuming single, multiple applications as well as accumulation has also been performed.	Addressed
4(26)	Vol. 3, B.8.6.2 PECsw – FOCUS	DK: Results from step 1 & 2 of the FOCUS PECsw estimation is missing in the DAR	It was obvious that acceptable risk (TER) cannot be demonstrated on the basis of the FOCUS steps 1 and 2.	Addressed

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(27)	Vol. 3, B.8.6.2 PECsw – FOCUS	DK: The version of FOCUSsw software used for step 3 and 4 is not given the text or tables.	Swash version v.1, Macro v.4, PRZM v.1, Toxswa v.1	Addressed RMS to consider in a corrigendum or amended DAR.
4(28)	Vol.1, list of endpoints, PECgw	AT: The PECgw-values for the metabolite Myclobutanil butyric acid should be mentioned in the endpoint list.	The listing of endpoints has been amended.	Addressed
4(29)	Vol 3, B.8.6.2, Predicted environmental concentration in surface water	UK: As spray drift may be a significant source of surface water contamination for this substance, we would propose that the FOCUS surface water models are also run assuming a single application pattern of the a.s. in case this results in a higher PECsw value compared to the multiple application pattern.	The simple drift calculations assuming single, multiple applications as well as accumulation had also the aim to verify this issue.	Data requirement FOCUSsw simulations at step 3 and 4 to be repeated for a single application for each intended use as these simulations are expected to give the highest PECsw concentrations appropriate for the short term risk assessment to free living aquatic organisms. The applicant has indicated that the data have been sent to the RMS (December 2006).
4(30)	Vol 3 B 8.6.2 Predicted environmental concentrations in surface water PECsw pg 8-33	DAS: Under the PECsw and PECsed calculations: DAS believes that it is inappropriate to use spray drift tables as the primary method of aquatic exposure assessment. This is because the FOCUS sw scenarios have been prescribed for use in the aquatic risk assessment for List 3A molecules.	See point 4(25) Both calculations have been reported (simple drift calculations and FOCUS calculations)	Addressed

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
4(31)	Vol 3, B.8.6.2, PECsw p. 8-30-32 Vol. 1, List of endpoints PECsw p. 49	EFSA: The simply calculated spray drift PEC should not have been presented as FOCUSsw approaches are available and are required for the assessment. The FOCUSsw values should be in the list of endpoints. As the FOCUSsw aquatic exposure assessment has drift as the predominant route of entry, was it checked that a single application (with the resulting higher spray drift %) did not result in higher global maximum PECsw than the multiple application simulations currently reported? As the modelling used a very long sediment half life (626 days) was it confirmed that accumulation in sediment from use over successive years is not an issue for this substance? See section 8.7.3 page 217 of SANCO/4802/2001 rev.2 final (May 2003), where this issue is discussed.	See point 4(25) The FOCUS sw values are presented in the listing of endpoints. the simple drift calculations assuming single, multiple applications as well as accumulation had also the aim to verify the accumulation over years.	Data requirement FOCUSsw simulations (step 4) to be repeated for the multiple application pattern for each crop of the intended use to account for potential accumulation from use in successive years as outlined in section 8.7.3 page 217 of SANCO/4802/2001 rev.2 final (May 2003), as these simulations are expected to give the PECsw concentrations appropriate for assessing the long term risk assessment to free living aquatic organisms and will give the highest PECsediment required to complete the sediment dweller risk assessment. The applicant has indicated that the data have been sent to the RMS (December 2006).
4(32)	Vol 3, B.8.6.1, PECgw p 8-26-29 Vol. 1, List of endpoints PECgw p 52-53	EFSA: What were the crop interception values used when defining the soil application rate used in simulations? Please report the kinetic formation fraction that was used in the PECgw calculation for myclobutanil butyric acid. Clarify how the normalised geomean butyric acid DT50 of 10 days was calculated. The value EFSA calculated is 15.6 days? Please specify what the difference in the input values (application timing and crop interception) used to produce the 'realistic case and worst case' results reported were.	The DT50 have been converted considering the gravimetric water content at 10 pKa. The mean is 10 d at 25°C, 14.5°c at 20°C. The crop interception factors are reported in the listing of endpoints – table with "80th percentile annual average leachate concentration in µg/L". The differences of crop interception factors are due to slight changes in the application timing. These changes have no significant impact on the resulting PECs.	Open point RMS to prepare an addendum to clarify: - the kinetic formation fraction that was used in the PECgw calculation for myclobutanil butyric acid. - the butyric acid DT50 for each of the 4 soils at experimental and then FOCUS reference conditions with the normalisation calculations used explained. - what the difference in the input values (application timing and crop

PEC in surface water and in ground water (B.8.6)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				interception) used to produce the 'realistic case and worst case' results reported were.
4(33)	Vol 3, B.8.6.1, PECgw p 8-26-29 Vol, List of endpoints PECgw p 52-53	EFSA: Modelling is only presented using the model FOCUS PELMO 3.3.2. In line with the EFSA PPR Panel opinion of September 2004 (question No 2004-58) the modelling exercise should be repeated using the PEARL model.	This new data requirement should be considered at MS level.	Data requirement Applicant to provide new groundwater modelling for myclobutanil and myclobutanil butyric acid ensuring the FOCUS reference condition DT50 for myclobutanil butyric acid is correctly calculated in line with FOCUS guidance (the EFSA calculated this DT50 to be 15.6 days) and the formation fraction of butyric acid from myclobuanil used in modelling is clearly reported and reflects FOCUS guidance. Modelling to use FOCUS PEARL in addition to FOCUS PELMO or FOCUS PRZM. The applicant has indicated that the data have been sent to the RMS (December 2006).

