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section 0 – General comments

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)
0(1)	Vol 1, 1.3.1 name and address applicant	NL: Schirm has taken over (the dossier from) DuPont? It is kind of confusing to see references being made to a dossier submitted by DuPont while the applicant is Schirm.	Indeed, the dossier for the active substance lenacil was transferred from Du Pont de Nemours (France) S.A.S to Dr. Schirm AG as of 24. October 2000.	Addressed.

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(1)	Vol. 4, C.1.1. Method of Manufacture p.4	EFSA: in the description of the synthesis pathway [redacted] is mentioned, however the formula drawn is rather [redacted] which seems to been used in the manufacture. Also the name [redacted] is not the adequate one in the first reaction before acidification	RMS fully agrees with comment of EFSA. [redacted] is the correct name for the presented structural formula. The correct name for the [redacted] In case an updated DAR will be issued, these errors will be corrected.	Addressed: RMS to correct the name of the two compounds in a corrigendum
1(2)	Vol. 4, C.2.2-2. Identity of isomers, impurities and additives in technical material p.8	EFSA: information on the level of [redacted] of [redacted] should be given. It was agreed at PRAPeR 06 to require this information due to the fact that the [redacted] evel (expressed in moles) can influence the (eco)toxicological as well as the physical and chemical properties of the formulation	RMS agrees that the level of [redacted] should be given.	Point of clarification for the applicant: Applicant to provide information on the level of [redacted] of [redacted]
1(3)	Vol 4 C.1.1, manufacturing process	UK: Reaction time and temperature should be provided for the method of manufacture.	This is considered to be process engineering information, which is generally not required according to Commission Directive 94/37/EC.	Addressed.

Identity (B.1, Annex C)				
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1(4)	Vol 4 C.1.1, manufacturing process	UK: Full discussion of the source of the impurities found in the technical material should be provided.	Such information was not available in the dossier. The notifier waived the request of the RMS as follows: *"There is no obligation under point 1.10 to describe how the specified impurities are probably formed. The only requirement is to comment on the possible formation of particularly undesirable impurities (nitrosamines and dioxins). Based on the structures, it is not considered likely that dioxins and nitrosamines will be formed. […]"*	Addressed.
1(5)	Vol. 4, C.1.2.3-1 Analytical Profile of Batches p.9	EFSA: the dates of manufacture for the batches should be given	Dates of manufacturing were not reported in the study report (Wittig, 2000). It is considered to be very likely that the batches were produced in the period between 1998 (former 5-batch analysis study report by Hansen is dated 1998) and 2000 (analysis by Wittig was performed in July/August 2000).	Addressed.

Identity (B.1, Annex C)				
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1(6)	Vol 4, C.1.2.3, analytical profile of batches	UK: Compound 4, 7 and 8 have been listed in the 5 batch analysis but stated to be not analysed. It is unclear if this means the impurities have been sought but not found or not sought.	As indicated in Table C.1.2.3-1, the compounds 4, 7 and 8 were not analysed for in the study by Wittig (2000), which means they were not sought for. Those compounds were added to the table only to enable an easier comparison, if deemed necessary, with the results of the other (non-representative) batch analyses (Table C.1.2.3-2 and Table C.1.2.3-3), in which those compounds were sought for. Please also note that the 5-batch analysis study by Wittig (2000), which is the only 5-batch analysis that was submitted as being representative for current production, shows an analytical closure of at least [redacted] See also comment 1(7).	Addressed. See also comment 1(7)
1(7)	Vol. 4, C.1.2.3-1 Analytical Profile of Batches p.9	EFSA: if impurities 4, 7 and 8 were not analysed for in the representative batches, are they included only for the reason that in the other- non representative –batches were analysed for? If so, why impurity 11 is not included, which was analysed for and also detected in the old batches?	Interpretation by EFSA is correct. RMS acknowledges that for consistency, also impurity 11 could have been included in the table. See also comment 1(8)	Addressed See also comment 1(6) and 1(8)

Identity (B.1, Annex C)				
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1(8)	Vol 4, C.1.2.3, analytical profile of batches	UK: Compound 11 has been sought in the 5 batch analysis data presented in Table C.1.2.3-3 but not in Table C.1.2.3-1, although the notifier states that the data provided in Table C.1.2.3-2 and C.1.2.3-3 are not relevant it should be clarified if this impurity is no longer considered likely (see also comment at Vol 4 C.1.1.).	In the older analysis of batches (Hansen, 1998), impurity 11 was - if detected - found at maximum [redacted] and hence, this compound would not be considered as significant impurity. In addition, it should be noted that the 5-batch analysis study by Wittig (2000), which is the only 5-batch analysis that was submitted as being representative for current production, shows an analytical closure of at least [redacted] Therefore, in the hypothetical case that compound 11 was present also in the technical material analysed by Wittig (2000) (and not found because not sought for), this would probably have been at insignificant concentration levels.	Addressed See also comment 1(7)
1(9)	Vol 4, C.1.2.3, analytical profile of batches	UK: Analytical closure should not include those impurities which were quantified as <1 g/kg.	See comment 1(10)	See comment 1(10)
1(10)	Vol 4, table C.1.2.3-2, comments below table	NL: If a concentration is below the LOQ („less than' values), then it cannot be taken into account for the analytical closure.	RMS agrees. However, in this case, analytical closure is still above [redacted] when results „< LOQ' are not considered.	Addressed. See also comment 1(9)
1(11)	Vol 4, C.1.2.3, analytical profile of batches	UK: Compound 9; If the values in the 5 batch analysis data have been quantified as [redacted] this is how the values should be presented and utilised in the calculation of analytical closure.	Having considered the manufacturing process and the raw materials used therein, the RMS is of the opinion that it can be reasonably assumed that the measured [redacted] from [redacted] Therefore, the expression of the s[redacted]content as [redacted] was considered to be acceptable.	Open point: The expression of the content of impurity 9 in the five batch to be discussed in a meeting of experts

Identity (B.1, Annex C)				
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1(12)	Vol 4, C.1.2.3, analytical profile of batches	UK: It appears that several starting materials and intermediates have not been sought in the 5 batch analysis (see also comment at Vol 4 C.1.1.).	Please note the analytical closure of more than [redacted] in the 5-batch analysis study by Wittig (2000).	Open point: To be discussed in a meeting of experts whether the 5-batch analysis study (Wittig, 2000) sufficiently covers the analytical profile of lenacil technical.
1(13)	Vol 4, C.1.2.3, analytical profile of batches	UK: The analytical profile of tox batches has not been provided.	For the majority of batches used in toxicological and ecotoxicological studies, the purity was provided (see Table C.1.2.3-4 and Table C.1.2.3-5). Given the identity of the significant impurities specified (Table C.1.2.3-6), it is questionable whether the absence of the full analytical profile of the tox batches is really a matter of concern in this case.	Addressed. See point 2(51)
1(14)	Vol 4, C.1.2.3, analytical profile of batches	UK: Water content in Table C.1.2.3-1 has been measured by loss on drying and therefore the method used is not specific	RMS agrees: drying at 110°C and measuring loss of weight cannot be generally considered as specific for the determination of water content. To be discussed in a meeting of experts whether the specification as „loss on drying' can be accepted, taking also into account the manufacturing process and the raw materials used for synthesis of lenacil.	Open point: The acceptability of the water measurement by „loss on drying' to be discussed in a meeting of experts.
1(15)	Vol. 4, C.1.2 production plant[redacted]	AT: Is plant[redacted]obsolete? If not, details (address etc..), information on production process, current representative batches, and an assessment on equivalence according to guidance document 10597 is required.	Indeed, the manufacturing plant[redacted] is obsolete and was not supported for Annex I inclusion. The provided data specifically related to this plant were evaluated and reported in the DAR, but were not taken into account in the overall conclusion on technical specification.	Addressed.

Rapporteur: BE

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(16)	LOEP Appearance	FR : In the Vol. 3 B.2.1.7, purity of 99% is for PGAI which is described as a liquid, please RMS clarify if the appearance listing in the LOEP is this of the technical substance and so corrected by 98.6%	Both the TGAI and PGAI tested, had a purity of approximately 99% and were described as being light beige solid material. The entry in the LoEP is therefore consistent with the results reported in Vol.3 B.2.1.7.	Addressed.
1(17)	LOEP Partition coefficient	FR : For better comprehensibility, please RMS homogenise result at pH 7 : "1.69" in the LOEP and "1.70" in Vol 3 B.2.1.13	Log Pow at pH 7 = 1.7 In the study, 2 determinations were performed with 1.69 and 1.70 as individual results. Minor point	Addressed. See also comment 1(18)
1(18)	Vol 1, LOEP, log Pow	NL: The value at pH 7 is not consistent with the value in volume 3 (1.70 and 1.69).	See comment 1(17)	See comment 1(17)
1(19)	Vol. 1, List of endpoints p.40	EFSA: instead of not applicable in the fields for melting and boiling point probably would be more correct to write that decomposes above 270oC	Entry in LoEP has been amended to "*Not applicable (decomposition above 270°C)"*, which should be comprehensible.	Addressed.

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(20)	Vol.3 B.2.2.15 Stability after storage for 14 days at 54°C	FR considers that this study is required to assure if the plant protection product is stable at 54°C. Even if a shelf life study is provided as maximal temperature reached during this study was 31°C, no data are provided on the stability at higher temperature. If the formulation is not stable at 54°C, FR thinks that an advice has to be added on the label.	See comment 1(21)	See open point in comment 1(21)
1(21)	Vol. 3, B.2.2.15 Stability after storage for 14 days at 54oC p.2-16	EFSA:The stability of the preparation after storage for 14 days at 54 °C according to the Directive should be provided	RMS acknowledges that this is a requirement of Directive 94/37/EC. However, according to GIFAP monograph N°17, the accelerated test is to be performed to generate data that may be extrapolated to propose a shelf life for the product.	Open point: The necessity to request the „accelerated' storage stability testing of the preparation if a shelf life study is available to be (re-)discussed in a meeting of experts. See also comment 1(20)
1(22)	Vol.3 B.2.2.22 Suspensibility	FR : Please RMS clarify why the suspensibility has been realized and accepted at 0.5 g a.s / L while the minimal recommended concentration is 0.3 g a.s / L.	The overall results for suspensibility (before and after storage) were considered to be unsatisfying. Even at 0.5 g a.s./L, the suspensibility was found to be below the FAO limit (i.e. 60%). A sprayability test is considered necessary in order to demonstrate good performance of the formulation under field conditions with respect to suspensibility. See comment 1(25)	Open point: The acceptability of the suspensibility study to be discussed in a meeting of experts

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(23)	Vol 3, B.2.2.22, suspensibility	NL: Was suspensibility determined analytically or gravimetrically? It seems a sprayability test will be required (at MS level?).	Suspensibility was determined analytically by means of HPLC-UV. See comment 1(25)	Addressed. See also comment 1(25)
1(24)	Vol 1, 4.2 (page 93) Suspensibility and wettability	Notifier: Venzar 80 WP has been sold for over 30 years and has performed satisfactorily in the field in many countries including Belgium, France and the UK. The notifier has received no complaints over the sprayability of the product and no complaints of poor efficacy linked to sprayability. Venzar 80 WP product labels already include a statement warning users that agitation should be started before loading and maintained during spraying. The notifier agrees with the RMS that this issue can be addressed at member state level during the re-registration of Venzar 80 WP. Evidence of satisfactory importance and homogeneity of the diluted spray solution in the form of efficacy data will be submitted in the biological assessment dossier to member state authorities.	Further evidence, demonstrating acceptable performance of the preparation under field conditions, should be required at member state level. See comment 1(25)	See point of clarification in comment 1(25)

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(25)	Vol 3, table B.2.2.-2, shelf life results	NL: Change of properties does not seem shocking – properties do not change dramatically. The variance in results seem to be within acceptable limits. NL would probably be content with a sprayability test as the suspensibility is too low and wetting is too slow.	Further evidence, demonstrating acceptable performance of the preparation under field conditions, should be required at member state level.	Point of clarification for the applicant: Applicant to provide information demonstrating acceptable performance of the preparation under field conditions See also comment 1(24)
1(26)	Vol 1, level 4, 4.2, ppp data	NL: NL agrees with the RMS that this data can be handled at MS level.	See comments 1(24) and 1(25)	See point of clarification in comment 1(25) and also comment 1(24)
1(27)	Vol 3, B.2.2.19, shelf-life	NL: The summary suggests the product was stored in paper only, while in B.3 the cardboard box appears to be sealed or laminated with LDPE. Is the assumption that the same packaging as described in B3 was used correct?	Indeed, it was confirmed by the applicant that the same commercial packaging as described in Vol.3 (B3) as „Bag in Box' was used in the shelf life study (1 kg sealed cardboard box with an inner paper bag lining; the inner paper bag is lined with LDPE).	Addressed.

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(28)	Vol 3, B.3.5.1.1, table B.3.5.1.1.-1	NL: No. 3 under material/bag mentions a HDPE film of 20 „my'? What are „my'? Micrometers?	„my' appears to be a measuring unit for the material strength of foils.	Point of clarification for the applicant: Applicant to clarify the unit used in table B.3.5.1.1-1 No. 3 under material/bag

Classification and labelling (B.4)

For comments on classification and labelling see the relevant sections.

Rapporteur: BE

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(29)	Vol.3 B.5.1.1 Method Hansen, 1998 – Report No. AMR 3747-96)	FR : Please RMS clarify why the linearity of this method is accepted while only 3 standard solutions were used.	The HPLC-UV method used in the batch analysis study Wittig (2000) is suitable for the determination of lenacil content in the technical material.	Open point: The acceptability of the linearity determination of method (Hansen, 1998 – Report No. AMR 3747-96) to be discussed in a meeting of experts
1(30)	Vol. 4 annex C.1.2.4 Methods of analytical for the determination of impurities (Wittig, 2000 – Report No. PR00/015)	FR thinks that analytical method using ICP-OES has to be validated as other method. Even if it is a well-established technique, validation data have to be provided.	Linearity and accuracy data were not provided for the ICP-OES method. Following waiver was received from the applicant: *"ICP-OES is a well established technique for inorganic analysis and is generally accepted as being linear and acceptably accurate for all purposes."* RMS can agree that full validation data should have been provided for this method.	Open point: The acceptability of the ICP-OES method (Wittig, 2000 – Report No. PR00/015) to be discussed in a meeting of experts
1(31)	Vol.3 Annex C.1.2.4 Methods of analytical for the determination of impurities (Hansen, 1998 – Report No. AMR 3747-96)	FR : A typo is appeared in the table. For linearity, only concentration range are reported in the table not r^2 while the column is described as "Linearity r^2 (conc. Range)"	Noted However, RMS believes this minor error causes no problems with the interpretation of the results.	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(32)	Vol.3 Annex C.1.2.4 Methods of analytical for the determination of impurities (Hansen, 1998 – Report No. AMR 3747-96)	FR : According to the doc SANCO 3030/099 rev.4, LOQ has to be determined as the lowest concentration tested, at which an acceptable mean recovery with an acceptable RSD is obtained. In this part, LOQ is defined in function of ratio S/N, please RMS clarify.	According to Commission Directive 96/46/EC, the establishment of a validated LOQ is only required for relevant impurities. It is our interpretation that for non-relevant impurities, LOQ can be estimated based on S/N ratio and does not necessarily have to be supported by validation data. In addition, please note that sufficient validation data for the impurity methods were presented in the study report by Wittig (2000), where a LOQ of 1 g/kg was established on the basis of accuracy and precision.	Addressed.
1(33)	Vol 1, 4.5 (page 93)	Notifier: Since a fully validated method for the determination of lenacil residues in sugar beet is available for monitoring purposes, the notifier considers that there is no need for additional information to be submitted.	RMS agrees that a fully validated method for the determination of lenacil residues in sugar beet is available for monitoring purposes (Mende, 2002 and Turnbull, 2003). Concerning the applicability of a multi-residue method: see comments 1(35) and 1(36).	See open point in comment 1(35)
1(34)	Vol 1, level 4, 4.5, RAM for plant material	NL: Either more data is required or not. It is unclear what the RMS wants the notifier to do.	See comments 1(35) and 1(36)	See open point in comment 1(35) See also comments 1(33) and 1(36)

