PEER REVIEW REPORT ON **TOLYLFLUANID** 04.04.2005

TABLE OF CONTENTS

Comments on the Draft Assessment Report (DAR) on tolylfluanid

End of commenting period: 15 October 2003

Date	Supplier	File
17.10.2003	Greece	01_tolylfluanid_comment_GR.doc
14.10.2003	Sweden	02_tolylfluanid_comment_SE.doc
15.10.2003	Denmark	03_tolylfluanid_comment_DK.doc
15.10.2003	United Kingdom	04_tolylfluanid_comment_UK.doc
08.10.2003	Notifier	05_tolylfluanid_comment_NOT.doc
03.10.2003	Netherlands	06_tolylfluanid_comment_NL.doc
15.10.2003	United Kingdom	07_tolylfluanid_comment_UK.doc
14.11.2003	Germany	08_tolylfluanid_comment_DE.doc

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, Point B.7.3, Definition of the residue	EL: The residue definition as stated for products of animal origin (parent compound and metabolites) is rather vague. The relevant metabolites should be specified in the residue definition.	
(2)	Vol. 3, Point B.7.4, Use pattern	EL: The use in grapes should be more specific and should clarify whether it involves both table and wine grapes. For strawberries it is not clarified if the use outdoors and/or indoors is intended.	
(3)	Vol. 3, Point B.7.5, Identification of critical GAPs	EL: To out opinion the critical GAPs should be identified on the basis of the zones. Different critical GAPs should be identified for Southern and Northern Europe, if different GAPs are intended. In the cases where a greenhouse use is intended for a crop along to the outdoor uses, and this greenhouse use differs than that outdoors, then, a separate cGAP for this greenhouse use should be identified.	
(4)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: In Table B.7.6-1, 2 for pome fruits in Northern Europe, if the number of applications and the application rate per hl are taken to be within 25% of those in cGAP only seven trials are according to the critical GAP for Northern Europe. If the trials with reduced over 25% number of application (7 instead of 15) are accepted that would raise the number of trials to nine, but a justification for this deviation for the number of applications based on the persistence	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
		of the a.s. should be provided.	
(5)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: In relation to comment 2, in Table B.7.6-3 the type of grapes, wine or table should be stated as the MRLs are calculated on that basis.	
(6)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: The trials of Table B.7.6-6 for grapes cannot be used for MRL calculation as the application rate per ha is 50% below that in the critical GAP for Southern Europe.	
(7)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: In relation to comment 2, in Table B.7.6.-13, for strawberries, the field of use (outdoors or indoors) is not stated.	
(8)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: On the basis of the residue levels presented in Tables B.6-17, 18, 19, 20 and 21, the greenhouse use appears to be more critical than those in field. Therefore, the calculation of MRL for tomatoes and by extrapolation for aubergines, should be based only on this data from greenhouse trials.	
(9)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: Table B.6-22. For peppers only two trials in greenhouse are according to critical GAP (the two in the Netherlands). The rest of the trials are with very low compared to the critical application rate per ha (50% below). Six (6) more trials according to the cGAP for peppers indoors are required.	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(10)	Vol. 3, Point B.7.6, Residues arising from supervising trials	EL: The trials of table B.7.6-.32 cannot be used for MRL calculation as the number of applications is reduced from 3 to 2 and there are enough (8) trials in table B.7.6.31 conducted according to the critical GAP for Southern Europe.	
(11)	Vol. 3, Point B.7.9, Livestock feeding studies	EL: For clarity and transparency reasons, the calculated by the Rapporteur intake of residues for beef and dairy cattles should be presented clearly, in a form that would enable the read to see the figures (residue levels, transfer factors) used for these calculations.	
(12)	Vol. 3, Point B.7.13, Proposed EU MRLs and justification for the acceptability of those MRLs	EL: From Point B.7.6. as well as in this point it is not clear on which basis these MRLs were calculated by the Rapporteur. If they have been calculated by pooling the relevant data of the two zones (Northern and Southern Europe), we strongly oppose such an approach. On the contrary we would accept the approach and on the basis of our previous comments (2-10), i.e. to perform separate calculations of MRLs for Southern and Northern Europe and greenhouse and then for the MRL proposal, select the highest calculated.	
(13)	Vol. 3, Point B.7.13, Proposed EU MRLs and justification for the acceptability of those MRLs	EL: Were the average transfer factors obtained under point B.7.8 taken into account for the MRL proposals?	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(14)	Vol. 1, Level 4, Point 4.2.7	EL: Six (6) more residue trials according to the cGAP for peppers indoors are required.	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Volume 3, point B.9.2 Effects on aquatic organisms (fish, aquatic invertebrates, algae)	GR: When reviewing the reports it is clearly that the end points used for the risk assessment for Daphnia derives from the static test while for fish the notifier prefers end points from flow-through tests. We fully agree with the suggestions made from the RMS.	