Comments received on reporting table, section Environmental fate and behaviour (B.8)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
4 (3) Vol.1, list of endpoints, route of degradation in soil –	FR	FR agrees with AT comment. Major deviations are identified and a new photolysis study should be requested. Despite the UV-spectrum of myclobutanil, results indicate a slow photodegradation (about 10% in 30 days). It seems that this degradation process cannot neglected in comparison to the microbial degradation.	The initial proposal of addressed has been updated to an open point for discussion in a meeting of experts.

Comments received on reporting table, section Environmental fate and behaviour (B.8)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
supplemental studies, soil photolysis and Vol. 3, B.8.1.1.3. soil photolysis			
4(3)	UK	The UK agrees with the comment from AT that the soil photolysis study had too many deficiencies to be considered reliable. However we also feel that based on the absence of significant absorption above 290nm, it is unlikely that the myclobutanil would be susceptible to significant photolytic breakdown. This argument was accepted for the non-submission of aqueous photolysis study later in the DAR. Overall we propose that the soil photolysis study be not relied on, but that further information is not required in this case.	The initial proposal of addressed has been updated to an open point for discussion in a meeting of experts.
4(13) and 4(15)	UK	Provided that the final LOEP is clear that there was definitive evidence of dependence of pH on soil sorption, and that the use of mean Koc values is acceptable, the UK is content that the point can be closed.	Noted. The point must remain open until the LoEP has been updated.
4(29)	UK	We agree that a data requirement should be set for the Applicant to address the potential PECsw arising from single applications using the FOCUSsw models.	Noted
4(29)	NOT	**Data requirement** *FOCUSsw simulations at step 3 and 4 to be repeated for a single application for each intended use as these simulations are expected to give the highest PECsw concentrations appropriate for the short term risk assessment to free living aquatic organisms.* **DAS:** The required simulation **is available** and was sent to RMS.	Noted The fact that the information was already provided to the RMS has been added to the reporting table.
4(29)	RMS	The notifier has calculated PECsw by means of the FOCUS software for the supported uses (90 g/ha in apples, 48 g/ha in grape, 4 applications with a 10 day interval). We do not see why the notifier should recalculate PEC for a use which is not supported (single application) The comment of UK seems to imply that the FOCUS software does not produce appropriate PECsw in the case of multiple applications. If this is the case this comment should be transferred to the FOCUS steering group in order to revise the software.	Please read the FOCUSsw scenarios report which states that because of the overall 90th spray drift approach described, single applications as well as multiple applications have to be simulated when spray drift is a significant route of entry to surface water. The software

Comments received on reporting table, section Environmental fate and behaviour (B.8)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
			tools have to be used following the guidance contained in the FOCUSsw scenarios report.
4(31)	NOT	**Data requirement** *FOCUSsw simulations (step 4) to be repeated for the multiple application pattern for each crop of the intended use to account for potential accumulation from use in successive years as outlined in section 8.7.3 page 217 of SANCO/4802/2001 rev.2 final (May 2003), as these simulations are expected to give the PECsw concentrations appropriate for assessing the long term risk assessment to free living aquatic organisms and will give the highest PECsediment required to complete the sediment dweller risk assessment.* **DAS: DAS:** The required simulation **is available** and was sent to RMS.	Noted The fact that the information was already provided to the RMS has been added to the reporting table.
4(31)	RMS	On the basis of the available PECsed, the chronic TER for sediment dwelling organisms are in the range 725-23000. Before requiring new FOCUS PEC calculations, EFSA should check whether it is really necessary in term of risk assessment	The peer review had not (yet) required new simulations. Until December 2006, this was just a proposal by EFSA to be commented on. This RMS comment here does not address the issue over the use of TWA values for the free living organisms. If it were to be agreed that water TWA should be used in the risk assessment then the new simulations requested in the data requirement proposal would be required to satisfactorily complete the risk assessment. Considering all the comments received (including that from the UK that the uses of TWA in the aquatic risk assessment should be discussed further) EFSA proposes to maintain the data requirement.
4(31)	UK	The UK recognises the need to assess the potential for accumulation of sediment residues. However the UK suggests that MS may wish to discuss the appropriateness of the standard FOCUSsw models to fully determine the accumulation potential. For example, it could be argued that for a substance with such a long sediment DT50 of 626d, the FOCUS models based on dynamic water bodies with presumably only a 7 year simulation run (6 year warm-up, 1 year output) may not represent the worst case as residues may be continuing to accumulate at the end of the simulation period.	This issue is already covered in the FOCUSsw scenarios report. Please read section 8.7.3 page 217 of SANCO/4802/2001 rev.2 final (May 2003), where the guidance on what should be done in terms of a step 4 simulation is described.
4(32) and 4 (33)	UK	The UK agrees that this information will be useful and should be provided in an Addenda or, preferably an updated LOEP.	Noted.