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 1, level 4, 4.5, Methods of analysis p.93 Vol. 3, B.5.2.1 Analytical method for residues in plants p.5-6	EFSA is of the opinion that the study Tillkes, 1998 addresses the demonstration of the applicability of DFG S19, even if it the validation does not fully comply with the requirements of guidance document 825/00, as a fully validated method for monitoring in sugar beet is available	It should be discussed in a meeting of experts what (level of) information should be provided in order to demonstrate the applicability of a multi-residue method sufficiently.	Open point: The necessity to provide further data to demonstrate the applicability of the multi-residue method to be discussed in a meeting of experts. See also comments 1(33), 1(34) and 1(36)
1(36)	Vol. 3, B.5.2.1	DE: Conclusion of Tilkes, 1998: Because only 1 recovery experiment per level was reported, we consider this study as being not acceptable. If RMS agrees, please state clearly.	Indeed, the RMS considered this study as being not acceptable, because the validation data package does not comply with SANCO/825/00. See also comment 1(35)	See open point under comment 1(35) See also comments 1(33), 1(34)
1(37)	Vol.3 B.5.5.3 Table B.5.5.3-1 Summary of analytical methods(residue) for soil, water and air	FR thinks that method *Brodsky and Zietz, 1990* cannot be considered as fully validated on the range from 0.05 to 2.55 mg/kg as only two samples were analysed at 2.55 mg/kg.	RMS agrees. The method was fully validated as primary method in the range 0.05 to 0.5 mg/kg.	Addressed: RMS to correct the range in the table B.5.5.3-1 in a corrigendum
1(38)	Vol. 3, B.5.3.1 analytical method residues in soil	AT: Method Brodsky and Zietz is not acceptable as primary method since the numbers of replicates are too low. Therefore it should be deleted from the list of endpoints.	At the fortification levels 0.05, 0.1 and 0.5 mg/kg, 5 replicate recovery determinations were done and therefore, the method is considered acceptable as primary method in the range 0.05 to 0.5 mg/kg. It should be noted that the fully validated HPLC-MS/MS method (Mende, 2003), which is more sensitive (LOQ=0.02 mg/kg) and highly specific, is available for enforcement purposes.	Open point: The acceptability of method Brodsky and Zietz as primary method 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)
1(39)	Vol. 3, B.5.2.2	DE: Method of Wittig, 2002: We agree that one UV spectrum of a standard is shown in this study. But this was a spectrum of a pure standard without any information on its concentration level. Therefore, we do not agree with the RMS that confirmation of the primary method was acceptable. Therefore a data gap exists and a confirmatory method for the determination of the active substance in drinking water and surface water is missing. According to SANCO confirmation by UV-spectra requires "an UV- spectrum under the conditions of the determination". From our point of view this requires the comparison of UV-spectra of standard and fortified real sample generated by LC-DAD at the LOQ. This is not done in the study.	Before the DAR was finalised, the RMS asked this question to the applicant, who provided the following answer: *"[…] Identity is primarily confirmed by comparison of retention times against standard solutions of lenacil. This is supported by the comparison of UV spectra, which has been reported in a GLP study so presentation of the raw data should not be required. HPLC/DAD is an inherently self-confirmatory technique."*	Open point: The necessity to require a confirmatory method for determination of residues in water to be discussed in a meeting of experts See also comment 1(40) and 1(41)
1(40)	Vol 3, B.5.3.2, RAM for water	NL: In general, NL does not consider DAD as highly specific. At below 230 nm UV spectra are never specific and therefore the identity is insufficiently confirmed using the wavelengths mentioned. NL believes a confirmatory method is required.	The detection wavelengths stated in the report are 200, 212 and 270 nm.	See open point in comment 1(39) See also comment 1(41)

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(41)	Vol. 3, B.5.5.3, Vol. 1, 2.2.3 (p. 16), List of End points (p. 43), 4.5 (p. 93)	DE: We consider analytical methods for water (drinking water, surface water) as being not fully validated. A confirmatory method for drinking water and for surface water is missing. (please refer to comment *[1(39)]*). Please correct the respective text sections and tables.	See comment 1(39)	See open point in comment 1(39) See also comment 1(40)
1(42)	Vol. 3, B.5.3.3 analytical method residues in air	AT: The method is not sensitive enough (LOQ = 0.1 mg/m3) to cover the concentration C (0.048 mg/m3) as required according to guidance document 825/00. A new method/validation must be provided.	Indeed, the validated LOQ of the method is below the relevant concentration C, which was estimated following the guidelines described in SANCO/825/00 rev.7. However, it should be noted that the difference between validated LOQ and concentration C is quite small. In addition, lenacil is a very slightly volatile compound (see B.2.1.5) and furthermore, it should be kept in mind that there is already a safety factor of 100 included in the AOEL and an additional safety factor of 10 for the calculation of concentration C. Therefore, the request for further data may not be necessary in this case.	Open point: The acceptability of the air method with the validated LOQ to be discussed in a meeting of experts See also comment 1(43)
1(43)	Vol. 3, B.5.3.3 Analytical method for residues in air p.5-11	EFSA: The LOQ = 0.1 mg/m^3 is higher than the concentration C (0.048 mg/m^3) required according to guidance document 825/00. A new method/validation must be provided	See comment 1(42)	See open point in comment 1(42)

2. Mammalian toxicology

Toxicokinetics (B.6.1)				
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)
2(1)	Vol. 3, B.6.1, ADME (Toxicokinetics)	DE: It seems that oral absorption of lenacil in fact will increase with repeated dosing but the oral absorption rate is usually based on the results obtained after single application of a low dose. Unfortunately, the amounts found in bile are not tabulated in the DAR. According to our national evaluation, however, oral absorption following the single low dose will account for about 70 % only. This point should be discussed on the PRAPeR meeting since a change in the view might result in a need for correction of the AOEL.	The radioactivity levels in the bile are tabulated in table B.1.6-5 (title correct, but erroneously stated as „urine' in the 3th column of the table). Indeed, usually, the oral absorption is calculated based on the results obtained after application of a single low dose. The absorption of a compound is largely determined by the capacity to cross semi permeable membranes and depends strongly from its physical chemical properties, concentration at the site of contact, dissolution of the substance, gastric emptying rate and intestinal motility. In the repeat dosing study, the same low dose as in the single dose study was used but administered 7 times with a time interval of 24 h. Therefore, RMS considers that repeated dose study is well adapted for estimation of oral absorption. After a single oral low dose of lenacil, oral absorption= 63% (females) and 82% (males) increasing to 85-89% after repeated low dose. Females excrete more unchanged parent compound after a single low dose, an effect disappearing after repeated dosing. This could suggest that lenacil induces its own metabolism and therefore bioavailability. When the mean value of the various oral absorption values (see table B.6.1-4) is calculated, 79.92% is obtained. If bile excretion is added to urinary excretion,	Open point: Oral absorption to be discussed at an experts' meeting. See also points 2(3), 2(4), 2(5)

Toxicokinetics (B.6.1)				
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)
			single oral low dose, an oral absorption value of 64-73% of the dose is obtained: this approach was not used as bile and urinary excretion were not measured in the same study.	
2(2)	Vol 4, C.1.2.3, batches used in toxicity testing	UK: In the absence of specific details, we would like to have assurance that the material used in the toxicity testing was produced using the same manufacturing method as used in the full production plants (therefore likely to have a similar impurity profile) rather than in a small lab based system.	We assume that the same method was used and that the purity of a material produced in a small lab based system could be lower than that obtained in the full production plants.	Addressed See point 2(51)
2(3)	Vol 3, B.6.1, Absorption, distribution, excretion and metabolism	UK: Does the RMS consider that the increased absorption seen following repeat low dosing is a result of an increase in the activity of gut micro flora?	RMS does not know if an increase in the activity of gut microflora could be related to an increase in oral absorption of lenacil. Despite the fact that the nature of metabolites could suggest a role of intestinal microflora, such kind of metabolites could also result from involvement of liver CYPs which are also inducible. It appears that lenacil induces its own metabolism and bioavailability is better after repeated dosing.	See open point on point 2 (1) See also points 2(4), 2(5)
2(4)	Vol. 3, B.6.1 Toxicokinetics Oral absorption. Page 3	EFSA: According to the summary RMS states that “based on urinary excreted radioactivity after a single dose, oral absorption represents 63-82% of administered low dose level” but according to table B.6.1-4 this value correspond to the sum of urine + faeces –parent. Please, could the RMS clarify this point?	It is correct that the estimated absorption after single treatment corresponds to the sum of urine + faeces – parent. Table B.6.1-4 shows the distribution of metabolites of lenacil in urine and faeces after low, high and repeated low dose. Five different metabolites are suggested by the different radioactive peaks, all appearing in urine, faeces and bile. Parent compound in faeces is not included in the estimation of oral absorption because the part of	See open point on point 2(1) See also point 2(3), 2(5)

Toxicokinetics (B.6.1)				
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)
			parent compound is probably related to a non absorbed part.	
2(5)	Vol. 3, B.6.1 Toxicokinetics Oral absorption.	EFSA: RMS proposes to take the values of repeated dosing (85%) into account for setting the correction factor for oral absorption based on urinary and faeces excretion considering the metabolites excretion. The inclusion of metabolites excretion as absorbed and the use of the values of repeated dosing for setting the oral absorption should be further discussed.	- Use of repeat dose: In the repeat dose study, the same dose of lenacil as that used in the single low dose was used. The interval of 24 hours between each dose makes that the absorption process has the time to be completed and interference at the site of absorption with the next dose is improbable. After repeated dosing, accumulation in the body could occur but this should not affect oral absorption. The absorption of a compound is largely determined by the capacity to cross semi-permeable membranes and depends strongly from its physical chemical properties, concentration at the site of contact, dissolution of the substance, gastric empting rate and intestinal motility. - Inclusion of metabolites excreted as absorbed: usually, metabolism occurs after absorption but metabolism in the gut lumen and wall could also occur without passage in blood. Bacterial flora in the gut, the environmental pH and oxidative or conjugative enzymes present in the intestinal epithelial cells can all contribute to the metabolic process. In the case of lenacil, identical metabolites were identified in urine, bile and feces and these hydroxylated metabolites could therefore result from metabolism by gut microflora but also by the liver. These metabolites, if formed only in the gut, could then be absorbed as suggested by the presence of metabolites in bile and urine.	See open point on point 2(1) See also points 2(3), 2(4)

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)

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(6)	Vol. 3 B6.3.2.1 page 17, Oral 90-d toxicity Vol. 3 B6.10, Page 63. Short term toxicity Vol. 1, page 18-21 point 2.3, Impact on human and animal health	Notifier: Additional information pertinent to discussions about possible target organs and possible effects on thyroid function affecting determination of adverse effect levels was submitted by the Notifier in the dossier. The Notifier requests inclusion of this information at relevant points in the summary of repeated dose toxicity evaluations. Alterations to text and endpoints are requested on basis of arguments relating to thyroid function tests and adaptive liver responses.	In the DAR, additional information was included under each point when necessary as "comment from the company". Some more detailed discussions are included in the addendum.	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 B6.3.2.2 page 21, Oral 90-d toxicity - dog	Notifier: Discussions relating to the adaptive nature of the hepatic response have been partially included in the DAR as a comment from Notifier. The Notifier requests expansion of this comment to include more details pertinent to the "adaptive response argument".	In the DAR, additional information was included under each point when necessary as "comment from the company" RMS considers that a full evaluation of liver effects was not performed and therefore the conclusion of liver effects as adaptive could not be reached.	Addressed
2(8)	Vol. 3 B6.3.4, Page 22 Summary of short term toxicity Vol. 3 B6.10, Page 63. short term toxicity	Notifier: A revised table of results is proposed with different endpoints taking into account the adaptive liver response and additional thyroid function tests.	See addendum	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(9)	Vol 3, B.6.3.2.1, Oral 90-day toxicity (mouse), B.6.10.3, AOEL	DE: It is difficult to assess whether the effects on blood (in particular leucopenia) im mice at dose levels of 1000 ppm and above are toxicological relevant since a dose response is lacking. The NOAEL is rather seen at 1000 ppm (157 mg/kg bw/d) than at 100 ppm (15.5 mg/kg bw/d). At least, because of this uncertainty and also the wide dose spacing, it is doubtful whether this study may in fact provide the most suitable basis to derive the AOEL. Instead, the 90-day study in rats might be used.	RMS agrees that a dose response is lacking but is probably related to a saturation process of oral absorption at high doses as suggested in the ADME part of the DAR: at single dose as high as 1000 mg/kg bw (corresponding to 5000 ppm in mice) oral absorption is very low (0-7%). Repeated dosing increased the absorption of the low dose but it is unknown if this applies to a high dose. Therefore, RMS considers that the lack of dose effect results from a low oral absorption with a plateau in the toxic effects.	Open point: The NOAEL of 15.5 mg/kg bw/d from the 90-day mouse toxicity study to be discussed by the experts. See also open point on point 2(28) See also points 2 (19) 2(10) ,2(29) 2(31) 2(32)
2(10)	Vol 3, B.6.3, Short term toxicity	UK: The mouse is clearly the most sensitive species, rat and dog similar	No further comments	See open point on point 2(9) See also points 2(28) 2(29) 2(31) 2(32)

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.6.4.1.3, In vitro mammalian cytogenetics	UK: More details are required on the positive findings in chromosome aberration test. From the table it appears that the aberrations did not include any gaps it would be useful to know if there was any increase in a single aberration or a spectrum.	See addendum	Addressed

Long-term toxicity and carcinogenicity (B.6.5)				
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)
2(12)	Vol. 3 B6.5.2, page 37 Carcinogenicity in the rat	Notifier: Request for inclusion of additional comment relating to the derivation of the NOEL and NOAEL values in this study – see text in column 3.	See addendum	Addressed

Long-term toxicity and carcinogenicity (B.6.5)				
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)
2(13)	Vol. 1, 2.1.4, Classification and labelling	DE: A possible need for classification and labelling for carcinogenicity (R40) on the basis of thyroid and mammary tumours in female rats should be discussed on the PRAPeR meeting. Lung tumours in male mice must also be taken into account. If a carcinogenic effect is recognized and a NOAEL for oncogenicity is set for a particular substance (as this was the case in the DAR), allocation of R40 will usually follow unless it can be proven that the findings were certainly not relevant for humans. In contrast, R64 as proposed by the RMS is not supported since the reduction in body weight gain in offspring during lactation was confined to a very high dose of 50000 ppm that was also parentally toxic and was not accompanied by a delay in any further developmental landmarks.	Allocation of R40 was not proposed as RMS considered that : 1) the increase in malignant mammary adenocarcinoma was outside the historical control data of the laboratory but within the data of Charles River Han Wistar rats in 2003 and therefore considered **as questionable**. However, RMS agrees that the topic deserves further discussion. 2) thyroid adenoma are not a basis for classification: the adenoma are within historical control data. 3)Lung tumors in male mice: Incidences of adenoma and adenocarcinoma, taken separately, were not statistically increased. There was no statistical significance with the Fisher exact test at p=0.05 for any dose group. There was no decrease in alveolar tumor latency; most tumors were observed in mice killed at terminal sacrifice. There was no increase in focal hyperplasia of type II alveolar cells. There was no shift in tumor cell anaplasia. Allocation of R64: we agree that the effects are confined to a very high dose but classification is a hazard and not a risk. Parental toxicity was not so evident in the 2 generation studies.	Open point: Carcinogenic properties and proposal for classification and labelling for carcinogenicity (R40) to be discussed in an experts' meeting. See also points 2 (14) 2 (15), 2(16), 2 (17) 2(18) Open point: Proposal for classification and labelling with R64 based on reduction in body weight gain in offspring during lactation to be discussed in an experts' meeting. See also points 2(19), 2(21), 2(23), 2(24) 2(50)
2(14)	Vol. 3, B.6.5.1 and B.6.5.2, Long-term toxicity and carcinogenicity in the	DE: If follicular cell adenoma and carcinoma are combined, the incidence in female rats over the course of the study was 3, 0, 3, and 8	Agreement: the incidence of malignant thyroid carcinoma in females was not correctly reported in the DAR and is 1/0/1/0 **and not 2/0/2/4** in females.	See open point in comment 2(13) See also points 2(15), 2(16), 2(17) 2(18) RMS to consider the amendments in a