section 4 - Environmental fate and behaviour (B.8)

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, 2.5, PEC values	SE: The scenarios chosen for PECsoil, groundwater, surface water and sediment do not appear to include the worst case scenarios, e.g. 15 applications in apples/pears at 1.125 kg as/ha and 6 applications in hops at 3 kg as/ha.	
(2)	Vol. 1, 2.5.2.3, PECsoil	SE: PECsoil should generally be calculated by use of realistic worst case DT50. In this case, mean DT50 values for a.s. and DMST were used. The FOCUS-scenarios used take worst-case conditions for leaching on board, by use of worst case weather and soil scenarios. Therefore, mean DT50 values are acceptable for PECgroundwater, but not for PECsoil. We realize though that in this case the risk assessment is not likely to change by this.	
(3)	Vol. 1, 2.5.3.3, PECsw	SE: Generally, realistic worst-case DT50 values should be used for calculation of PECsw. In this case, it appears that both mean and worst-case values were used. The use of mean values should be justified.	
(4)	Vol. 3, B.8, PEC values	SE: The scenarios chosen for PECsoil, groundwater, surface water and sediment do not appear to include the worst case scenarios, e.g. 15 applications in apples/pears at 1.125 kg as/ha and 6 applications in hops at 3 kg as/ha.	

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(5)	Vol. 3, B.8.3 PECsoil	SE: PECsoil should generally be calculated by use of realistic worst case DT50. (see further comment on Vol.1)	
(6)	Vol. 3, B.8.6 PECsw	SE: Generally, realistic worst-case DT50 values should be used for calculation of PECsw. (see further comment on Vol.1)	

section 5 - Ecotoxicology (B.9)

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, 2.6 Risk assessment scenarios	SE: The scenarios chosen for risk assessments do not appear to include the worst case scenarios, e.g. 15 applications in apples/pears at 1.125 kg as/ha and 6 applications in hops at 3 kg as/ha.	
(2)	Vol.1, 2.6.1 Effects on birds	SE: The toxicity endpoint from short-term dietary study and reproduction study should consistently be expressed as daily dose (mg as/kg bw per day), in order to take into account the different feed intake between laboratory and wild animals. The difference in feed intake depends mainly on different energy expenditure of the animals, and on different energy and moisture content of the food in the laboratory compared to that in the field.	
(3)	Vol.1, 2.6.1 Effects on birds	SE: In the exposure assessment , RUD in accordance with Appendix II of Guidance Doc 4145 should have been used.	
(4)	Vol. 1, 2.6.3 Effects on wild mammals	SE: The toxicity endpoints should consistently be expressed as daily dose (mg as/kg bw per day), in order to take into account the different feed intake between laboratory and wild animals. The difference in feed intake depends mainly on different energy expenditure of the animals, and on different energy and moisture content of the food in the laboratory compared to that in the field.	
(5)	Vol. 1, 2.6.3 Effects on wild mammals	SE: In the exposure assessment , RUD in accordance with Appendix II of Guidance Doc 4145 should have been used.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(4)	Vol.1, Appendix 3 Effects on aquatic species	SE: Please include and make clear the RMS's final risk assessment with regard to fish in the list of endpoint. From pages 502-502 and Table B.9.2.10-24 in Annex B we understand that the RMS's final assessment applies an assessment factor of 3 to NOEC 60 µg/l, resulting in acceptable risk at 5-15 m sprayfree zones. We can agree to that conclusion. It is important however to point out that at lower pH conditions than used in the studies, and at > 4 applications/season, the conclusion is more uncertain. Use of assessment factor lower than, say 3-5, is not justified in this case, since the outdoor microcosm had some shortcomings and since the HC5 approach in itself has not yet been generally adopted.	
(5)	Vol.1, Level 4 Bioconcentration study	SE: Bioconcentration studies should in accordance with OECD TG be performed at two concentrations to identify potential concentration dependency. The requirement can be dealt with as confirmatory.	
(6)	Vol. 3, B.9 Risk assessment	SE: The scenarios chosen for risk assessments do not appear to include the worst case scenarios, e.g. 15 applications in apples/pears at 1.125 kg as/ha and 6 applications in hops at 3 kg as/ha.	
(7)	Vol.3, B.9.1.4 Risk assessment birds	SE: The toxicity endpoint from short-term dietary study and reproduction study should consistently be expressed as daily dose (mg as/kg bw per day).	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(8)	Vol.3, B.9.1.4 Risk assessment birds	SE: In the exposure assessment , RUD in accordance with Appendix II of Guidance Doc 4145 should have been used.	
(9)	Vol. 3, B.9.3 Risk assessment mammals	SE: The toxicity endpoints should consistently be expressed as daily dose (mg as/kg bw per day).	
(10)	Vol. 3, B.9.3 Risk assessment mammals	SE: In the exposure assessment , RUD in accordance with Appendix II of Guidance Doc 4145 should have been used.	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol 3, B.9.2.10 and Vol 1, 2.6.2	DK: IN our view some of the endpoints used for fish in the higher tier risk assessment for fish should be reconsidered.	Re: Acute risk assessment based on HC_5 We have seen no information to validate the assumption that the higher values are outliers and therefore can be excluded from the HC5 calculation leading to a higher endpoint (33 micrg/l) than if all values are included (17,5 microg/l) – thus the later value should be used. Re Acute NOEC HC_5 We do not agree to this approach and find that this value should be deleted from the endpoint list. Furthermore it seems that the data are not normaly distributed and as such the analysis is invalid (In Table B.9.2.19-6 the Kolmogorov-S test is significant).