Comments received on reporting table, section Environmental fate and behaviour (B.8)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
4(33)	NOT	**Data requirement** *Applicant to provide new groundwater modelling for myclobutanil and myclobutanil butyric acid ensuring the FOCUS reference condition DT50 for myclobutanil butyric acid is correctly calculated in line with FOCUS guidance (the EFSA calculated this DT50 to be 15.6 days) and the formation fraction of butyric acid from myclobuanil used in modelling is clearly reported and reflects FOCUS guidance. Modelling to use FOCUS PEARL in addition to FOCUS PELMO or FOCUS PRZM.* **DAS: DAS:** The required simulation **is available** and was sent to RMS.	Noted The fact that the information was already provided to the RMS has been added to the reporting table.
4(33)	RMS	The notifier submitted his dossier in November 2003. At this time, PEC gw calculation by means of one FOCUS model was requested. Almost one year later (September 2004), an EFSA panel recommends to use PEARL and PELMO in parallel. We have therefore reservation to set new requirements that were not known at time of submission. If EFSA considers that modelling by means of PEARL and PELMO has to be provided, this new rule should have been discussed and at least communicated to the notifiers and to the rapporteurs. Moreover, it seems that EFSA does not apply this new rule uniformly to all the substances that are now under revision in the list 3A. (for example, one model software for acequinocyl and flonicamid discussed during the Praper meetings of November) In absence of harmonized treatment of the dossiers, we consider that PECgw with another model should not be requested for myclobutanil.	The EFSA accepts that the PPR opinion was published after the dossier was submitted. However, the original modelling in the dossier appeared to have incorrect parameterisation regarding myclobutanil butyric acid, so there was a proposal for additional modelling to be requested. This new request of course is later than the PPR opinion so it is possible for it to be incorporated in a new submission. Hence the proposal made. The panel opinion indicates 2 models are only required when the concentrations approach the drinking water limit. In the examples of flonicamid and acequinocyl the predicted concentrations were significantly below the drinking water limit. Therefore the EFSA would not make this comment for these substances even if there had been a requirement for the modelling to be updated. For myclobutanil the use of a second model may change (increase) the number of scenarios above the drinking water limit or show the metabolite to breach the 0.75µg/L assessment level.

5. Ecotoxicology

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(1)	Vol. 3, B.9.1.3, Subchronic and reproductive toxicity to birds	NL: Albinism was observed, which might reduce life expectancy in the field. From the summary it is not clear in which group(s) this occurred and if it has a connection with the dose rate.	Twenty young birds out of the offspring of one parent pen at the treatment level of 130 ppm. We consider this not dose-related.	Addressed
5(2)	Vol. 3, B.9.1.8 Risk assessment for birds and B.9.3 Idem for mammals	NL: If the risk of consumption of drinking water should only be assessed for leafy crops, this should be put down in an EFSA agreement list.	This was said by EFSA at the EPCO meeting 22.	Open point: The issue of risk to birds and mammals from intake of contaminated drinking water is still under debate and will be further addressed in the revised Guidance document. For the mean time it is proposed that issue is dicussed in the experts' meeting.
5(3)	Vol. 3, Refined risk assessment for the long-term exposure of small herbivorous mammals, pg 9-40	DAS: For the refinement of the risk assessment for long term effects on mammals in orchards, a foliar interception factor of 70% was used for foliage development. It should be made clear that the risk assessment presented in the dossier shows that applications can be made at an earlier stage than foliar development, that being at flowering. Using an interception factor of 65% for flowering, the risk assessment must be taken one more step, but acceptable risk is shown in the dossier for 2 applications at flowering and 2 at foliage development. **DAS would like to make it clear that applications can be made to orchards at the flowering stage.**	An acceptable risk has been determined for mammals using an interception factor of 70 %. We consider that sufficient information is available to show that at least one use is acceptable. Refinement of the risk assessment should be made at MS level.	Open point: RMS to clarify how the residue unit value (RUD) of 22.8 in the refinement was derived and to calculate a long-term TER for mammals for the use of myclobutanil in apples with 2 applications during flowering (65% interception) and 2 applications at a stage when foliage is developed (70% interception) in an addendum.

Birds and mammals (B.9.1 and B.9.3)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(4)	Vol. 3, B.9.1.1 and B.9.1.2; Acute oral and dietary toxicity to birds, p.401	EFSA: It is noted that the purity of the technical material used in the studies was only 84.5% while the technical specification is 92.5%. This seems not to have been considered.	We have seen this "deficiency" but we considered that it is not appropriate to require new vertebrate studies.	Open point: To be discussed in an expert's meeting if the endpoint values for acute and short term should be corrected for the low content of a.s. For the evaluated uses the outcome of the risk assessment would not be changed.
5(5)	Vol. 3, B.9.1.2 Avian dietary toxicity	EFSA: For what period was the mean food consumption and body weights calculated?	For the bobwhite quail : 5 day test period. For the mallard duck : 5 day test period.	Addressed

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(6)	Vol. 3, B.9.2, Aquatic risk assessment	DK: The results of the risk assessment applying FOCUS step 1 and 2 should be presented.	See also comment 4(26). It was obvious that acceptable risk (TER) cannot be demonstrated on the basis of the FOCUS steps 1 and 2.	Addressed