Long-term toxicity and carcinogenicity (B.6.5)				
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)
	rat, thyroid tumours	in the control and three dose groups (Table B.6.5.2-1) suggesting a treatment-related effect with a combinded incidence of 16 % at the highest dose level. However, an incidence of 4 top dose females with carcinoma could not be found in the summary of the original study report. The RMS is asked for clarification.		revised DAR or corrigendum
2(15)	Vol. 3, B.6.5.1 and B.6.5.2, Long-term toxicity and carcinogenicity in the rat, mammary tumours	DE: If the combined incidence of mammary adenoma and adenocarcinoma is considered (0, 3, 6, 8), there is evidence for a significant and dose-related increase. However, it must be noticed that a tenfold increase in the dose level produced only a marginal increase in tumour frequency. The relevance of this findings should be discussed on the PRAPeR meeting.	Agreement.	See open point in comment 2(13), See also points 2(14) 2(16), 2 (17) 2(18)

Long-term toxicity and carcinogenicity (B.6.5)				
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)
2(16)	Vol 3, B.6.5, carcinogenicity	UK: We agree with the RMS conclusions on the tumours apart from the lung tumours in the mouse. The only two Historical Control groups did not have any carcinomas and the 7000 ppm males were well over the Historical Control value for the combined incidence. It would have been useful to have the incidence for lung tumours for all groups from the 2 studies from which the Historical Control data have been derived (assuming the test compounds didn't cause lung tumours!). Overall based on the data presented the tumours should be considered as treatment related rather than „equivocal toxicological significance', and consider the need for Cat 3 classification.	no comments	See open point on point 2(13) See also points 2(14) 2(15), 2 (17) 2(18)
2(17)	Vol. 3, B.6.5. Long-term toxicity and carcinogenicity. Carcinogenic properties	EFSA: With regard to carcinogenicity RMS states that equivocal findings were found in rats (mammary gland tumour) and mice (lung alveolar tumor and hepatocellular adenoma). The carcinogenicity properties should be further discussed based on findings outside the historical control data.	agreement	See open point on point 2(13) See also points 2(14) 2(15), 2 (16) 2(18)

Long-term toxicity and carcinogenicity (B.6.5)				
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)
2(18)	Vol. 3. B.6.5 Long-term toxicity and carcinogenicity. Historical control data	EFSA: Could the RMS clarify whether the laboratory control data is relevant to the strain used in the long-term studies, also with regard to the date of the study?	The company did not provide the date of laboratory control data. The study was terminated in 2004. It appears that the historical control data from the laboratory have a background incidence different from those reported by Charles River in 2003, but we suppose that as they were provided by the company, they are relevant as well as those reported by Charles River.	Point of clarification for the applicant: Applicant to submit laboratory control data including all details (dates, strain, number of animals, etc) for liver and lung tumours in mice and for mammary gland tumors in rats. See also open point on point 2(13) See also points 2(14) 2(15), 2 (16) 2(17)

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(19)	Vol. 3 B6.6.1, page 44 Two generation reproduction toxicity in the rat Vol. 3 B6.6.3, Page 53-54. Summary of reproductive toxicity and teratogenicity	Notifier: The Notifier disagrees with the conclusion of the RMS to classify the active substance with R64. In the DAR the RMS proposes further discussion in relation to this classification. The notifier requests inclusion of arguments from the dossier summaries in the DAR which conclude that R64 is not required (see Column 3) and amendment of the conclusions.	It was proposed in the DAR to discuss this point in the PRAPeR meeting.	See open point on point 2(13), See also points 2(21) 2(23) 2(24) 2(50)

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(20)	Vol. 3 B6.6.1, page 44 Two generation reproduction toxicity in the rat	Notifier: The notifier requests inclusion of the discussion of thyroid function tests in relation to interpretation of multigeneration study endpoints in the DAR.	See addendum	Addressed.
2(21)	**B.6.6.1 Two generation reproductive toxicity in the rat (Annex IIA 5.6.1)**	FR: agrees with the RMS that the reduction of weight gain in F1 and F2 offsprings during lactation should be considered as adverse; however a labelling with R64 should be accompanied by a labelling with, at least, an R63 phrase.	No further comments	See open point on point 2(13), See also points 2(19) 2(23) 2(24) 2(50)
2(22)	**General comment**	FR: in the short and long term studies, lenacil caused various alterations –sometimes dose related- of the thyroid gland in rats as well as in dogs. As stressed by the RMS, as the mechanism has not been clearly elucidated, these effects should be considered relevant for humans.	No further comments	Addressed
2(23)	Vol 3, B.6.6.3, reproductive toxicity	UK: In the absence of a lactating goat study we agree with R64 classification	Metabolism studies in lactating animals were not necessary. RMS agrees that it could indeed be helpful to have some information in other species.	See open point on point 2(13), See also points 2(19) 2(21) 2(24) 2(50)
2(24)	Vol.3, B.6.6. Reproductive toxicity. Proposal for classification. R64.	EFSA: As RMS already mentioned on page 45, the proposal to classify Lenacil as R64 based on decreased body weight in offspring during lactation should be discussed and agreed on.	agreement	See open point on point 2(13), See also points 2(19) 2(21) 2(23) 2(50)

Neurotoxicity (B.6.7)				
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)

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(25)	Vol 3, B.6.8.1, toxicity of metabolites	UK: Provided the levels of metabolites are low compared to parent we are content with the RMS assessment. Therefore it would be useful if levels (for both impurities and parent) were given (in plants and potential for groundwater).	The metabolites have been identified and concentration was estimated by calculation to be below 0.1 µg/L. No further evaluation for toxicological relevance is necessary.	Addressed Plant metabolites IN-KC943 and IN-KQ961 could be considered as equivalent or less toxic as Lenacil. After confirmation by the residue and environmental fate groups the definition of the relevance of some metabolites might be requested.
2(26)	Vol. 3, B.6.8.1 Toxicological studies on metabolites.	EFSA: Could the RMS confirm if the metabolites found in various environmental compartments can be considered as the same or less toxicity as Lenacil?	As explained in the DAR the metabolites found in various environmental compartments are structurally similar to the parent compound and metabolites identified in the rat. Therefore, RMS considers that the toxicological evaluation is covered by the dossier of the parent. The different metabolites should be considered as equivalent or less toxic as lenacil.	Addressed See point 2(25)
2(27)	Empty row			

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(28)	Vol. 3 B6.10.1, Page 68. ADI Vol. 1, page 23 point 2.3.2, ADI	Notifier: The Notifier proposes an ADI of 1.18 mg/kg/day. The notifier requests inclusion of a table summary of revised endpoints on which to base derivation of the ADI in the DAR taking account of thyroid function and adaptive liver responses in long term toxicity studies..	See addendum	Open point: The setting of reference values to be confirmed in an experts' meeting See also points 2(9), 2(10) 2(29) 2(30) 2(31) 2(32)
2(29)	Vol. 3 B6.10.3, Page 69. Vol. 1, page 17 point 2.3.4, AOEL	Notifier: The Notifier proposes an AOEL of 4.12 mg/kg/day. The notifier proposes inclusion of a table summary of revised endpoints on which to base derivation of the AOEL in the DAR taking account of thyroid function and adaptive liver responses in short and long term toxicity studies.	RMS has noted the proposals from the company.	See also points 2(9) 2(10) 2(28) 2(31) 2(32)
2(30)	Vol. 3, B.6.10.1, ADI	DE: A slightly lower ADI of 0.12 mg/kg bw instead of 0.14 mg/kg bw is proposed. The RMS proposal is agreed to derive the ADI from the NOAEL in the long-term study in rats. However, the numeric value is usually set on the basis of the lower mean dietary intake if there is a difference between sexes. For lenacil, this was 12 mg/kg bw/d in male animals.	No further comments	See also points 2(28) 2(32)

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(31)	Vol. 3, B.6.10.3, AOEL	DE: A somewhat higher systemic AOEL of 0.3 mg/kg bw/d instead of 0.16 mg/kg bw/d is suggested. On one hand, the NOAEL in the 90-day study in mice is not considered an appropriate basis (see comment above). Instead, the AOEL should be derived from the NOAEL in the 90-day rat study (40.6 mg/kg bw/d) that is nearly equal to the NOAEL in the 90-day dog study (44 mg/kg bw/d). If, furthermore, an oral absorption rate of only 70 % is assumed (see comment above), a rounded figure of 0.3 mg/kg bw/d would result.	For the reasons explained in 2(9), RMS does not consider the WBC effects in the mice irrelevant. The findings are consistent throughout the experiment (wk6-7 and wk 13), and the plateau-effect could be explained by a possible saturation at the quite high top-dose. The modification of the correction factor for oral absoprtion is, in our opinion, not necessary as we consider that the repeat dose is well adapted for estimation of oral absorption	See also points 2(9) 2(10) 2(28) 2(29) 2(32)
2(32)	Vol 3, B.6.10.1, 6.10.2 and 6.10.3, reference values	UK: The reference values proposed are acceptable.	No further comments	See also points 2(9) 2(10) 2(28) 2(29) 2(31)

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(33)	Vol. 3 B6.11.3, Page 71 Acute inhalation toxicity to rats of Venzar 80 WP.	Notifier: A complete copy of the report is available and has been submitted to include pages originally omitted in error.	Noted.	Addressed

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(34)	Vol. 3 B6.12, Page 74 Dermal absorption.	Notifier: Comments relating to derivation of the correct dermal absorption values for diluted and undiluted forms of lenacil are included in the DAR but the references cited to support the Notifier's argument have been omitted. We request inclusion of the references. See column 3 for full reference.	No comments	Addressed

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(35)	Vol. 3, B.6.12, Dermal absorption	DE: For the concentrate, 1 % dermal absorption should be assumed whereas the more appropriate value for the dilution might be 16 %. The approach taken by the RMS to include the amount retained in skin is supported. However, if it is possible to distinguish between different layers of *stratum corneum* because values for individual tape strips are given, the first strips (1 and 2) may be excluded also in an *in vitro* study on human skin since it is very unlikely that this material on the surface would become available under *in vivo* conditions. This would give lower values than proposed by the RMS but much higher percentages than suggested by the notifier.	Indeed, tape strips 1-2 could have been excluded for estimation of dermal absorption. RMS considered the exclusion of the first two strips providing a value of 0.88% (rounded to 1%) value for the concentrated, and 15.5% for the diluted lenacil, instead of the former values 2.7% and 34.2% formerly proposed. A new estimation of operator exposure was performed using the new values of dermal absorption. The amendments are introduced in the addendum.	Addressed

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(36)	Vol 3, B.6.12, dermal absorption	UK: The dermal absorption section could be more transparent. The RMS firstly states that a dermal absorption rate of 2.7% for the concentrate and of 34.2% for the diluted formulation can be derived based on treated skin plus receptor fluid in line with SANCO/222/2000 rev. 7 Guidance. They then go on to indicate that you can exclude the first couple of tape strips. They state that the exclusion of stratum corneum values from total absorption is in accordance with recommendations from the Standing Committees on Plants (2002) and Cosmetics (2003). And give a lower set of values, not very clearly laid out. But the RMS OpEx calculations use 2.7 and 34.2%. Overall UK would be happy to exclude the first couple of tape strips to give values of 0.88 and 15.5% (high and low doses).	- It is the company who stated that: the exclusion of stratum corneum values from total absorption is in accordance with recommendations from the Standing Committees on Plants (2002) and Cosmetics (2003) - The initial estimation of dermal absorption proposed by the company was 0.018% and 0.4% for high and low dose respectively, excluding material recovered in the *stratum corneum*. The values of 2.7% and 34.2% as proposed by the RMS in the DAR in table B.6.12.2-1 result from the sum of dose in receptor + skin+ dose on tape strip 1-2, + 3-5 + 6-8. - we agree that the first 2 tape strips could be excluded giving lower dermal absorption values of 0.88 rounded to 1% and 15.5% (high and low doses). - In the DAR, an estimation of operator exposure was performed using dermal absorption values excluding and including the first 2 tape strips. - in the addendum a correction of dermal absorption is proposed.	Addressed
2(37)	Vol.3, B.6.12 Dermal absorption. Absorbed dose.	EFSA: RMS considered as absorbed dose the dose in the receptor + skin + dose on tape strips (1-8). Nevertheless, the first two tape strips could be considered as not absorbed since they can be lost by desquamation.	We agree, see explanations above.	Addressed

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)

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(38)	Vol. 3, B.6.15.1 (page 76) Estimation of operator exposure: data used for the calculation	Notifier: Operator body weight should read 60 kg (UK model) **and 70 kg (German model)**	agreement	Open point Operator, worker and bystander exposure to be confirmed at a meeting of experts. See also points from 2(39) to 2(49).
2(39)	Vol. 3, B.6.15.1 (page 76) Estimation of operator exposure: Table B.6.15.1-1	Notifier: The exposure estimated using UK POEM is reduced for operators using RPE during mixing/loading (as permitted in the UK model) in addition to gloves during mixing and loading and application.	a new estimation of exposure was performed taking into account a lower value of dermal absorption. See addendum. RMS does not assume the use of RPE, considering that such a protection is unrealistic.	See also points from 2(38) to 2(49).

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(40)	Vol. 3, B.6.15.1 (page 77) Estimation of operator exposure: Table B.6.15.1-3 and Conclusions Vol. 1, 2.3.6 Operator exposure (page 24). Vol. 1 List of endpoints (page 45)	Notifier: The exposure estimated using UK POEM is less than the AOEL (77%) for operators wearing RPE (FFP2 particle filtering mask) during mixing and loading in addition to gloves during mixing and loading and application.	RMS considers that the use of RPE is not realistic for such a compound. As Venzar 80 ia a wettable powder, the use of another package could reduce exposure.	See also points from 2(38) to 2(49
2(41)	Vol. 3, B.6.15.1 (page 76) Estimation of operator exposure: Table B.6.15.1-2	Notifier: The values in Table B.6.15.1-2 are not presented in the same way as those in Table B.6.15.1-1. Currently, the tables imply that estimated exposure using the German model is higher than with the UK POEM. The notifier suggests that the values in Table B.6.15.1-2 are corrected for dermal absorption values (the values proposed by the RMS) to be consistent with Table B.6.15.1-1.	In the German model, dermal exposure is estimated and reported in the table while in the UK model it is the dermal absorbed dose that is reported . This explains why estimated exposure look to be higher in the German model.	See also points from 2(38) to 2(49

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(42)	Vol. 3, B.6 Appendix: (page 85) Estimation of the exposure (page 88-89)	Notifier: There are errors in the spreadsheets for exposure calculated by UK POEM. In addition, amended calculations showing how exposure is reduced by RPE (FFP2 particle filtering mask) during mixing and loading.	A new estimation of operator exposure is proposed in the addendum.	See also points from 2(38) to 2(49
2(43)	Volume 3, B.6.15, Exposure data	DE: Exposure data should be recalculated with the proposed AOEL and the proposed dermal absorption [see comment 7 and 8].	New exposure estimate are reported in the addendum taking into account the modified dermal absorption value	See also points from 2(38) to 2(49
2(44)	Volume 3, B.6.15.4, Estimation of worker exposure	DE: It cannot be excluded that re-entry is necessary soon after application e.g. for irrigation or monitoring purposes. Therefore, a quantitative assessment of re-entry exposure should be given.	Indeed**.** quantitative assessment of re-entry exposure is included in the addendum	See also points from 2(38) to 2(49
2(45)	Vol. 3, B.6.15.3 Estimation of bystander exposure	UK: The bystander exposure estimate uses a dermal absorption value of 0.4% (the value proposed by the notifier) rather than 34.2% (the value used by the RMS in the operator exposure estimates).	This is corrected in the addendum	See also points from 2(38) to 2(49

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(46)	Vol. 3, B.6.15.4, Estimation of worker exposure	UK: As „Venzar 80 WP' is applied as a post-emergence treatment (BBCH 10-31), it is possible that workers inspecting a treated crop may be exposed to dislodgeable foliar residues of lenacil. It is, therefore, considered appropriate to evaluate worker exposure (taking into account the maximum total dose).	Worker exposure is evaluated in the addendum	See also points from 2(38) to 2(49
2(47)	Vol. 3, Annex B „Appendix: estimation of the exposure'	UK: It is noted that the both exposure estimates using the UK POEM seem to have an error in row 12 („Dermal exposure to formulation'). The value presented here (16.47 mg/day in both estimates) relates to inhalation, rather than dermal, exposure. However, it is noted that this error does not affect the calculation.	agreement	See also points from 2(38) to 2(49
2(48)	Vol.3, B.6.15.3 Bystander Exposure. Input values.	EFSA: the input values should be checked since dermal absorption was considered 0.4% when the proposal by RMS was initially 34.2% for the dilution (see B.6.12). In addition, body weight of 60 kg is considered more appropriate.	Agreement, see addendum	See also points from 2(38) to 2(49
2(49)	Vol. 3, B.6.15.4 Worker Exposure	EFSA: some activities such as inspection could be considered in the worker exposure assessment.	Agreement, see addendum	See also points from 2(38) to 2(48).

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)
2(50)	Vol. 3, B.4.1 (page 56) Vol 1, 2.1.4 (page 16) Proposed classification of the active substance	Notifier: The notifier does not agree with a classification of R64. (see Mammalian toxicology (B.6) comment 5)	No comments	See open point on point 2(13) See also points 2(19), 2(21), 2(23), 2(24)
2(51)	Vol.3, B6 General	EFSA: Is there any toxicologically relevant difference between the batches produced by [redacted], 1998 and the ones produced by [redacted], also with regard to proposed current specification?	First of all, it should be noted that lenacil manufactured by [redacted] or by [redacted] is of very high purity reaching [redacted]% and [redacted] especively. Lenacil produced by [redacted] contained 2 impurities: compound 4(see vol C) at [redacted] (toxicologically equivalent to parent compound) and compound 7 at 1[redacted], which are not detectable in the [redacted] batches where all impurities are <1/kg. [redacted] is not more used. One impurity (compound 11) in the [redacted]-[redacted]batches is present at [redacted] a somewhat higher concentration than the others. This impurity has a structure very similar to the parent coumpound and is considered as equivalent to the parent compound from a toxicological point of view. RMS concludes that there are no relevant differences between the lenacil produced by [redacted]a and by [redacted]also with regard to proposed current specification.	Addressed. There are no toxicological relevant differences between the lenacil produced by [redacted] and by [redacted] also with regard to proposed current specification. The batches used in the toxicological studies cover the technical specification.

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)
2(52)	Vol.3, B6 General	EFSA: Could the RMS clarify whether the batches used in the toxicological studies were in accordance with batches produced by [redacted] 1998 and/or [redacted] 1998 and/or [redacted] 2000?	The tox studies were usually performed with a compound having a purity of 98.60%. This degree of purity is very similar to that of [redacted] and [redacted]	Addressed See point 2(51)

3. Residues

Storage Stability (B.7.0)				
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.7.14, storage stability of residue samples	UK: Additional storage stability data are required to support the residue trials in which samples were stored for 26 months.	**02.2009:** The residue trials referenced F-95-001-RES were performed at the phenological growth stage BBCH GS 14 and 19 i.e., not covering the critical BBCH GS 31. RMS agrees to require further frozen storage stability data to support these trials if the meeting of experts considered these trials as acceptable.	Data gap: Frozen storage stability data covering the 26 months to be submitted if the trials can be considered as acceptable. See also open point in comment 3(11).
3(2)	Vol. 3, B.7.14, Storage stability of residue samples	EFSA: In the residue trials samples have been stored frozen for up to 26 months. Storage stability of lenacil residues has been only proven for 254 days. Storage stability data are required to support trials in which samples were stored for more than 254 days.	**02.2009:** See point 3(1).	See data gap in comment 3(1).

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(3)	Vol. 3, B.7.1.1, Metabolism, distribution and expression of residues of lenacil in Sugar Beets	DE: We suggest to change the reported harvest intervals (refer to days after last, not first application). Tabular presentations and the text should be amended accordingly.	**02.2009:** RMS confirms that the reported harvest intervals refer to the number of days after the first application.	Addressed.
3(4)	Volume 1, 2.4, Plant metabolism	EFSA: In Volume 1, 2.4 the RMS states: „A non-negligible polar metabolites fraction was also characterized in sugar beet foliage at harvest (37.9 % of TRR; 0.06 mg/kg) but no further tentative characterisation/identification was attempted.' It should be clarified if identification/characterisation of metabolites was sufficient.	**02.2009:** RMS presented a more detailed assessment of the sugar beet metabolism study in the Addendum-February 2009. This polar fraction was a mixture of several polar metabolites, some of which could be hydrolysed by β-glucosidase suggesting the existence of glucose conjugates. No single polar metabolite in sugar beet exceeded 10 % TRR and no further structure elucidation of these polar metabolites by Mass Spectrometry was attempted. This study was performed at BBCH GS 14 and 16. It is therefore assumed that the level of the recovered radioactive residues in sugar beet leaves would have been higher when performing the study at critical BBCH GS 31. A lower ratio of conjugates/non conjugated metabolites in the extracts would probably also be observed.	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(5)	Vol 3, B.7.2, metabolism in livestock	UK: The requirement for metabolism studies has been compared to animal feed intake on a dry weight basis. This comparison should be made to intake as received. However, it is agreed that animal metabolism data are not required.	**02.2009:** According to the current guidance document, the livestock feed intake must be reported on a dry weight basis.	Addressed.
3(6)	Vol. 3, B.7.2, Metabolism in livestock	EFSA: Intake calculations provided in the DAR show that for beef cattle and pigs the trigger value (0.1 mg/kg diet dry matter/day) is exceeded. A metabolism study on ruminants is required. A metabolism study on pigs is required if the metabolic patterns differ significantly in the rat as compared to ruminants. See also comment (10), residue trials.	**02.2009:** Although the trigger value is exceeded, this case is border line since the feed intake was calculated using the residue values of 0.04 and 0.03 mg/kg on sugar beet tops with leaves generated by residue trials performed at BBCH GS 37, 38. Based on the available residue trials, there is a non-residue situation in the roots and a very low residue situation in the leaves with tops. RMS is of the opinion that a metabolism study on ruminants is not required. A metabolism study on pigs is therefore also not required.	Open point: Experts meeting to discuss if metabolism studies on livestock are required.

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(7)	Vol 3, B.7.3, Definition of the residue	UK: It is stated that the critical GAP growth stage was not covered by the metabolism data provided, but that this was considered acceptable. This statement requires further justification.	**02.2009:** See also point 3(4). It is most likely that the metabolic profile of Lenacil in sugar beet won't be changed when the active substance is applied at a later stage (BBCH GS 31 instead of BBCH GS 14 and 16) since there is no major difference in the phenological stage (4- to 6-leaf stage and beginning of crop cover). Hydroxylation on the C5 cycle is the main step of degradation of the parent Lenacil followed by further glucoside conjugation. Performing the metabolism study at a later stage (BBCH GS 31), the level of total radioactive residues would be higher in leaves with tops but with a slower rate of conjugation. The available study is considered as acceptable and sufficient to cover the metabolism of sugar beet.	Addressed.

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(8)	Vol.3 B.7.3 Definition of the residue	NL: Please further clarify why IN-KC943 is considered non-toxicologically relevant. For example: better soluble and probably fast excreted.	**02.2009:** The metabolites IN-KC943 and IN-KQ961 were generated by hydroxylation of the parent compound on the C5 cycle of the molecule. This is a step of detoxification in plants. Those metabolites are structurally similar to the metabolites recovered in the rat. In rat metabolism, hydroxylation on C5 and C6 cycles is the main step of degradation of the parent Lenacil. IN-KC943 and IN-KQ961can therefore be considered as covered by the available toxicological dossier. These metabolites are as toxic as the parent or less toxic.	Open point: Meeting of experts to discuss the residue definition in plant matrices. See also point 2(25)
3(9)	Vol. 3, B.7.2, Definition of residues	EFSA: The RMS states that the metabolism study is considered as valid despite of the fact that the notified growth stage of application was not covered by the metabolism study. However, the RMS does not provide a justification for this conclusion.	**02.2009:** See points 3(4) and 3(7).	Addressed.

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(10)	Vol. 3, B.7.2, Definition of residues	EFSA: In the toxicology section the question was raised if the metabolites found in various environmental compartments can be considered as the same or less toxicity as lenacil. On the basis of the decision concerning IN-KQ961 it should be discussed if this metabolite needs to be included in the residue definitions.	**02.2009:** N-KC943 and IN-KQ961 can be considered as covered by the available toxicological dossier. These metabolites are as toxic as the parent or less toxic. RMS refers to the detailed metabolism study presented in the Addendum-February 2009. The metabolite IN-KC961 was not recovered in the sugar beet leaves as it is explained in the metabolism study: HPLC analyses showed a peak that matched the retention time of IN-KQ961 (hydroxylated Lenacil), indicating the presence of this metabolite. Later results indicated that IN-KQ961 showed a similar retention time to that of IN-KC943-glucoside and the peak corresponding to IN-KQ961 could be IN-KC943-glucoside or a mixture of the 2. Therefore, the peak was isolated for further β-glucosidase hydrolysis and this peak matched the retention time of IN-KC943, indicating the existence of IN-KC943 glucose conjugate before hydrolysis with no detectable amount of the metabolite IN-KQ961. This metabolite should not be included in the residue definition both for monitoring and risk assessment.	See open point in comment 3(8). See also point 2(25)

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(11)	Vol. 1, List of End points, summary of residue data (p. 49) Vol. 3, B.7.6.1, Residues resulting from supervised trials	DE: Samples from 4 trials (referenced as F-95-001-RES) were stored for 26 months, but storage stability for lenacil was only documented for a period of 8.5 months. Therefore, the corresponding data should not be used for the MRL calculation and should not be underlined in the residue tables. Tabular presentations and the text should be amended accordingly.	**02.2009:** RMS agrees not to accept these trials for MRL setting. So, the actual valid database is presented as follows: *North*: -Roots:4x<0.02 mg/kg -Leaves:<0.02-<0.02-<0.02-0.04 mg/kg *South*: -Roots:3x<0.02 mg/kg -Leaves:<0.02-<0.02-0.03 mg/kg	Open point: Meeting of experts to discuss acceptability of the residue trials carried out in Northern Europe.
3(12)	Vol.3, B7.6.1 Residues resulting from supervised trials, p13	FR: Only three trials have been performed in southern Europe. According to guideline 7029/VI/95 rev5, a complementary trial should be submitted for sugar beet.	**02.2009:** RMS agrees.	Data gap: Further trials covering SE necessary to complete the residue database. (Meeting of experts to discuss the number of trials necessary).
3(13)	Vol 3, B.7.5, identification of critical GAPs	UK: We think there may be a typo. Spray concentration does not agree with application rate and water volumes for use pattern provided in Table B.7.4-1.	**02.2009:** RMS agrees. The applicant is requested to provide clarification on that.	Point for clarification: Spray concentration does not agree with application rate and water volumes for use pattern provided in Table B.7.4-1. Notifier to clarify.

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(14)	Vol 3, B.7.6 supervised trials	UK: It is not clear from the method details submitted which methods are considered acceptable to support the residue trials. The methods suitability as enforcement methods also appears to have been considered. In addition some of the methods have also been considered in B5. For each of the methods full details of any omissions in the validation data should be provided and a conclusion on the acceptability of the method for pre-registration purposes. In addition it should be made clear if any of the residue trial data cannot be accepted due to the absence of supporting method validation data.	**02.2009:** Clarification on the acceptability of the analytical methods used both for enforcement and for pre-registration requirements was presented in the Addendum-February 2009.	Partly addressed. Open point: RMS to consider presenting relevant validation data for method Hamburger R., 2002 in an addendum to the DAR. Open point: Meeting of experts to discuss if methods used in residue trials (Tillkes, 1998; Mende 2002; Hamburger, 2002; Witte, 2006) comply with guidance document SANCO/3029/99 concerning methods of analysis in support of pre-registration requirements and therefore are suitable to support the respective residue trials.
3(15)	Vol 3, B.7.6.1 residues resulting from supervised trials	UK: Several residue trials have been considered acceptable with an earlier growth stage than indicated by the critical GAP.	**02.2009:** See point 3(11)	See open point in comment 3(11).
3(16)	Vol. 3, B.7.6, Residue trials, analytical methods used	EFSA: From the presentation in the DAR it is not clear which of the analytical methods were used in the following residue trials: Germany 2001: G01N003R-G01N006R, Portugal 2002: P02N001R and Spain 2005: 688479.	**02.2009:** See point 3(14)	Addressed in addendum – residue data (February 2009).

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(17)	Vol. 3, B.7.6, Residue trials, analytical methods used	EFSA: Analytical method Tillkes, 1998: EFSA agrees to the conclusion of the RMS that the validation data are not complete. However, the validation data for methods used in residue trials should comply with guidance document SANCO/3029/99 concerning methods of analysis in support of pre-registration requirements.	**02.2009:** RMS notes the remark. See point 3(14)	See second open point in comment 3(14).
3(18)	Vol. 3, B.7.6, Residue trials, analytical methods used	EFSA: Analytical method Hamburger, 2002 and Mende, 2002: Information on some of the parameters (linearity, precision – repeatability) required by guidance document SANCO/3029/99 and the conclusion of the RMS concerning the acceptability of the method are missing.	**02.2009:** The validation data package of the analytical method **(**Hamberger R., 2002 – Report No. 20011048/E2-FPSB) was similar as for the analytical method (Mende, 2002 – Report No. 20011048/E1-FPSB). The overall validation data package provided for analytical method (Mende, 2002 – Report No. 20011048/E1-FPSB) is considered to be sufficient to demonstrate that the HPLC-MS/MS method is suitable for the determination of Lenacil in sugar beet (leaves and roots) with a LOQ of 0.02 mg/kg (see also point B.5.2.1 –Vol3, B(5)).	See open points in comment 3(14).

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(19)	Vol. 3, B.7.6, Residue trials, analytical methods used	EFSA: Analytical method Witte, 2006: An independent laboratory validation is required for methods used for monitoring but not for methods used in residue trials only.	**02.2009:** RMS notes the remark.	Addressed.
3(20)	Vol. 3, B.7.6, Residue trials	EFSA: Criteria for assessing the validity of the reported supervised trials are not mentioned in the DAR. It is noted that several studies which were not carried out according to the notified cGAP (esp. concerning GS) were accepted and that no full data set for Southern Europe has been submitted. Only few results for residues in leaves from trials carried out according to the cGAP are available and therefore only tentative dietary burden calculations could be carried out.	**02.2009:** RMS agrees. See also point 3(11).	See open point in comment 3(11) and data gap in comment 3(12).

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)

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(21)	Vol.3, B7.3, Definition of the residue in animal, p7 AND Vol.3, B7.8.2 Livestock feeding studies in lactating cows or goats, p 17	FR: According to results of the dietary burden calculation, animal intake is above the trigger value: 0.135 mg/kg diet (dry weight basis) for beef cattle and 0.12 for pig. According to guidelines 7030/VI/95 rev3 and 7031/VI/95 rev4, a livestock metabolism and a feeding study- should be required.	**02.2009:** See point 3(6).	See open point in comment 3(6).

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(22)	Vol3.B7.9 Residues in succeeding or rotational crops, p17	FR: Arguments justifying the non requirement of succeeding and rotational crop study is acceptable only for rotational crop. In case of “growth problem”, this argument is no more acceptable because the substitution crop will be sown/planted in a shorter interval. Moreover, it appears that residues are detected in sugar beet leaves (0.04 mg/kg), so attention should be focused on potentially succeeding leafy crops.	**02.2009:** In case of “growth problem”-crop failure, it is only possible to sow beets and spinach resistant to Lenacil (selectivity of the herbicide) as substitution crops because of the phytotoxicity of Lenacil.	Open point: Meeting of experts to discuss if further information or studies concerning rotational/succeeding crops are required.