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(7)	Vol. 3, B.9.2.8 Effects on algal growth	AT: For the acute toxicity study with *Scenedesmus subspicatus* (Ellgehausen, 1987) only the E_bC_{50} – endpoint is mentioned. In our opinion, also the E_rC_{50} – endpoint should be reported.	In this study only E_bC_{50} was calculated. The notifier is asked to calculate E_rC_{50}.	Data requirement: Notifier to calculate the E_rC_{50} from the study with *Scenedesmus subspicatus* (Ellgehausen, 1987). The applicant has indicated that the data have been sent to the RMS (December 2006).
5(8)	Vol. 1, LOE Toxicity data for aquatic species	AT: The endpoints for the formulation used in the risk assessement should also be highlighted in bold.	The List of Endpoints is amended.	Addressed
5(9)	Vol. 3, B.9.2.11 Acute toxicity of the preparations	NL: It would be good to also express the endpoints as mg a.s./L, and to include both in the LoE (mg form./L as well as mg a.s./L).	Corrections are made in the update of September of section B9. The List of Endpoints is amended.	Addressed. List of endpoints has been updated.
5(10)	Vol. 3 B.9.2.13, Residue data in fish	DE: The study indicating a log Pow of 2.56 was actually not accepted by the RMS and should not be mentioned here. Since the log Pow appears to be close to 3 and a BCF study might be triggered by this value, the requirement for a new log Pow study should be discussed in order to determine a reliable value.	See also comment 1(7). Very likely the log P_{OW} is around 3 and therefore it is up to the meeting to decide whether a BCF study is required.	Open point: Experts' meeting to discuss whether a BCF study is necessary See comments 5(45) and 1(7).
5(11)	Vol. 3, B.9.2.16, Exposure and risk assessment for aquatic organisms	DE: The RMS is asked to put out more clearly that risk mitigation measures are needed to show acceptable risks for aquatic organisms when myclobutanil is used in apples.	See comment 5(17).	Open point: The reporting of the risk assessment for aquatic organisms to be discussed in an experts' meeting. See also column 4 at comment 5(17)

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(12)	Vol 3, B.9.2.16: Exposure and risk assessment for aquatic organisms	UK: It is not explained very clearly why it is necessary to go straight to using FOCUS Steps 3 and 4, or that different buffer zones are applied to different water bodies. It is also noted that the RMS has used 21-day time-weighted average PEC_{SW} for calculation of the chronic fish and aquatic invertebrate TERs. According to SANCO/3268/2001 (Section 3.3) the use of time-weighted average PEC_{sw} are only appropriate if exposure conditions in the environment are predicted to differ significantly to that in the toxicity studies (taking in to account the fate and behaviour profile of the active substance) and if good information is available on time to onset of effects in the toxicity studies. In the absence of this information, intial PEC values should be used in the chronic assessment and in any case the use of TWA PEC_{sw} has little effect on the outcome of the aquatic risk assessment.	See also comment 5(6). Calculations were performed with TWA PEC_{sw} because there was indeed an unrealistic exposure regime in the relevant toxicity tests, according to SANCO/3268/2001.	Open point: The use of TWA PEC_{sw} in the risk assessment for aquatic organisms to be discussed in an experts' meeting.
5(13)	Vol 3, B.9.2.16, Risk assessment to sediment dwelling organisms	UK: It is noted that the RMS has used 21-day time-weighted average sediment PEC for calculation of sediment dwellers TERs. The spiked water NOEC from the chironomid study has been converted to be a NOEC in sediment (Section B.8.2.9). It is suggested that the sediment dweller TERs should be calculated using a ratio of the spiked water NOEC with the initial surface water PEC. The use of time-weighted average PECs would also need to be fully justified, as discussed above.	According to EPCO meeting 22 it was recommended by EFSA to convert the endpoint expressed in mg/L water to mg/kg sediment and compared with PEC_{sed}. However, we think that it is more correct and relevant to conduct the risk assessment based on NOEC and PEC expressed in mg/L. Corrections are made in the update of September of section B9 and in the List of Endpoints.	Open point: MS to discuss the risk to sediment dwelling organisms with focus on a. Conversion of NOEC water to NOEC sediment b. Use of mean NOEC value (mean of concentration in sediment) c. Use of TWA PEC sediment versus plateau level (see comment 4(31) The risk from the representative uses

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				seem to be low, but the assessment should be discussed from a general point of view.
5(14)	Vol. 3, B.9.2.2 – Fish juvenile growth test, p. 9-15	DAS: The use of the chronic endpoint from the rainbow trout 21-day chronic study is inappropriate for risk assessment purposes since the study was not performed at a high enough concentration to produce a LOEC. Therefore, the NOEC from this study is an artifact of the study concentrations and is not accurate. The true NOEC for chronic effects of myclobutanil on fish should be from the fish early life-stage toxicity test with the fathead minnow (B 9.2.3). The fish early life-stage toxicity test is also a more sensitive test than the 21-day study. Therefore, the endpoint is more robust. **The correct endpoint is 0.98 mg a.s./L.**	Calculating the chronic risk to fish based on NOEC of 0.2 mg/L for rainbow trout or based on NOEC of 0.98 mg/L for fathead minnow will not alter the risk assessment.	Open point: The choice of chronic endpoint for fish to be discussed in an experts' meeting.
5(15)	Vol. 3, 9.2.9 Effects on sediment dwelling organisms, p. 9-27	EFSA: We propose to use the NOEC of 4.98 mg a.s./L derived in the study and compare it with the PEC sw value since it was a water spiked study.	See comment 5(13).	Addressed. List of endpoints amended.
5(16)	Vol. 3, B.9.2.16; Exposure and risk assessment for aquatic organisms	EFSA: Please check that a single application (with a higher spray drift %) doesn't give rise to higher PECsw (see EFSA comment in fate section). Should these PECsw values be worst case, please calculate new TER values.	From comment 4(1) „EFSA: The simply calculated spray drift PEC should not have been presented as FOCUSsw approaches are available and are required for the assessment." EFSA should explain what they really wish as PEC calculations.	Open point: RMS to clarify whether FOCUS modelling using a single application (with the resulting higher spray drift %) did not result in higher global maximum PECsw than the multiple application simulations currently reported, and if necessary to correct the TER calculations using the highest

Aquatic organisms (B. 9.2)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
				global max values. See also comment 4(31)
5(17)	Vol. 3, B.9.2.16; Exposure and risk assessment for aquatic organisms	EFSA: It is stated that the acute risk is acceptable since all TER values are exceeding the trigger value. However, risk mitigation is required in 8 out of 10 scenarios. This should be indicated more clearly. Tables like the one agreed for the list of endpoints EPCO No E 4, revision 4 (September 2005) could preferable be used.	We consider that the Table "Toxicity/exposure ratios for the most sensitive aquatic organisms" is sufficiently clear. This table contains the columns : - application rate - **distance** - TER - Trigger	Open point: The list of end points has been updated to include worst case scenario and water body type. However, it is proposed to discuss the presentation of the risk assessment for aquatic organisms in an experts' meeting as a general point.

Bees and non-target arthropods (B.9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(18)	Vol. 1, LOE Hazard quotient for honey bees	AT. The hazard quotients should be given as </> values in accordance with the toxicity endpoints.	The List of Endpoints is amended.	Addressed. List of end points has been amended.
5(19)	Vol.3, B.9.5.1 Effects on non-target arthropods	NL: Relevant endpoint for risk assessment is corrected mortality (and effect on reproduction), not reduction of beneficial capacity, according to ESCORT 2. Preferably L(E)R50's are calculated.	See comment 5(27).	Addressed. List of end points has been amended.

Bees and non-target arthropods (B.9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(20)	Vol. 3, B.9.5.1, Semi-field bioassay with *A. rhopalosiphi*	NL: Methods used are not very clear. Were only hop plants sprayed, or both hop and barley plants? Were effects only tested for after the 4rd spraying?	It was clearly mentioned in the DAR : - untreated barley plants - bioassay 1: after 1st treatment and bioassay 2: after 4th treatment	Addressed
5(21)	Vol.3, B.9.5.4 Risk assessment for non-target arthropods	NL: Pardosa is not mentioned in the risk assessment, although a study is available. IOBC classifications are generally not used anymore.	Corrections are made in the update of September of section B9.	Addressed
5(22)	Vol.1, LoE, NTA	NL: It might be helpful to describe the semi-field and field study in more detail (crop, country etc) in the LoE.	See comment 5(28).	Addressed. List of end points has been amended.
5(23)	Vol 3, B.9.5.3: Effects of the formulation on non-target terrestrial arthropods	UK: In the evaluation of the field study conducted with *Typhlodromus pyri*, the RMS concludes that there were no adverse effects on *Typhlodromus pyri* populations following nine applications of 'Systhane 20 EW'. The RMS acknowledges the very low mite population in the untreated control, which remained low for the duration of the study. The UK is concerned that the poor performance of the untreated control may have masked treatment related effects. It is noted that the mite population in the positive control, treated with propineb, were in fact greater than the untreated control on some of the sampling dates. The UK has concerns regarding the reliability of the study and believes the validity of the study should be considered further.	Indeed, mite populations were low at start but increased during the study for the untreated control. We consider that the study is valid (n° of replicates, observation on the predatory mites and spider mites). Moreover, this study has been performed at the application rate of 9 x 90 g a.s./ha and 9 x 180 g a.s./ha , while the maximum application rate in apple is 4 x 90 g a.s./ha.	Open point: The field study conducted with *Typhlodromus pyri* to be discussed in an experts' meeting. See also comments 5(24) and 5(26).

Bees and non-target arthropods (B.9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(24)	Vol 3, B.9.5.4: Summary of effects, exposure and risk assessment for non-target arthropods	UK: The RMS has concluded that the effects seen on other crop relevant species in tier I studies (e.g. *Coccinella septempunctata*) should be considered further at Member State level; the assessment has not been followed further to higher tier studies. The UK considers that this deficiency in higher tier data/assessment should not be left as a Member State issue. As the potential risk to crop relevant species has not been sufficiently addressed and the fact that the field study with *Typhlodromus pyri* is of questionable validity, it is proposed that the risk to non-target arthropods requires further consideration prior to Annex I listing of myclobutanil.	We disagree, see comment 5(23). Acceptable risk has been shown for *Typhlodromus*, *Aphidius*, *Chrysoperla* and *Pardosa*. Considering the fact that in other dossiers an evaluation of only *Typhlodromus* and *Aphidius* seems to be sufficient to the MS and EFSA, we believe that our requirement of further data at MS level is well balanced	Open point: The risk to NTA to be discussed in an experts' meeting and in particular the need for further studies with crop relevant species. See also comment 5(26).
5(25)	Vol. 1, 2.6.3 Effect on other arthropods, pg 37 Vol. 3 B.9.5.4 Risk assessment for non-target arthropods, pg 9-57	DAS: DAS agree with the RMS that myclobutanil poses an acceptable risk to terrestrial non-target arthropods. However, as the DAR is intended to meet the requirements of safe uses according to 91/414/EEC the comment relating to additional testing at the MS level seems inappropriate *as no risk to non-target arthropods has been identified*. DAS do recognize that each MS may have its own local requirements but this is beyond the scope of the DAR and request that the comment be removed.	See comment 5(24).	See comments 5 (23, 24, 26)