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(23)	Vol 3, B.7.9, residues in succeeding or rotational crops	UK: The information provided is not sufficient to conclude that less than 10% of the active substance would be present after 30 days. The RMS has indicated that due to the long interval between application and harvest the information is sufficient, however this does not address plant back after crop failure	**02.2009:** See point 3(22). In case of crop failure, only beets and spinach can be sown after soil ploughing.	See open point 3(22).
3(24)	Vol. 3, B.7.9, Residues in rotational crops	EFSA: DT90 values of up to 283 days have been found for lenacil in field studies. Therefore significant residues of lenacil in soil have to be expected up to the planting time of rotational crops and the possible uptake of residues in following crops has to be addressed.	**02.2009:** As already mentioned in the DAR under point B.7.9, Lenacil is rapidly degraded in soil. In laboratory studies, the DT_{50} values ranged between 7 and 15 days at 20˚C in five EU soils. In field studies, the DT_{50} value in three soils in the Northern EU region ranged between 23 and 52 days. Values from a fourth study (Spain) were discounted as there was no rainfall after application and no irrigation was applied. These conditions would not apply to sugar beets that require regular rainfall or irrigation for development.	See open point 3(22).
3(25)	Vol. 3, B.7.10, Re-entry interval, withholding period	EFSA: Residues of up to 19 mg/kg (day 0) have been found in sugar beet leaves after application of lenacil. Therefore, the requirement of a re-entry period and the prohibition of the feeding of sugar beet tops after thinning and crop failure should be addressed.	**02.2009:** No re-entry period was proposed since Lenacil is intended to be used on sugar beet. Livestock are not supposed to be grazed on such an area. Thinning out the sugar beet crop is not relevant anymore nowadays (seeds selection). It is not expected that sugar beet leaves after the crop failure (30 days) will be fed to livestock.	Open point : Meeting of experts to discuss the requirement of a re-entry period and/or the prohibition of the feeding of sugar beet tops after thinning and crop failure taking into account the practices in different countries.

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(26)	Vol. 1, List of End points (p. 50), Vol. 3, B.7.11, Estimates of the potential and actual exposure through diet and other means	DE: The acceptability of the chronic intake by consumers should be recalculated with the proposed ADI of 0.12 mg/kg bw [see comments to mammalian toxicology (6)].	**02.2009:** The chronic dietary intake risk assessment was recalculated according to EFSA PRIMo with the proposed ADI of 0.14 mg/kg bw/day. The calculation is presented in the Addendum – February 2009.	Addressed in addendum – residue data (February 2009).

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)

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. 3, B.8.1.1.1, Aerobic Degradation in Soil	Notifier: Typographical error, page 8-2, final paragraph, second sentence. „Radioactivity of the Soxhlet extracted soil' should be replaced by „Radioactivity in the Soxhlet extracted soil'	The amendments will be done in preparation of the PRAPER meeting	Addressed
4(2)	Vol. 3, B.8.1.2.1, Aerobic Degradation	Notifier: Typographical error, page 8-8, first paragraph, final sentence. „Up t0' should be replaced by „Up to'.	The amendments will be done in preparation of the PRAPER meeting	Addressed
4(3)	Vol. 3, B.8.1.2.1, Aerobic Degradation	Notifier: Typographical error. Page 8-13, second paragraph. „The major degradation product Metabolite IN-KF313 reached maximum level of 14.7% AR after 14 days; Metabolite IN-KE121 reached maximum level of 13.9 % AR after 14 days' should be replaced by „The major degradation product Metabolite IN-KF313 reached a maximum level of 14.7% AR after 14 days; Metabolite IN-KE121 reached a maximum level of 13.9 % AR after 14 days'.	The amendments will be done in preparation of the PRAPER meeting	Addressed
4(4)	Vol. 3, B.8.1.2.1, Aerobic Degradation	Notifier: Typographical error, page 8-17, third paragraph, final sentence. Duplication of to.	The amendments will be done in preparation of the PRAPER meeting	Addressed

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(5)	Vol. 3, B.8.1.2.1, Aerobic Degradation	Notifier: Table 8.1.2.1-16. Observed DT50 values for Sheringham and Wick soils should be given as 12 and 10 days, respectively. The data will then be consistent with the report by Shaw (2004) and allow the derivation of DT50 (reference conditions) for these soils as shown in the table.	The amendments will be done in preparation of the PRAPER meeting	Open point: RMS to clarify which DT_{50} values for IN-KE121 are the proper values for Sheringham and Wick soils and if necessary, to normalize these values to FOCUS reference conditions in an addendum. Note: the ‚k' values of these DT_{50} values are reported in Table B.8.1.2.1-13 originating from the report of Shaw (2004). See open point in 4(13). See also comment for point 4(6).
4(6)	Vol. 3, B.8.1.2.1, Aerobic Degradation	Notifier: Proposed geometric mean for IN-KE121 based in the data given in Table 8.1.2.1-16 should be 5.0 days and not 5.1 days as written.	The amendments will be done in preparation of the PRAPER meeting	See open point in 4(13). See also comment for point 4(10).
4(7)	Vol. 3, B.8.1.3.1, Soil Dissipation Testing	Notifier: Typographical error, page 8-21, fourth paragraph, final sentence. Delete final parenthesis.	The amendments will be done in preparation of the PRAPER meeting	Addressed
4(8)	Vol 1. List of End Points, Rate of Degradation in Soil	Notifier: The geometric mean soil degradation rate for lenacil should be given as 10.25 days to be consistent with the value shown in Vol 3. B.8.1.2.1, page 8-17.	The amendments will be done in preparation of the PRAPER meeting	See open point in 4(55).

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 End Points, Rate of Degradation in Soil	Notifier: The geometric mean soil degradation rate for IN-KF313 should be given as 11.5 days to be consistent with the value shown in Vol 3. B.8.1.2.1, page 8-18. The table identifier for IN-KF313 should state geometric mean rather than arithmetic mean.	The amendments will be done in preparation of the PRAPER meeting	See open point in 4(55).
4(10)	Vol 1. List of End Points, Rate of Degradation in Soil	Notifier: The geometric mean soil degradation rate for IN-KE121 should be given as 5.0 days and the DT50 value for IN-KE121 at 20°C pF2/10kPa should be corrected from 3.0 to 7.3 days.	The amendments will be done in preparation of the PRAPER meeting	See open point in 4(55).
4(11)	Vol 1. List of End Points, Rate of Degradation in Soil	Notifier: The field DT_{50} and DT_{90} values for lenacil are not consistent with those given in Vol 3. Table 8.1.3.1-2. The DT_{50} values should be 25, 28, 18 and 88 days for the French, German, German and Spanish soils, respectively. The corresponding DT_{90} values should be 84, 91, 61 and 291 days, respectively.	The listing of endpoints has been amended	See open point in 4(55).
4(12)	Vol 1. List of End Points, Rate of Degradation in Soil	Notifier: The maximum formation of IN-KF313 in the Ruckhaltebecken sediment is incorrectly given as 2.7% after 120 days. The correct value should be 3.0% after 88 days.	The amendments will be done in preparation of the PRAPER meeting	See open point in 4(55).

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(13)	B.8.1.2, Rate of degradation (Annex IIA 7.1.1.2.1, Annex IIIA 9.1.1.1.1), B.8.1.2.1, Aerobic degradation, Derivation of the DT_{50} soil used for the PEC calculations (p. 16)	DE: The study by Berg (1994a) was conducted at pF 2.5 (see page 6) and consequently no correction factor for water content is needed for the three soils (Hillsdale, Sassafras, Tama). The study by Theis (2003) presents as measured MWHC a water content of 51 ±4 Grav.-% (see page 2). Since the study was performed at 40 % of MWHC the water content was 51 %*0.40 during the study and not 27 %*0.40 (see page 16). The correct water content during the study was 20.4 Grav.-% which is wetter than the FOCUS default of 19 %. Consequently no correction factor for water content is needed for the soil (Speyer 2.2). The study by Girkin (2003) presents for each of the four soils both, a measured water content for MWHC (0 bar) and for the matric potential (1/3 bar). Consequently no FOCUS default values must be used. (1) for water content at reference condition pF 2: values at 1/3 bar can be used directly. (2) for water content of the study: the values for on page 16 are	The RMS has considered that the study of Berg 1994 is not valid to derive DT50. There is clearly an absence of degradation during the 2-4 first weeks of the experiment. The evolution of the a.s. and metabolites up to termination of the study is abnormal.	Point of clarification for the applicant: Regarding the studies by Theis (2003), Girkin (2003), Berg (1994a) and Berg (1994b): a) correctly classify the soils b) appropriately normalize the soils to soil moisture (e.g without normalization, where the soils were wet enough) and to temperature where necessary c) calculate the geometric mean values of the normalized DT_{50} values from the studies by Theis (2003) and Girkin (2003) d) calculate the geometric mean values of the normalized DT_{50} values considering all studies e) calculate the mean values of the kinetic formation fractions of the metabolites Before the normalization procedure and derivation of the mean values it should be considered that f) DT_{50} values for IN-KE121 for Sheringham and Wick soils might be corrected based on the open point for the comment 4(5) (rounding) g) DT_{50} and kinetic formation fraction for IN-KE121 from the

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)
		not correct and the values from page 8 should be used: Wolston 54.44 %*0.40 = 22.2 Grav.-%; Wick 37.9 %*0.40 = 15.2 Grav.-%; Whimple 77.46 %*0.40 = 31.0 Grav.-%; Sheringham 39.46 %*0.40 =15.8 Grav.-%. Since all four soils have been wetter than at reference condition no correction factor for water content is needed.		Theis study should not be used h) DT_{50} and kinetic formation fraction for the metabolites derived from the Whimle soil should be used (currently missing from the LoEP) Open point: MS experts to agree on the DT50 and kinetic formation fractions for use in FOCUS simulations (PECsw & PECgw) for lenacil, IN-KF313 and IN-KE121. See also comments in 4(5), 4(16), 4(28), 4(31), 4(29), 4(32), 4(35), 4(41), 4(47), 4(65) and 4(66).
4(14)	B.8.1.2, Rate of degradation (Annex IIA 7.1.1.2.1; Annex IIIA 9.1.1.1.1), B.8.1.2.1, Aerobic degradation	DE: Experts at PRAPeR to discuss whether to include or to exclude the studies from Berg (1994a) from risk assessment.	See above	Open point: Experts to discuss the validity of the studies by Berg 1994a and 1994b and the possible use of the results in the risk assessment. RMS to provide scientifically relevant details of the studies by Berg (1994a and 1994b) (e.g. preparation and storage of the soils, microbial biomass) in an addendum which can facilitate the discussion of experts about the validity of these studies. See also open point in 4(13); See comments for 4(23), 4(33), 4(34), 4(36) and 4(37).

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(15)	B.8.1.2, Rate of degradation (Annex IIA 7.1.1.2.1; Annex IIIA 9.1.1.1.1), B.8.1.2.1, Aerobic degradation	DE: RMS to consider if the study Belasco, J.: Microbial Degradation of 2-^{14}C-Lenacil in soil, Document No. LLME-2-79, 1979 would add valid information concerning lenacil or metabolites of lenacil.	The RMS has not to consider the published study of Belasco 1979.	Addressed Note: Germany, the commenter, confirmed that the study does not present more adverse findings.
4(16)	p.17 ff.: Metabolites IN-KF313 and IN-KE121	DE: Please check the correction factor for water content (see our comment (1)) and use the measured values from the study.	The correction factor will be checked.	See open point for 4(13).
4(17)	B.8.1.3, Field studies (Annex IIA 7.1.1.2.2; Annex IIIA 9.1.1.2), B.8.1.3.1, Soil dissipation testing	DE: Please provide information on the kinetical model used (SFO ??) and the assessment of goodness of fit (see FOCUS deg.Kin. 2006 page 80 ff.). The two German sites show a large p-value which could indicate that the model used is not appropriate and a different kinetic model should be used.	The field data were not used for the derivation of DT50 for modelling. Moreover, the RA for soil organisms is based on initial PEC.	Open point: RMS to provide information on the used kinetic model and the assessment of the goodness of fit for the field dissipation study in an addendum. Note: in the study description FOMC kinetic model is referred, however the ratio between the reported DT_{50} and DT_{90} values indicate SFO kinetics for all the 4 experiments. In the LoEP SFO kinetics are indicated, however the DT_{50} and DT_{90} values are not the same.
4(18)	B.8.1.3, Field studies (Annex IIA 7.1.1.2.2; Annex IIIA 9.1.1.2), B.8.1.3.1, Soil dissipation testing	DE: RMS to check if the study Brodsky, J.: Determination of Residues of Lenacil in Soil, treated with Venzar, season 1989, BE-A-11-90-10-BF, 1990 should be considered.	The RMS has not to evaluate studies that are not available in the dossier.	Addressed Note: Germany, the commenter, confirmed that the study does not present more adverse findings.

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(19)	Vol. 3, B.8, p 17 Summary and assessment of studies on route and rate of degradation in soil – rate of degradation	FR : Please, could you explain why the max field DT50 was not retained for the calculation of PECsoil for lenacil whereas the field dissipation study was considered acceptable.	The RMS considers that the long DT50 that has been observed in the study performed in Spain can be explained by the negligible degradation on a very dry soil during the 3 first months. The RMS considers that this study cannot be used to derive a meaningful DT50 for PEC assessment. The recalculation of the PEC soil with this DT50 is superfluous since the ecotoxicological risk assessment is based on the initial residue.	See open point for 4(21).
4(20)	Vol. 3, B.8, p 17 Table B.8.1.2.1-13 Summary and assessment of studies on route and rate of degradation in soil – rate of degradation	FR : Please, could you explain how the DT50 and kinetic fraction of IN-KF121 were calculated ? In the study of Theis (2003, speyer 2.2 soil) M14.0 and M15.0 are considered both to be IN-KF121. As a consequence, M14 and M15 should be added for the kinetic calculations. Could you please confirm if it was done are not ?	À voir avec le notifiant	See open points for 4(13) and 4(32).

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(21)	Vol. 3, B.8.1.3, p 21 Conclusions of the Field studies	FR: the RMS considered that the DT50 of 88 days can be considered as an outlier because the experiment was characterized hot soil temperature and almost no precipitation. These climatic conditions do not seem extreme for Spain and Southern Europe and have not to be considered as outlier. 26-31°C for soils seem to be reasonable for late spring-summer and 3 months with very low precipitation do not seem surprising. To consider such data as outlier, it should be explicitly compared to typical data. As a consequence, the DT50 of 88 days should be considered valid and should be used for risk assessment (PECsoil calculation at least).	See 4-19	Open point : MS to discuss in a meeting of expert whether the field experiment in Spain is considered as representative to European conditions and the DT_{50} of 88 days (alternatively 52 days) should be used or not for PECsoil calculations for lenacil. MS to discuss moreover the used application intervals, and that the PECsoil for the metabolites should be recalculated using the maximum observed instead of the kinetic formation fractions. See also comments for 4(19), 4(24), 4(30), 4(54), 4(55) and 4(56) and 4(64), point of clarification in 4(13).
4(22)	Vol. 3 B.8.1.3, field studies and LoEP	UK: There seems to be some inconsistency with DT50s listed for the field studies: values of 23 – 110 days listed in LoEP, whereas values of 18 – 88 days quoted in Vol 3.	The listing of endpoints has been amended.	See Open Point for 4(11). See also comment in 4(55).
4(23)	Vol 3 B.8.1.2.1, aerobic degradation in 3 soils	UK: The study by Berg (1994b) has been deemed invalid due to saturation of microbial processes. However, we consider that some evidence of this should be presented e.g. a range-finding study before the (longer) DT50s from this study are dismissed.	In the table B.8.1.2-2 (and on the graphs in the study report), no degradation has been detected during at least 14 days for the 3 soils. Considering the time constraints of the RMS, we consider that sufficient information is already available in the DAR to withdraw this study.	See Open Point for 4(14).

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(24)	Vol. 1, level 2, Chapter 2.5	NL: Max field DT50 is to be used for PECsoil. After leaving out the Spanish trial (DT50 88 days), this is the DT50 of French trial of 52 days. Check interval for multiple appl. lysimeter application may not be worst-case (this could be a single application of 500 g a.s./ha) NL: w/s: stated that only 1 major metabolite occurred, M20.5 (=IN-KF313). Later on also M15 is mentioned, which also seems to be major. Maybe just the phrasing needs revision (since from B8 only IN-KF313 appears to be major).	The max PEC for one application has been considered in the risk assessment for terrestrial organisms. 2 applications of 200 and 300 g as/ha have been done at 2 weeks interval. We consider that a single application or 2 applications at 2 weeks interval are similar in terms of concentrations in water after 1-4 years leaching. M15 is similar to IN-KE121	See Open Point for 4(11). See Open Point for 4(21).