Bees and non-target arthropods (B.9.4 and B.9.5)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(26)	Vol.3, B.9.5.4; Summary of effects to NTA	EFSA: The dose rates applied in the first tier studies with *T. pyri, A. rhopalosiphi, Coccinella* and *Pardosa* do not cover the maximum application rate in apples, and not in vine either if a multiple application factor is considered. Since the studies were not of a dose-response design, no LR_{50} could be derived and consequently no HQs were calculated. However, since effects were observed and the dose rates didn't cover the proposed uses, further studies with *Coccinella* are considered necessary in addition to the available semi-field and field studies with *T. pyri* and *A. rhopalosiphi.*	See also comment 5(24). Acceptable risk has been shown for *Typhlodromus*, *Aphidius*, *Chrysoperla* and *Pardosa*. Considering the fact that in other dossiers an evaluation of only *Typhlodromus* and *Aphidius* seems to be sufficient to the MS and EFSA, we believe that our requirement of further data at MS level is well balanced	See open point in comment 5(24)
5(27)	Vol. 1, List of endpoints, Effects on other arthropod species	EFSA: Please report % effects on mortality and reproduction instead of reduction in beneficial capacity. Please also report the effects based on dose rate of a.s./ha. For the extended tests the 50% trigger value is from ESCORT II and not from Annex VI.	The List of Endpoints is amended. Corrections are made in the update of September of section B9.	Addressed. List of endpoints has been amended.
5(28)	Vol. 1, List of endpoints, Effects on other arthropod species	EFSA: Please add information on crop, application interval and location (for the field study) in the box for field or semi-field studies.	The List of Endpoints is amended.	Addressed. The list of endpoints has been amended.

Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(29)	Vol. 3, B.9.7 effects on other soil non-target macro-organisms	AT: The evaluation of the two litter-bag studies should be consistent. The first study (Galicia, 2002) was not considered valid as no effects were observed in the positive control. The second study (Mallet, 2004) was accepted, though even no positive control was tested. We think that this is contradictory and a short comment to address this issue should be included. Further, a final conclusion/risk assessment on the results of the litter-bag studies should be added.	See comment 5(37).	Open point: The suitability of the litter bag study by Mallet (2004) to address the risk to OM breakdown to be discussed in an experts meeting. See also comment 5(34)
5(30)	Vol.3, B.9.6.6, First tier risk assessment of the formulation Systhane 24E	NL: Is this formulation comparable to Systhane 20EW?	See comment 5(35).	Addressed See 5(35)
5(31)	Vol.3, B.9.7, Effects on other soil non-target macro-organisms	NL: In the risk assessment, nothing is said about the litterbag study.	See comment 5(34).	Addressed. See 5(34)
5(32)	Vol.1, LoE	NL: Why are the litterbag study, studies on non-target plants and sewage treatment not included in the LoE?	See comment 5(44).	Addressed See 5(44)
5(33)	Vol.3, B.9.8.4 Risk assessment for soil micro-organisms	NL: Results of the studies should be compared to the PECs before concluding that the risk is acceptable.	See comment 5(39).	Addressed See 5(39)

Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(34)	Vol 3, B.9.7: Effects on other soil non-target macro-organisms (and soil organic matter breakdown)	UK: The soil DT90 values for myclobutanil are well in excess of 1 year and (according to Annex point 10.6.2) the need for a litter bag is clearly triggered irrespective of the assessment on collembola. There has been no assessment of effects on OM breakdown using the submitted studies. We note that the mean soil concentrations achieved in the Mallet, 2004 study (up to 0.146 mg a.s./kg soil) are substantially below the peak plateau PECsoil values of 0.359 mg a.s./kg and 0.672 mg a.s./kg determined for vines and apples respectively. The suitability of this study to address the risk to OM breakdown should therefore be discussed.	According to the EPFES Guideline the litter bags should be placed at 5 cm soil depth and the top 10 cm of the test soil should contain the FOCUS PEC_{soil} plateau concentration at a soil depth of 20 cm. The annual cumulative dose is applied subsequently. In the study of Malllet (2004), the concentration in soil immediately after the last application PEC_{soil} at 5 cm in apples is 0.672 mg a.s./kg soil corresponding to 0.168 mg a.s./kg soil at 20 cm. This last concentration was achieved in the actual test, namely 0.1247 – 0.1460 mg a.s./kg soil at 10 cm depth. Detailed calculations are presented in the update of September of section B9.	See open point in comment 5(29)
5(35)	Vol. 3, B.9.9.6.3, Acute toxicity of the formulation to earthworms	EFSA: It is noted that the in the acute formulation toxicity study with earthworms Systhane 24E was used. However since a reproduction study with the lead formulation is available the results from this study can be used to assess the risk from the formulation.	Systhane 24 E is a more concentrated formulation containing similar solvent compounds. Therefore, data from studies with Systhane 24 E are considered as a worst case and suitable for assessing the effects of Systhane 20 EW. Clarification is provided in the update of September of section B9.	Addressed

Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(36)	Vol. 3, B.9.6.6 Risk assessment for earthworms	EFSA: At least for the first tier risk assessment the peak PEC_{soil} following the last application on top of the accumulation plateau should be used regarding the risk for soil organisms in case that there are several applications foreseen (Agreed in EPCO 17, Jan-Feb 2005). Please calculate new TER values.	"EFSA: The EFSA can agree to the use of the longest single first order laboratory DT50 for myclobutanil of 574 days to calculate an accumulated PEC in soil. However field data would probably provide a more realistic estimate." Worst case PECsoil considering accumulation of the a.s. during several years were used in the risk assessment. We consider that the PEC and the TER must not be revised.	Addressed. As the used DT_{50} can be assumed to be worst case no futher action is necessary.
5(37)	Vol.3, B.9.7; Effects on other soil macro-organisms	EFSA: A litter bag study is triggered based on the persistence of myclobutanil in soil. It is not clear why the study by Galicia (2002) was stated not acceptable while the study by Mallet (2004) is considered acceptable. A positive control is lacking in both studies and it is not clear if the concentrations in soil at the start of the study covered the long-term pluriannual plateau over years plus the additional application for the season.	According to the EPFES Guideline, the annual cumulative application should be made in 1 dose on bare soil or on soil with only little plant cover. The study of Galicia (2002) was conducted in grassland and no analytical measurement of the actual concentration of myclobutanil was performed. It is expected that the applied myclobutanil was intercepted by the grass and therefore there is no indication that the straw in the litter bags was exposed to the correct dose of myclobutanil. The study of Mallet (2004) is acceptable because measurements of actual myclobutanil concentrations were performed. Clarification is provided in the update of September of section B9. See also comment 5(34) : According to the EPFES Guideline the litter bags should be placed at 5 cm soil depth and the	Addressed

Earthworms and other soil non-target organisms (macro and micro) (B. 9.6, B.9.7 and B.9.8)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			top 10 cm of the test soil should contain the FOCUS PEC_{soil} plateau concentration at a soil depth of 20 cm. The annual cumulative dose is applied subsequently. In the study of Malllet (2004), the concentration in soil immediately after the last application PEC_{soil} at 5 cm in apples is 0.672 mg a.s./kg soil corresponding to 0.168 mg a.s./kg soil at 20 cm. This last concentration was achieved in the actual test, namely 0.1247 – 0.1460 mg a.s./kg soil at 10 cm depth. Detailed calculations are presented in the update of September of section B9.	
5(38)	Vol.3, B.9.7; Effects on other soil macro-organisms	EFSA: In the risk assessment for *Folsomia* the PEC_s from long-term pluriannual plateau over years plus the additional application for the season should have been used. TER values would however still be above the trigger.	See comment 5(36).	Addressed. As the used DT_{50} can be assumed to be worst case no futher action is necessary.
5(39)	Vol.3, B.9.8.2, Impact of the formulation on soil microbial activity	EFSA: It was noted that the study on effects on soil microbial activity used the formulation Systhane 24E. Nothing is stated about the comparability with the lead formulation. It was also noted that the application rate just covers the peak PEC_s but no exaggerated dose rate was tested. We consider this as necessary especially for persistent substances as myclobutanil.	See also comment 5(35). According to SANCO/10329/2002 the concentrations used in the test must cover the maximum PEC. The maximum PEC_{soil} (concentration in soil immediately after last application) is 0.672 mg a.s./kg soil in apples. The concentration tested with soil micro-organisms was 0.76 mg a.s./kg soil, so we consider this issue addressed. Clarification is provided in the update of September of section B9.	Addressed

Other non-target organisms (flora and fauna), sewage treatment (B.9.9 and B.9.10)				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(40)	1, LOE Non-target plants	AT: "Effects on non-target plants" are missing in the LOE.	See comment 5(44).	Addressed
5(41)	Vol. 3, B.9.10 Effects on sewage treatment	NL: It is not clear how the risk assessment is performed (it is only concluded that the risk is acceptable).	No guidance is given for the risk assessment. The conclusion is restricted to an EC_{50} value for activated sludge of 71 mg a.s./L. Corrections are made in the update of September of section B9.	Addressed

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
5(42)	Vol. 1, Point 2.6 Effects on non-target species, and Vol. 3, B.9 Ecotoxicology	DE: Myclobutanil belongs to a group of fungicides for which a general concern about a potential for endocrine disrupting effects in humans and wildlife can be stated because of its mechanism of action (triazole fungicides, inhibiting sterol biosynthesis). As myclobutanil in addition shows a rather persistent behaviour this aspect should be included in the risk assessment for the relevant non-target species groups.	The possible endocrine effects are taken in to consideration by the reproduction studies in setting a NOEC. Therefore we consider that this issue is addressed.	Open point: The issue of potential for endocrine disruption and whether further studies should be required (e.g. fish full life cycle study) to be discussed in an experts' meeting. The risk to mammals should be revisited following the outcome of the dicussions in the section mammalian toxicology.
5(43)	Vol. 3, B.9 General	EFSA: A full specification of the material used in all studies should be provided by the applicant and the compliance with the specification of the technical material should be assessed.	According to the OECD Guidelines the study reports must contain the chemical identity data including purity of the active substance. The information on the purity is reported for each	This comment refers to the data requirement in Annex IIA '8. Ecotoxicological studies Test substance