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(25)	Vol. 3, B.8.1.1.1 and 8.1.2.1 (route and rate of degradation in soil)	NL: USA soils discarded partly because of high application rates, this explanation alone is not enough to leave these soils out, since for the 10 C study also a high application rate was used. So only the poor storage can be used as reason to discard these USA soils. Alternatively a remark could be made about the high application rate in the 10 C study. Comparison of lab and field DT50 values (page 8-16 and 8-17) (argumentation for use of lab values also for PECsoil) is not based on values given in LoEP. From the LoEP it appears that a value of 52 days should be used for PECsoil calculations (see remark (5)). Please check consistency. Degradation scheme (p 8-19) does not seem complete (major IN-KE 121 not presented).	The main argument to discard the study of Berg 1994 with USA soils is the fact that no degradation has been observed at days 0 to 14. This can be related to poor storage conditions There was a mistake in the listing of endpoints. The listing has been amended. M14.0, M15.0 is similar to IN-KE121	See Open Point for 4(14). See Open Point for 4(55). See Open Point for 4(21). See Open Point for 4(32). See also comment in 4(20)
4(26)	Vol. 3, B.8.1, aerobic degradation in soil	AT: classification error: soil type in table B.8.1.1.1-1 should be sandy loam and not loamy sand.	Soil type proposed in the original study report. This has no impact on the final outcome of the RA.	Addressed Notes: this has no impact on normalization. In the LoEP the classification of the soils are not indicated, however these should be included in the relevant boxes instead of the names of the soils. See also comment in 4(55).

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(27)	Vol. 3, B.8.1.2, Rate of degradation	AT: Only soils with pH < 7 were chosen	The RMS has considered that sufficient information is available on the degradation of lenacil in soil (lab and field data) and therefore requirement of additional data at higher pH is not necessary.	Open point: MS to discuss whether any requirement of additional data for the degradation of lenacil and its metabolites in soil at higher pH is necessary.
4(28)	Vol. 3, B.8.1.2, Rate of degradation	AT: p 8-8. classification errors – the soils types are not in USDA classification system; markings in the table (a and b) have no explanations.	Soil type proposed in the original study report. This has no impact on the final outcome of the RA.	See open point for comment 4(13). See also comment in 4(55). Note: errors in the soil classification can lead to errors in the normalization procedure.
4(29)	Vol. 3, B.8.1.2, Rate of degradation, p 8-16, Derivation of the DT_{50} soil used for the PEC calculations	AT: we consider the DT_{50} of 9.9 days an underestimation of the degradation of lenacil. Furthermore, calculations of arithmetic mean based on the 5 european soils did not provide DT_{50} of 9.9 days but of 10.6 days (based on table B.8.1.2.1-12). As well, arithmetic mean calculations of DT_{50} for metabolites were not consistent to the values from the notifier. And as mentioned by RMS, geometrical mean should be used.	The RMS will recheck the consistency of the listing of endpoints. However, these inconsistencies have no impact on the risk assessment.	See open point for comment 4(13). See also comments for 4(55), 4(65) and 4(66).

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(30)	Vol.3, B.8.1.3, Field studies	AT: p 8-21. DT_{50} of 88 days is considered by notifier and RMS as outlier since high soil temperature and low precipitations were recorded during the study. This value should be taken into consideration as worst case since such conditions are not exceptional for southern Europe.	The RMS considers that 3 months drought at early sugarbeet growth stages is not particularly favourable.	See open point for 4(21).

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(31)	General for Fate	EFSA: In the studies by Berg the used soils called Hillsdale and Sassafras are really similar, might could not be handled as two different soil types in the fate assessment. RMS is asked to check the organic carbon content of these soils (in the adsorption/desorption study much lower OC content is reported than values reported in the degradation studies. This inconsistency may come from that somewhere OC%, somewhere else OM% is reported, but it could lead incorrect Kfoc calculation). Moreover the MWHC values of these soils seem to be unrealistically low. Could RMS please clarify whether these soils used in different fate studies come from the same source and give it's view on the point raised in this comment? Moreover please clarify the organic carbon content of these soils and make re-calculations where necessary.	The RMS has checked the soil properties that were used in the degradation study and in the adsorption study when preparing the DAR.	Point of clarification for the applicant: To provide a table of OM% and OC% content, the maximum water holding capacity and the actual wet content (used in the degradation studies) for the soils used in all Berg studies (list references). See also point of clarification in 4(13) and open point in 4(47).

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(32)	Vol. 3, B.8.1, Route and rate of degradation Page 8-3	EFSA: RMS pls clarify how was DT50 value calculated for metabolite IN-KE121 from the Theis study as the identity of this metabolite is not seem to be confirmed. The text says that metabolites M14.0 and M15.0 were cyclohexanone derivatives - similar to IN-KE121, but it do not say that any metabolite is identical with IN-KE121 (in Appendix 2 of chapter B.8 M15.0 seems to be identical with IN-KE121, but this is not in line with the text or the figures B.8.1-1 and B.8.4.4-1). If neither M14.0, nor M15.0 is identical with metabolite IN-KE121 than DT_{50} of 2.7 d should not be used in the RA, but the leaching potential of M15.0 should be addressed as this metabolites reached > 5% AR at two consecutive sampling time.		Point of clarification to the applicant: Applicant to clearly clarify that the exact identity or structures of the metabolites M14.0 and M15.0 are not available (however their structure are similar to IN-KE121) and confirm that the metabolite IN-KE121 was identified to be 3-cyclohexyl-6,7-dihydro-7-1H-cyclo pentapyrimidine-2,4,5(3H)-trione. Clearly indicate moreover, where the position of metabolite IN-KE121 is in the degradation pathway in soil. See also comments in 4(20), 4(25) and 4(42). Open point: RMS to remove the DT_{50} of IN-KE121 for the Speyer soil from the LoEP. The PEC values for the metabolite IN-KE121 without using this DT_{50} or the formation fraction calculated from the Theis study might need to be recalculated. See also comments in 4(11). Open point: MS to discuss in a meeting of experts whether to address the leaching potential of M15.0 is necessary. See also comments in 4(20).

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(33)	Vol. 3, B.8.1, Route and rate of degradation Study by Berg, 1994a	EFSA: RMS please clarify how long were the soils stored before using them in the study and describe the storage conditions. Please clarify whether the microbiological viability was determined before/during/after the experiments and please give scientifically sound explanation whether the study should be used in the RA or not. Alternatively DT_{50}/DT_{90} could be calculated discarding the lag-phases. Please check whether really OC% is reported or the values refer to OM%. Moreover please confirm whether the values indicated in the Table B.8.1.2.1-1 are referring to the MWHC and not to the actual water content (e.g. at pF 2.5) as at least the value of 12.1% for Sassafras soil seems to be too low.	According to the study, the soils have been stored moist under refrigeration at 4°C for less than 90 days. It is however clear that no degradation occurred during at least 14 days. The RMS does not believe it is reasonable to „restore“ the study .	See OP for comment 4(14).

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(34)	Vol. 3, B.8.1, Route and rate of degradation Page 8-7, Table B.8.1.2.1-2	EFSA: The category „Other polars' seems to contain 1 to 3 peaks. Please indicate the amount of this/these products individually in terms of %AR, as many of the values in this column are >5%. If the individual amount of any of these compounds reaches > 5% AR at two consecutive time point, GW assessment may become necessary. Met.B is increasing at the end of the study therefore GW assessment may be necessary for this compound. Even if that this study is suffering from some shortcomings the exclusion of these metabolites from the residue definition might not been justified. RMS pls. argue why these compounds were not further assessed.	The RMS considers it is not feasible to base the evaluation of soil metabolites on a study without degradation during at least 14 days.	See open point for 4(36).

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(35)	Vol. 3, B.8.1, Route and rate of degradation Study by Girkin, R., 2003 Page 8-8	EFSA: In the description of the experimental design 40% of MWHC as moisture content is mentioned, but it is not consistent with the values indicated in the Table B.8.1.2.1-3 (16.19 17.17 8.92 21.60 14.81 are not the 40% of 55.01 54.44 37.90 77.46 39.46, respectively). Could RMS please clarify what was the actual water content used for each soils and what superscript a and b in this Table meant?		See open point for 4(13).
4(36)	Vol. 3, B.8.1, Route and rate of degradation Study by Girkin, R., 2003 Tables B.8.1.2.1-4 to B.8.1.2.1-8	EFSA: RMS please clarify whether the soil samples before the last sampling were taken at day 91 or 88 (DAA) and which was used for the kinetic calculations. RMS please clarify why Polar B was not further addressed as this degradation product appeared at a level >10% AR (also „Polars' in the test at 10°C) and/or >5% at two times.	91 or 88 days is clearly a point of detail with no impact on the final RA.	Point of clarification for the applicant: to clarify whether Polar B, Met.B, category „Polars' or „other polars' from the studies by Berg (1994a) and Girkin, R. (2003) contain any common transformation products. Open point: Experts to discuss whether further consideration of Polar B and „Polars' from the study by Girkin, R., 2003 and category „Other polars' and the Met.B from the study by Berg (1994a) is needed. See also comment 4(14) and 4(34).

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(37)	Vol. 3, B.8.1, Route and rate of degradation Study by Berg, 1994b	EFSA: RMS pls give details on the results of the analysis of the aliquots extracted from the soils. Please clarify whether was or not any metabolite found in these experiments and which values were used for DT50/DT90 calculations for the metabolite IN-FK313. Moreover pls clarify the same questions as asked for study by Berg, 1994a (storage etc.).	It can be clearly seen in the study report that the study is not valid.	See open point for 4(14).
4(38)	Vol. 3, B.8.1, Route and rate of degradation Table B.8.1.2.1-11 & LoEP	EFSA: Some DT_{90} values slightly differ in the LoEP compared with the table in the DAR.	The listing of endpoints will be amended.	See open point in 4(55).
4(39)	Vol. 3, B.8.1, Route and rate of degradation Page 8-17, Table B.8.1.2.1-13	EFSA: As no metabolites IN-KE121 was observed/identified in study by Theis no degradation rate and kinetic fraction could be derived. RMS pls. clarify how these values were derive.	Metabolites 14.0 and 15.0 have been considered similar to IN-KE121.	See open points in 4(13) and 4(32). See also comment 4(20).

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(40)	Vol. 3, B.8.1, Route and rate of degradation Page 8-17 to 8-18 Derivation of DT_{50} soil used for the PEC calculations, Metabolites	EFSA: RMS please clarify the statistical and visual assessment of the fit of the parent compounds and metabolites of the kinetic analysis for each experiment, where the formation fractions and degradation rates of the metabolites were calculated. Please confirm whether both metabolites were associated with the parent directly. RMS please clarify whether the arithmetic mean of the formation fractions were used in the PEC calculations.	The RMS will check this.	Open point: RMS to include the statistical and visual assessment of the fit of the parent compounds and metabolites of the kinetic analysis for each experiment, where the formation fractions and degradation rates of the metabolites were calculated in an addendum. See also open point in 4(32).
4(41)	Vol. 3, B.8.1, Route and rate of degradation Tables B.8.1.2.1-15 and B.8.1.2.1-16 & LoEP	EFSA: RMS please clarify why the DT_{50} values from the Whimle soils were leave out from the tables and did not used for the RA. However to incorporate these results into the RA might lead to „better case' situation.	The RMS will check this.	Open point: RMS to include the DT_{50} values from the Whimle soils in the LoEP. The PEC values using these DT_{50} values and the pertaining to formation fractions might need to be recalculated. See also open point 4(13).
4(42)	Vol. 3, B.8.1, Route and rate of degradation Page 8-19	EFSA: RMS pls include/mention Metabolite IN-KE121 in the Figure (B.8.1-1).	The metabolite M15.0 is similar to IN-KE121	See Point of clarification to the applicant for comment 4(32).

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(43)	Vol. 3, B.8.1.3 Field studies Pollmann, B., 2003	EFSA: In the calculation of dissipation rates for the German trials the half of the LOQ were used, however the half of the LOD should be used in the case when the measured value is below the LOD and the second value below the LOD should not been used. Where a value is below the LOQ, but above the LOD the actual vale should be used, which may be true for these cases. RMS pls. clarify what was the LOD in this study and what were the actual measured residue values. The repetition of the fitting and the re-calculation of DT_{50}/DT_{90} values as recommended by FOCUS Kinetic guideline might be necessary if the results from this study are used in the RA.	The RMS takes note of the remark. The RMS however believes that a new fitting would not dramatically change the final outcome.	Addressed. See also open points for 4(17) and 4(21).

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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(44)	Vol. 3, B.8.2.4, Lysimeter and Field Leaching Studies	Notifier: Typographical error, page 8-28, first paragraph, second sentence. Duplication of for.	The amendments will be done	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(45)	B.8.2, Adsorption, desorption and mobility in soil (Annex IIA 7.1.2 and 7.1.3; Annex IIIA 9.1.2), B.8.2.1, Adsorption and desorption of the active substance and relevant metabolites (Annex IIA 7.1.2), Batch Equilibrium (Adsorption/Desorption) Study with IN-KF313 (Berg, D. S., 1996c)	DE: The metabolite IN-KF313 shows no correlation between Kf and OC-content but does show correlation between Kf and all three: pH, CEC and clay content. Please use worst case assumptions such as 10th percentile of 218 in the risk assessment.	According to the directive 91/414, the Koc of metabolites must be determined for 3 soils. The RMS does not understand how correlation/ absence of correlation has been determined between Kf, pH, CEC and clay content. The use of a worst case assumption seems arbitrary.	See open point in 4(47).
4(46)	Vol.3, B.8, p22 Adsoprtion/desorption studies	FR : Please, could you indicate if the preliminary test to determine the adsorption of the test substance on the surface of the test vessels was carried out and what the results were.	The information is available in the study report.	Open point: RMS to include information about the preliminary test to determine the adsorption of the test substance on the surface of the test vessels and its results.

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(47)	Vol.3, B.8, p24, Table B.8.2.1-5 Adsoprtion/desorption study	FR : In the adsorption study of IN-KF313 (Berg, 1996), the pH values lay in the small range of 6.3 to 6.8. Additionally, the Sassafras soil and the Hillsdale soil are very similar in texture, OC and CEC. We do not believe that these two soils should be considered different. Finally, the Kfoc values obtained for Tama (79 l/kg) and the values obtained for Sassafras and Hillsdale (823.8 and 769 l/kg) suggest that there may be a dependence of the adsorption to one soil parameter. However, with only 2 real different soils, such relation can only be suspected. We think that additional adsorption data are needed.	The RMS considers that no new adsorption study is necessary (short DT50, not present in the lysimeter)	Open point: In relation of the adsoprtion/desorption study of the metabolite IN-KF313 (Berg, D. S., 1996c), MS to discuss in a meeting of experts: a) similarity of Sassafras and Hillsdale soils b) narrow range of the pH of the used soils c) dependence of the adsorption to any soil parameter (pH, CEC, clay) d) to use the arithmetic mean or the (any) worst case K_{Foc} value for PEC calculations, and/or e) the need of additional adsorption data Open point: MS experts to agree on the K_{Foc} and 1/n values for use in FOCUS simulations for lenacil, IN-KF313 and IN-KE121. See also comments 4(31), 4(45), 4(52) and 4(66).
4(48)	Vol. 1 level 3 proposed decision	NL: In principle agreed but see comments on lysimeter study.	No comment	Addressed. See also open point for 4(50).

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(49)	Vol. 1 level 4 data requirements	NL: More data on unidentified lysimeter metabolites are considered necessary (either fate – e.g., substance properties- or ecotox data – e.g., toxicity studies with lysimeter leachates)	The 3 unknown metabolites are polar compounds. The RMS considers that they have been appropriately assessed .	See open point for 4(50).
4(50)	Vol. 3, B.8.2.4 Lysimeter studies	NL: Although efforts have already been made to identify M1, M2 and M3, we still think that more information is required, since these metabolites (or molecule fragments) show a high potential for leaching.	The 3 unknown metabolites are polar compounds. The RMS considers that they have been appropriately assessed .	Open point: MS to discuss in a meeting of experts whether there is a need for further information for the unidentified lysimeter metabolites M1, M2 and M3 for the EU level assessment. See also comment in 4(49).
4(51)	Vol.3, B.8.2.1 Adsorption and desorption of the active substance and relevant metabolites	AT: table 8.2.1-3, classification error – the soil types are not in USDA classification system	The contribution of each soil constituent is given in the table.	Open point: RMS to check the classification of the soils used in the adsoprtion/desorption studies and change the names of the soils with the soil types based on the USDA classification system in the relevant boxes of the LoEP.
4(52)	Vol. 3, B.8.2.1, Adsorption, desorption and mobility Berg, D. S., 1996c	EFSA: The soils Hillsdale and Sassafras used in this study are really similar based on the reported parameters. Moreover the pH range of the applied soils is narrow.	See comment 4(47)	See open point for 4(47).
4(53)	Vol. 3, B.8.2.1, Adsorption, desorption and mobility Kane, T., 2004	EFSA: The soil Elmton has a $CaCO_3$ content of 263.1 g/kg reported. Is this correct?	This value is reported in the Tier. This point can be checked with the notifier	Point of clarification for the applicant: to clarify whether is it correct that the Elmton soil in the study by Kane, T., 2004 had a $CaCO_3$ content of 263.1 g/kg.

Rapporteur: BE

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(54)	Vol.3, B.8, p 31 PECsoil	FR : PECsoil metabolites were calculated with formation fraction and not with maximal measured percentage in soil. This is not the recommended approach but can be considered as conservative for risk assessment.	The RMS takes note of the remark.	See open point for 4(21).
4(55)	Vol. 1 level 2 LoEP	NL: Route of degradation: please state temperature of study also for max. formed metabolites. Rate of degradation (lab): please indicate soil type (i.e. texture) in designated column for soil type, not (only) location. DT50 field non-normalised range from 23-110 days, while in Vol. 1 level 2 a DT50 field of 18-88 is mentioned. Were these normalised? If so then why does LoEP state that normalisation is not done. PECsoil: we disagree with the chosen max DT50 lab, instead non-normalised max field (52 days when Spanish trial is considered outlier) should be used. This does not affect the initial PEC for the single application, however (but does affect all other PECs). So, if this is the PEC used for TER calculation	The studies have been performed at 20°C The TER for soil organisms are based on the initial PEC soil. The structure of the metabolites is given at the end of the endpoints list. It is recommended to check the structure before indicating that the molecular weights are different. The consistency of the LoEP will be checked.	Open point: RMS to amend the LoEP taking into consideration all the inconsistency identified in the reporting table. RMS to highlight all the changes in the LoEP with a colour (yellow is already proposed by the RMS for changes in February 2009) as part of the track changes procedure. See also open point in 4(21). See also comments in 4(8), 4(9), 4(10), 4(11), 4(12), 4(22), 4(25), 4(26), 4(28), 4(38), 4(41), 4(51), 4(62) and 4(66).

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)
		then the ecotox RA does not change. Both metabolites are given the same molecular weight ((boxes method of calculation), this appears to be unlikely, please check. See also box PECsw/sed. PECsw/sed: the (geo)mean DT50system should have been used for the sediment compartment (instead of worst-case). RA is conservative and acceptable. PECgw: in Vol 1 it is stated that calculations were based on arithmetic mean DT50 values, in LoEP it states geomean (for the same values). Please mind consistency.		
4(56)	Vol.3, B.8.3 Predicted environmental concentration in soil	AT: Worst case from field studies should be used – 88 days, and maximum appearance should be used for metabolites and not the formation fraction.	This change would have no impact on the final outcome of the ecotox RA. The initial PECsoil have been used.	See open point for 4(21).

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(57)	Vol. 3, B.8.4.4, Water Sediment Study	Notifier: Typographical error, page 8-37, experimental design, first paragraph, first sentence. With and height are spelled incorrectly.	These errors will be checked	Addressed
4(58)	Vol. 3, B.8.4.5, Degradation in the Saturated Zone	Notifier: Typographical error, page 8-43, first sentence. The word no should be deleted.	These errors will be checked	Addressed
4(59)	Vol. 1, 2.5.3, Fate and Behaviour in Water	Notifier: Page 32, second paragraph, fourth sentence. To give the correct meaning to the sentence, the word „this' should be replaced by IN-KF313.	These errors will be checked	Addressed
4(60)	Vol. 3, B.8.4.4 Water/sediment study	EFSA: Please clarify when the experimental samplings were taken as this information is not perfectly clear from the text especially when compared with the heading of the tables (B.8.4.4-2 and B.8.4.4-3) and check whether the correct time points were used for the kinetic calculations. Moreover please clarify what is the difference between Recovery (mean) and Total recovery (mean) in the Tables B.8.4.4-2 and B.8.4.4-3.	Differences of one day in the sampling time has no impact on the kinetic evaluation. The first row "recovery (mean)" is the sum of water and sediment AR The second row is the mean of all the samplings points. This row is not useful and can be deleted.	Addressed Note: any error in the sampling time used in the kinetic evaluation has an impact on the outcome. Some sampling points in the tables of the DAR are inaccurately indicated.

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(61)	Vol.3, B.8, p 44 Table B.8.6.1-1 PECgw	FR : The water solubility of metabolites were defined by EPIWIN estimation and not with a laboratory study.	The RMS has considered this approach in the case of lenacil metabolites	Addressed
4(62)	Vol.3, B.8, p 44 Table B.8.6.1-1 PECgw, PECsw	FR: The geomean DT50 of the total system was applied to the sediment phase and a DT50 of 1000 days was used for the water phase as default value. From the experimental data (Table B.8.4.4-2 and B.8.4.4-3), the opposite might be also possible (i.e., degradation of lenacil happened in the water phase). It may be worthwhile to additionally calculate PECsw and PECsed with this option to evaluate the impact on the aquatic risk assessment.	The RMS considers that additional PEC calculations are not required.	Open point: MS to discuss in a meeting of experts whether additional PECsw and PECsed calculation is needed or not with the option of DT50 of 1000 days for the sediment phase and geomean DT50 of the total system for the water phase. See also open point 4(13). See also comment in 4(55).
4(63)	Vol.3, B.8, p 67 PECsw	FR : A step 4 to refine the aquatic assessment for drift should be carried out. See the ecotox comment 5(6).	Acceptable TER aquatic organisms have been calculated considering the Focus step 3 PEC.	Addressed Note: pending on the discussion on ecotoxicology, it is not excluded that there will be a need for further refinement of the risk assessment using FOCUS step 4 calculations.
4(64)	Vol 3 B.8.3, B.8.6, PEC in soil, groundwater and surface water (and LoEP)	UK: It is unclear why DT50s from field studies were not considered for use as input values for PECs, PECsw and PECgw.	It is generally recognized that lab data are preferred as input since they are only taking into account the intrinsic degradation.	Addressed See open point for 4(21). Note: for PECsoil the preferred input is rather field data.
4(65)	Vol 3 B.8.3, B.8.6, PEC in soil, groundwater and surface water (and LoEP)	UK: We consider that the chosen DT50 value of 9.9 days may under-estimate the degradation time for lenacil hence potentially under-estimating PECs, PECsw and PECgw	The RMS has indicated that PEC calculated with a DT50 of 9.9 or 10.25 would give similar results.	See open point in 4(13).

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(66)	Vol. 3, B.8.6.1 PEC groundwater and surface water Table B.8.6.1	EFSA: DT_{50} values used for PEC GW and SW calculations are neither the arithmetic mean nor the geomean (or median) values based on the considered dataset by the RMS (and all of them are shorter than the geomean). As the pH range of the soils used for the determination of adsorption/desorption for the metabolite IN-KF313 was narrow and two soils from the three were really similar to each other the worst case Kfoc value of 79 and 1/n of 1 should arguably be used for the calculations (or additional data would be needed). The same MW was used for the two metabolites, which might be correct, but should be confirmed/re-checked. As the present calculation may underestimate the risk for GW and SW (at least for GW in the case of the metabolite IN-KF313) re-calculation might become necessary.	The RMS considers that the results of the PECgw assessment and the results of the lysimeter study indicate that the contamination of groundwater by the a.s. or its metabolites IN-KF313 and IN-KE121 is limited. It is however up to EFSA to request new data and new PEC assessements.	See open point in 4(13). See also comments in 4(29), 4(47), 4(52), 4(55) and 4(65).

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(67)	Vol. 3, B.8.6.1 PEC groundwater and surface water Table B.8.6.1	EFSA: RMS pls clarify whether or not the calculated crop washoff factor was used only for SW calculations and please confirm that the crop half-life was not changed for the modelling. The change on crop washoff factor should be indicated in the relevant part of the LoEP.	This factor has certainly low impact on the final outcome of the PEC.	Open point: RMS to indicate in the LoEP the washoff factor used in the FOCUS calculations. Open point: RMS to clarify that the crop washoff factor was used only for SW calculations or for the GW calculations as well and that whether the crop half-life was or was not changed for the modelling in an addendum.
4(68)	Vol. 3, B.8.10 References relied on	EFSA: If the RMS belives that the studies by Berg (Berg, D. S. 1994a and Berg, D. S. 1994b) are not relied on they should be removed from the list of References relied on.	The study will be removed from the listing of endpoints	Open point: The studies by Berg (Berg, D. S. 1994a and Berg, D. S. 1994b) should be removed from the list of references relied on depending on the discussions on the validity of these studies during the peer review. See reporting table comment in 4(14).

Fate and behaviour in air and PEC in air (B.8.7-8.8)				
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)

Definition of the residues (B.8.9)				
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)
4(69)	Vol. 1, 2.5.1, Definition of the Residue Relevant to the Environment	Notifier: Justification for non-inclusion of IN-KE121 in the definition of the residue is presented in Vol 3, B.8.10. For completeness the justification in Vol 3 should be reproduced under Vol 1, 2.5.1.	We take note of the comment	Addressed.

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.9.1.2, Avian dietary toxicity test	FR: It would have been easier to agree with the RMS conclusion if the abstract of the study would have been more detailed, especially concerning the weight of birds.	**RMS (February 2009) :** There was a typing error, the calculation is based on a mean body weight of 26.2 g and a mean food consumption of 5.7 g/bird/day. The raw data have been inserted in the updated DAR.	Addressed
5(2)	B.9.1.8, Summary of effects on birds	NL: In the first sentence below table B.9.1.8-1 is mentioned: "The risk assessment for mammals….". „Mammals' should be „birds'.	**RMS (February 2009) :** This is corrected in the updated DAR.	Addressed
5(3)	B.9.1.8, Summary of effects on birds	NL: In table B.9.1.8-3 are a few mistakes: - „mall' should be „small'; - no value for ftwa should be mentioned for the long-term exposure because it concerns insects (in the table a value of 0.53 is mentioned). The value of the ETE is right.	**RMS (February 2009) :** This is corrected in the updated DAR.	Addressed
5(4)	Vol. 3, B.9.1.8 Summary of effects on birds – exposure and risk assessment for birds Table B.9.1.8-3	AT: To avoid misunderstandings the f_{twa} of 0.53 which is stated in the table should be deleted as it will not be used to calculate the long-term ETE for insectivorous birds.	**RMS (February 2009) :** Please refer to comment 5(3).	Addressed

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(5)	Vol. 3, B.9.1.2, Avian dietary toxicity	EFSA: The RMS states that LC_{50} was converted to daily dose based on mean bw of 5.7 g/bird but the mean weight at the start was 13.0-14.0 g. Could you please clarify? It would be more transparent to have raw data (i.e tables with the body weight and food consumption during the test)	**RMS (February 2009) :** Please refer to comment 5(1).	Addressed
5(6)	Vol. 3, B.9.1.3, Avian reproduction toxicity	EFSA: the raw data should be reported for causes of transparency (i.e tables with the body weight and food consumption during the test).	**RMS (February 2009) :** The raw data have been inserted in the updated DAR.	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.9.2.12, Effects on primary productivity and macrophyte biomass in field-based microcosms, B.9.2.16, Exposure and risk assessment for aquatic organisms	DE: We agree with the use of a NOEAEC of 22.1 µg as/L from the microcosm study by Jenkins (2005) for risk assessment. However an assessment factor of 3 as proposed by the RMS cannot be supported. We would propose the use of an assessment factor of five instead (see argumentation in column 3). The outcome of the risk assessment would change for 4 x 0.125 kg as/ha but risk would still be manageable by slight risk mitigation measures.	**RMS (February 2009) :** The report of the microcosm study (Jenkins C.A, 2005) has been revised, taking into account the comments raised in the reporting table. Some essential raw data have been added to the study summary in the updated DAR. An overall NOEAEC = 22.1 µg a.s./L was established. A NOEC of 22.1 µg a.s./L or higher has been defined for periphyton, phytoplankton, zooplankton and 10 out of 12 macrophyte species. A NOEAEC of 22.1 µg a.s./L has been determined for *Elodea canadensis*. Charophyta was the only macrophyte species with a NOEC < 0.4 µg a.s./L. RMS considers that setting the NOEAEC at 5.81 or 0.4 µg a.s./L is not appropriate since the functioning of the mesocosm is not impaired at 22.1 µg a.s./L.	Open Point 5.1 B.9.2.12, Effects on primary productivity and macrophyte biomass in field-based microcosms, (Jenkins, 2005). Several uncertainties (is not clear where the study was conducted, results of statistical analysis are not presented, the study was performed with a single application) can be observed in the outdoor microcosm study. Furthermore, some MS did not agree with the NOEAEC = 22.1 µg a.s./L, proposed by the RMS considering that at this endpoint it was noted that there were effects on *Elodea canadensis* and Charophyta. The endpoint for the microcosm study (Jenkins, 2005) as well as the assessment factor to be applied should be discussed by the MS experts in a meeting.
5(8)	Vol.3, B.9.2.8, Effects on algae	FR: It would have been more convenient to read the results of algae tests if they would have been presented in tables, instead of text.	**RMS (February 2009) :** The results were presented in tables in the updated DAR.	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(9)	Vol.3, B.9.2.8, Test on *P. subcapitata*, page 9-18	FR: In the study from Douglas and Handley (1988), is the E_rC_{50} really measured between 24 and 48 hours? Why is it not calculated at 72 hours? As long as no analytical measurement was conducted during the test, this study can not be accepted. It can only be considered as supporting data because it confirms results obtained in other tests. Therefore, values obtained should be deleted from the LoEP in vol.1.	**RMS (February 2009) :** RMS confirms that the E_rC_{50} is calculated for the period 24-48 hours. No further explanation is given in the study why it was calculated as such and not for the period 0-72 hours. The endpoints are in close agreement with the study of Flatman D., 2003c and are not deleted from the list of endpoints.	Open point 5.2 B.9.2 Effects on aquatic organisms, B.9.2.8 Effects on algae. The study by Douglas M.T. and Handley J.W., 1988 is regarded as not acceptable and should only be used as additional information. The endpoints of this study should be deleted from the list of endpoint by the RMS.
5(10)	Vol.3, B.9.2.11, Test on algae with the preparation, page 9-22	FR: As long as no analytical measurement was conducted during the test, this study can not be accepted. It can only be considered as supporting data because it confirms results obtained in other tests. Moreover, toxicity is in the same range as of the active substance itself. Therefore, values obtained should be deleted from the LoEP in vol.1.	**RMS (February 2009) :** Three studies with *Pseudokirchneriella subcapitata* were conducted (Flatman D., 2003c; Douglas M.T. and Handley J.W., 1988; Douglas M.T. and Halls R.W.S., 1993), leading to similar endpoints. Moreover, a microcosm study (Jenkins C.A., 2005) is available. The effects of lenacil on algae are investigated. The endpoint is acceptable and therefore not deleted from the list of endpoints.	See open point 5.6
5(11)	Vol.3, B.9.2.12, Microcosm study (Jenkins, 2005)	FR: We have several comments on this study: - PRC: the NOAEC proposed can not be retained because a recovery was observed for phytoplankton after 8 weeks, when lenacil can be applied up to 4 times a year with a maximum	**RMS (February 2009) :** Please refer to comment 5(7).	See open point 5.1

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)
		interval of 14 days. Only the NOEC of 22.1 µg a.s./L can be considered. - Concentrations: as long as initial measured concentrations were much lower than the nominal, even 3 hours after treatment, the endpoints have to be based on these initial measured concentrations, and not on the nominal ones. - General NOAEC: two species are more sensitive than the proposed NOAEC: Elodea Canadensis (NOEC = 5.81 µg a.s./L) and Charophyta (NOEC < 0.4 µg a.s./L), both expressed as nominal concentrations. Due to the very high sensitivity of Charophyta, and because only one treatment was applied to the microcosm, a global NOAEC can not ignore effects observed on these taxa. We then propose to use a NOEC based on the measured concentration of the lowest nominal one, i.e. 0.13 µg a.s./L.		