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
			study in the DAR. Therefore, the EFSA comment is not relevant.	(vi) A detailed description (specification) of the material used, as provided for under point 1.11 must be provided. Where testing is done using active substance the material used should be of that specification that will be used in the manufacture of preparations to be authorized except where radiolabelled material is used.' The purpose is to ensure that the test substance used in the studies comply with the technical specification also with regard to amount of impurities, especially relevant impurities. Data requirement: Applicant to submit information to address Annex II point 8 (vi). The applicant has indicated that the information will be submitted to the RMS by end of December 2006
5(44)	Vol. 1, List of endpoints, General	EFSA: Please use the EPCO No E 4, revision 4 (September 2005) template for the list of endpoints and fill in results for all groups of	The List of Endpoints is amended.	Addressed. The list of endpoints has been amended.

Other comments				
No.	Column 1 Reference to DAR (vol., point, page)	Column 2 Comments from Member States or applicant	Column 3 Evaluation by (RMS) rapporteur and - if available - (Co-RMS) Co-rapporteur	Column 4 Data requirement or Open point (if data point not addressed or fulfilled)
		organisms where relevant.		
5(45)	Vol. 3, IIA 2.8, partition coefficient Comment copied from section 1 comment 1(7)	DE: The study indicating a log Pow of 2.56 was actually not accepted by the RMS. Since the log Pow appears to be close to 3 and a BCF study for section 5 might be triggered by this value, the requirement for a new log Pow study should be discussed in order to determine a reliable value. The (other) log Kow of 2.89 was derived by estimation (McFarlane, 2005). However, with the KOWWIN program (v1.67; © 2000 U.S. EPA), a log Pow of 3.5 can be calculated and, moreover, the program's database indicates an experimental log Pow of 2.94 (reference: BioByte, 1995).	Taking into account the fact that the two estimated log Pow values (i.e. 3.5, as mentioned by DE and 2.89) significantly differ from each other and are around the trigger value of 3, the RMS considers that it is up to the meeting in ecotoxicology to decide whether a BCF study is required. The estimated value of the log Pow, mentioned by DE, has been included in an addendum to Vol.3 (B2) dd. September 2006.	See open point in comment 5(10). See comment 1(7).

Comments received on reporting table, section Ecotoxicology (B.9)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
5(3)	RMS	The TER calculations for the refined risk assessment for small herbivorous mammals were presented in the updated version of the section B9 and not in an addendum, since no new information was added compared to the original dossier. The long-term risk of myclobutanil for small herbivorous mammals in apples at 2 applications during flowering and at 2 applications during foliage development is acceptable. For the applications in apples during flowering an interception factor of 65 % is used, resulting in a refined RUD value of 26.6, this is 35 % of 76. For the applications in apples during foliage development an interception factor of 70 % is used,	An updated version of section B9 is not available (at least not for EFSA). In the version we have 70% interception has been used. Open point remains as it is in the RT.

Comments received on reporting table, section Ecotoxicology (B.9)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
		resulting in a refined RUD value of 22.8, this is 30 % of 76.	
5(7)	NOT	**Data requirement:** *Notifier to calculate the ErC50 from the study with Scenedesmus subspicatus (Ellgehausen, 1987*). **DAS: DAS:** The required calculation **is available** and was sent to RMS.	Noted. Data requirement remains for technical reasons.
5 (12), (13)	UK	It is noted that the RMS considers the use of time-weighted average PECs to be suitable for the aquatic risk assessment. However, the UK feels that further justification is required and therefore the UK agrees that the use of time-weighted average PECs for the aquatic risk assessment should be discussed at an expert meeting.	Noted. Open point 5(12) remains as it is in the RT. An open point was set at 5(13) to discuss the RA for sediment dwelling organisms.
5 (16)	UK	The UK agrees that the RMS should clarify whether the FOCUS global maximum PEC is greater following a single application. Consideration of whether this open point has been satisfactorily addressed should be made at an expert meeting.	Noted. Open point remains as it is in the RT.
5(16)	RMS	See comment 4(31) in the fate section.	Noted. Open point remains as it is in the RT.
5 (23), (24) and (26)	UK	The UK agrees that the validity of the non-target arthropod field study and whether the risk to non-target arthropods has been satisfactorily addressed should be discussed at an expert meeting.	Noted. Open point remains as it is in the RT.
5 (29), (35)	UK	It is noted that the soil DT_{90} is calculated to be greater than 1 year and therefore the risk to soil macro-organisms should be addressed with a litter bag study. The validity and appropriateness of the two submitted litter bag studies with regards to the predicted exposure is unclear and therefore the UK agrees that the risk to soil macro-organisms requires further consideration and should be discussed at an expert meeting.	Noted. Open point remains as it is in the RT.
5(43)	NOT	**Data requirement:** *Applicant to submit information to address Annex II point 8 (vi)*	Noted.

Comments received on reporting table, section Ecotoxicology (B.9)			
Reference to reporting table	MS / Notifier	Comment	EFSA response
		DAS: The information to address Annex II point 8 (vi) is being collected and will be available **by end of December 2006**	