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, Risk assessment for aquatic organisms, Point 5 Risk refinement for algae and plants	FR: Considering our previous comment, we propose to assess the refined risk to algae and aquatic plants using a NOEC of 0.13 µ a.s./L. The trigger value could be 3, as proposed by the RMS, because of the uncertainty on possible effects on these species that could occur after 4 treatments with 14 days interval and which are not covered by this study. With this endpoint modification, it is quite sure that there will be a need for further refinement of the risk assessment for algae and aquatic plants using Focus step 4 calculations.	**RMS (February 2009) :** Please refer to comment 5(7).	See open point 5.1
5(13)	Vol.1, LoEP, Effects on algae	FR: The first test on *P. subcapitata* was conducted during 96h, but the endpoints are reported for 72h. This should be mentioned in the table.	**RMS (February 2009) :** The list of endpoints has been amended.	Addressed
5(14)	Vol.1, LoEP, Effects on algae	FR: As long as the second test on *P. subcapitata* is not valid (see comment no 5(9)), the results should be removed from the LoEP.	**RMS (February 2009) :** Please refer to comment 5(9).	See open point 5.2
5(15)	Vol.1, LoEP, Effects on algae	FR: As long as the test on *P. subcapitata* with the preparation is not valid (see comment no 5(10)), the results should be removed from the LoEP.	**RMS (February 2009) :** Please refer to comment 5(10).	See open point 5.6

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(16)	Vol.1, LoEP, Microcosm study	FR: Considering comments no 5(11) and 5(12), the endpoint related to the microcosm study and the risk assessment for algae and aquatic plants should be modified.	**RMS (February 2009) :** Please refer to comment 5(11) and 5(12).	See open point 5.1
5(17)	Vol 3, B.9.2.16, risk assessment for aquatic organisms	UK: the acute and chronic risk to fish and aquatic invertebrates is acceptable; there is a potentially high risk to algae and aquatic plants and all first tier TERs at FOCUS Step 3 are below the appropriate Annex VI trigger value. It is noted that higher tier data that assessed the impact of lenacil on algae and aquatic plants has been submitted and assessed. One study assessed the impact of lenacil on macrophyte biomass following simulated spray drift contamination. The other study assessed the impact on primary productivity and macrophyte biomass in a microcosm. It would appear that on the basis of these data the proposed endpoint is 22.1 ug/l and that an uncertainty factor of 3 is proposed, resulting in a regulatory concentration of 7.4 ug/l. On this basis „safe' uses can be predicted in relevant scenarios. At the proposed endpoint of 22.1 ug/L it is noted that there were effects on Elodea and Charophyta in the microcosm study, whilst the NOEC for Elodea from the spray drift study was 10	**RMS (February 2009) :** Please refer to comment 5(7) and 5(29).	See open point 5.1

Aquatic organisms (B. 9.2)				
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		ug/L. On this basis, it is questioned whether the endpoint is sufficiently protective for Elodea. It is proposed that these two studies should be discussed at an Expert meeting.		
5(18)	B.9.2.12 Microcosm and mesocosm study	NL: It is concluded by the RMS that the overall NOAEC = 22.1 µg as/L, covering most of the species examined. NL does not agree with this endpoint. All species must be covered. The NOEAEC for *Elodea Canadensis* was 5.81 µg as/L. Significant, immediate impact on abundance and health was evident at the two higher treatments on days 7 and 14, without recovery within 8 weeks. Hence, NL is of the opinion that the NOEAEC of 5.81 µg as/L should be a better endpoint of the mesocosm study. However, the NOEC for *Charophyta* is even lower than the lowest dose (< 0.4 µg as/L). This is simply ignored by the RMS. Are there explanations why this species seems to be so sensitive? Dependent on the explanation this can lead to an even lower endpoint of the mesocosm study.	**RMS (February 2009) :** Please refer to comment 5(7).	See open point 5.1
5(19)	B.9.2.16 Exposure and risk assessment for aquatic organisms	NL: Default crop relevant buffer distances are mentioned for ditches, streams and ponds. If these are the standard buffer zones in the FOCUS scenarios they don't have to be mentioned here explicitly.	**RMS (February 2009) :** No comment.	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(20)	B.9.2.16 Exposure and risk assessment for aquatic organisms; 4-Risk assessment for aquatic plants	NL: As already stated NL is of the opinion that the NOEAEC of 5.81 µg as/L is a better endpoint of the mesocosm study. But then the effects at even the lowest dose for *Charophyta* must be explained in a sufficient way. Normally a safety factor of 3 is applied on the NOEAEC. But dependent on the explanation regarding the effects on *Charophyta* the endpoint may be even lower. It may be important to compare the FOCUS exposure profile with the toxicity profile, as described in a publication of Boesten et al. (Conceptual model for improving the link between exposure and effects in the aquatic risk assessment of pesticides. Ecotoxicology and Environmental safety, 2006) and also discussed in the Elink-workshops.	**RMS (February 2009) :** Please refer to comment 5(7).	See open point 5.1
5(21)	B.9.2.16 Exposure and risk assessment for aquatic organisms; 4-Risk assessment for aquatic plants	NL: In the last sentence of this paragraph a buffer zone is mentioned. But this is the default buffer zone for the pond scenario. For the other scenario's different default buffer zones are valid. If it are just default buffer zones it is not necessary to mention them here explicitly.	**RMS (February 2009) :** No comment.	Addressed
5(22)	List of endpoints	NL: Mesocosm test aquatic organisms: the NOEAEC of 5.81 µg as/L for *Elodea Canadensis* is not mentioned in the LoEP. NL does not agree with the NOEAEC of	**RMS (February 2009) :** Please refer to comment 5(20).	See open point 5.1

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)
		22.1 µg as/L. All of the species must be covered. See also point 5(18) and 5(20) of the afore mentioned comments.		
5(23)	Vol. 3, B.9.2 Effects on aquatic organisms, B.9.2.8 Effects on algae	AT: The study by Douglas M.T. and Handley J.W., 1988 is regarded as not acceptable and should only be used as additional information. Therefore we are of the opinion that the endpoint of this study should not be stated in the LoEP.	**RMS (February 2009) :** Please refer to comment 5(9).	See open point 5.2
5(24)	Vol. 3, B.9.2.16 Exposure and risk assessment for aquatic organisms	AT: The risk assessment based on the NOAEC derived from the mesocosm study should be discussed. On the one hand the used NOAEC of 22.1 µg a.s./L should be discussed regarding the effects on *Elodea sp.* (NOEC = 5.81 µg/L) and Charophyta (NOEC < 0.4 µg/L) and on the other hand the safety of factor of 3 should be questioned (regarding missing analysis of abundance and diversity of phytoplankton, application rate and potential of recovery).	**RMS (February 2009) :** Please refer to comment 5(7).	See open point 5.1
5(25)	Vol. 3, B.9.2.8, effects on algae, *Navicula pelliculosa* study	EFSA: in the “Flatman D., 2003b” study only the measured concentrations are reported. It is not clear which nominal concentrations were applied as well as the difference between the nominal and the measured concentrations.	**RMS (February 2009) :** Serial dilutions were made of a nominal concentration of 10 mg a.s./L, with a recovery in the range of 4.68 – 5.79 %. The results are based on mean measured concentrations. More details are presented in the updated DAR.	Open point 5.3 B.9.2.8, effects on algae, *Navicula pelliculosa* study. According to guidance SANCO/3268/2001 if the measured concentrations are very low compared to the nominal the validity of the test might be questionable. MS to discuss in an expert meeting the

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)
				acceptability of Flatman D., 2003b" study.
5(26)	Vol. 3, B.9.2.8, effects on algae, *Selenastrum capricornutum* study	EFSA: in the "Flatman D., 2003c" study only the measured concentrations are reported. It is not clear which nominal concentrations were applied as well as the difference between the nominal and the measured concentrations.	**RMS (February 2009) :** Serial dilutions were made of a nominal concentration of 10 mg a.s./L, with a recovery in the range of 33 – 41 %. The results are based on mean measured concentrations. More details are presented in the updated DAR.	Open point 5.4 B.9.2.8, effects on algae, *Selenastrum capricornutum* study. According to guidance SANCO/3268/2001 if the measured concentrations are very low compared to the nominal the validity of the test might be questionable. MS to discuss in an expert meeting the acceptability of Flatman D., 2003c" study.
5(27)	Vol. 3, B.9.2.10, effects on aquatic plants, *Lemna* study	EFSA: in the "Flatman D., 2003d" study only the measured concentrations are reported. It is not clear which nominal concentrations were applied as well as the difference between the nominal and the measured concentrations.	**RMS (February 2009) :** Serial dilutions were made of a nominal concentration of 10 mg a.s./L, with a recovery in the range of 37 – 44 %. The results are based on mean measured concentrations. More details are presented in the updated DAR.	Open point 5.5 B.9.2.10, effects on aquatic plants, *Lemna* study. According to guidance SANCO/3268/2001 if the measured concentrations are very low compared to the nominal the validity of the test might be questionable. MS to discuss in an expert meeting the acceptability of Flatman D., 2003d" study.

Aquatic organisms (B. 9.2)				
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5(28)	Vol. 3, B.9.2.11, acute toxicity of the preparation, *Selenastrum capricornutum* study	EFSA: Since the study was not acceptable, it cannot be used in risk assessment. It should be deleted from the LoE and from the list of studies relied on. A new valid study could be useful to address potential highest sensitivity of algae to the formulation with respect to the active ingredient. According to the available data, algae and aquatic plants drive the risk assessment. The submitted higher tier studies address particularly the effects on aquatic plants. Therefore if algae are more sensitive the available data could be not sufficient to address the risk to algae.	**RMS (February 2009) :** Please refer to comment 5(10) and 5(15).	Open point 5.6 Vol. 3, B.9.2.11, acute toxicity of the preparation, *Selenastrum capricornutum* study. The validity of the study should be discussed by the experts in a PRAPeR meeting.
5(29)	Vol. 3, B.9.2.12, aquatic organisms, microcosm and mesocosm study (Taylor S.A., 2004)	EFSA: The RMS states that the "Taylor S.A., 2004" study is not acceptable. Was the study not accepted because the concentrations were not determined analytically? This study confirms the highest sensitivity of *Elodea canadensis* observed in the outdoor microcosm study (Jenkins C.A., 2005). Therefore, the study could be useful to cover uncertainties observed in such outdoor microcosm study (see related EFSA comment). Could the RMS please re-evaluate the acceptability of the study?	**RMS (February 2009) :** As indicated in the DAR, only four macrophyte species were tested in a laboratory microcosm test. Since an outdoor, more elaborated microcosm study (Jenkins C.A., 2005) is available, RMS decided to base the risk assessment on the last one.	Open point 5.7 B.9.2.12, aquatic organisms, microcosm and mesocosm study (Taylor S.A., 2004). The acceptability of the (Taylor S.A. 2004) should be discussed in an experts meeting.
5(30)	Vol. 3, B.9.2.12, aquatic	EFSA: several uncertainties can be observed	**RMS (February 2009) :**	See open point 5.1

Aquatic organisms (B. 9.2)				
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	organisms, microcosm and mesocosm study (Jenkins C.A., 2005)	in the outdoor microcosm study (Jenkins C.A., 2005). From the summary reported in DAR, it is not clear where the study was conducted. Could the study be considered acceptable for both the northern and southern EU intended uses? (The sunlight is a limiting factor for macrophyte growth). The results of the statistical analysis of the different parameters are not reported (i.e. PRC). Could the influence on growth rate/abundance of other limiting factors (for instance O_2, Nitrate, sulphate, phosphates) be excluded? It would be better to have the results of the additional water chemistry analysis. The study was performed with a single application. Could a single application be considered to cover the intended uses (1 to 4 applications, 7 to 14 days interval)? How could be explained the presence in the study of the species reported under the paragraph "*other macrophytes species*" at page 9-31? Could the observations related to these species be considered reliable? One of the most sensitive species (*Charophyita*) belongs to this group, thus it would be better to have more details.	Please refer to comment 5(7).	

Aquatic organisms (B. 9.2)				
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		In general, it would be appreciated to have a more detailed summary with all the necessary raw data .		

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(31)	B.9.4.8 Exposure and risk assessment for bees	NL: In the last sentence it is mentioned that sugar/fodder beets are non-flowering crops. This is true, but it is no argument for low risk to bees, because flowering weeds may also be an attractive source for bees.	**RMS (February 2009) :** Lenacil is an herbicide, therefore no weeds will be present in the field.	Addressed
5(32)	Vol. 3, B.9.4.1, Acute toxicity to bees	EFSA: RMS states that the acute oral toxicity study of Hoxter K.A. *et al* 1994a, is not acceptable because the endpoint is not expressed in µg a.s./bee. Anyhow, it would be better to report the study result (i.e. the resulted endpoint).	**RMS (February 2009) :** LC_{50} oral (*Apis mellifera*, 48 h) > 1000 mg a.s./L NOEC oral (*Apis mellifera*, 48 h) = 1000 mg a.s./L However, no information was given in the study on the actual amount of honey, containing the test substance, that was consumed by the bees. Therefore, RMS does not accept the study results, whether it is expressed in mg a.s./L or µg a.s./bee. More details are presented in the updated DAR.	addressed
5(33)	Vol.3, B.9.5.4 Summary of effects, exposure and risk assessment for non-target terrestrial arthropods	AT: The HQ-approach is only validated for *Aphidius rhopalosiphi* and *Typhlodromus pyri*. Therefore, it should not be used for the risk assessment of *Chrysoperla carnea* and *Aleochara bilineata*.	**RMS (February 2009) :** Noted. The risk assessment for *Chrysoperla carnea* and *Aleochara bilineata* is amended accordingly.	Addressed

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(34)	Vol.1, List of Endpoints, Effects on other arthropod species	AT: HQ values of *Aleochara bilineata* and *Chrysoperla carnea* should not be listed in the LoEP (see above).	**RMS (February 2009) :** Noted. The list of endpoints has been amended accordingly.	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(35)	Vol.3, B.9.6.4, Subchronic effects on earthworms	FR: It is surprising that the effect on earthworm reproduction at the application rate of 32 kg a.s./ha is not significantly different from the control, with an inhibition of reproduction around 20%. There is no information in the text about the statistical test used in this study. Could the RMS complete the abstract and confirm that an inhibition of reproduction of 20% is not significant? This has to be checked also for the other application rates, as a dose-response is not clear in this test.	**RMS (February 2009) :** For the number of offspring, the Dunnett's test was performed to compare the treated groups with the control. No statistically significant results were found. The coefficient of variation of the number of offspring in the control group was 19.74 %. More details are presented in the updated DAR.	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(36)	Vol. 3, B.9.9 Effects on other non –target organisms (flora and fauna)	EFSA: it is surprising that lenacil does not cause adverse effects on non-target plants, as though it is a non-selective herbicide which inhibits the chlorophyll synthesis. How can this be explained?	**RMS (February 2009) :** Lenacil is mainly absorbed via the root system but also by the leaves. Movement within the plant is primarily via the xylem from the roots to the leaves where it acts by inhibiting photosynthesis. Lenacil, when used according to label recommendations, provides selective control or suppression of a range of key annual weeds in sugar and fodder beet, including: *Anagallis arvensis*, *Anthemis* spp., *Chenopodium album, Diplotaxis erucoides, Fumaria officinalis, Malva sylvestris, Papaver rhoeas, Polygonum convolvulus, Silene* spp., *Stellaria media, Capsella bursa-pastoris, Sinapis arvensis, Raphanus raphanistrum, Amaranthus retroflexus, Mercurialis annua, Polygonum aviculare.* Lenacil is applied to small plants (uptake by the roots) and is active against dicotyledonous plants.	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)