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(2)	Vol 3, B.9.2.10 and Vol 1, 2.6.2	In our view the TER values accepted for the higher tier risk assessment for fish and invertebrates are to low – and thus the risk and the extend of needed buffer zones underestimated.	Fish The microcosm studies potentially underestimate the risk due to decreased bioavailibility of the testsubstance in these systems (high pH, turbidity, dense macrophyte population), which is recognised by the RMS but not taken into account in the risk assessment – i.e. in the refinement of TERs. Furthermore it should be considered that these studies only include 4 applications whereas the intended use is up to 15 applications ! In our view at least a TER of 10 should be applied. Invertebrates: The indoor microcosm study with daphnids does only include daphnids and as such can not be used to lower the TER for invertebrates in general. In our view a TER of 100 for acute effects would still apply for this study. The outdoor microcosm study on the other hand is an aquatic community study (this is not clear in volume 1) – and as such can be used to lower the TER, however as above there are limitations to the study (high pH – which increases hydrolysis) and only 4 applications were made. So again we find that a TER of 10 would be more appropriate for this study.

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	Vol. 1, appendix 3, list of endpoints. Toxicity data for aquatic species Toxicity/exposure ratios	DK: The NOEC HC_5 – acute studies value should be deleted and the results of the microcosm studies for fish and invertebrates should be included. DK: The NOEC HC_5 – acute studies value should be deleted and the TERs should be revised to take into account further uncertainties.	See comments above. See comments above.

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 4, C.1.3.11 Technical specification	UK: CONFIDENTIAL INFORMATION – FAXED SEPARATELY TO RMS/EFSA	
(2)	Vol. 3, B.5.3.1	UK: Volume 3, page 51 Only limited recovery data are available for soil – additional recovery data are required.	

section 2 - Mammalian toxicology (B.6)

2. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 1, 2.1.4 Classification and Labelling	UK:The active substance and products should be classified with regard to inhalation toxicity/irritation regardless of particle size.	
(2)	Vol. 3, B.6.3.2.2 Short-term toxicity studies	UK: Decreased activities of the liver enzymes AST, ALT and AP are not considered to represent an adverse effect.	
(3)	Vol. 3, B.6.3.2.5 Short-term toxicity studies	UK: The RMS should justify the NOAEL proposed for this study (80 mg/kg bw/d), when elevated bone fluoride was seen at 20 mg/kg bw/d.	
(4)	Vol. 3, B.6.4.1.5 Genotoxicity studies	UK: A reduction in survival index at the highest concentration is considered to be sufficient indication of cytotoxicity; this study is therefore acceptable.	
(5)	Vol. 3, B.6.4.1.6 Genotoxicity studies	UK: The RMS is asked to clarify whether any assessment of the number of small colonies was made in this mouse lymphoma assay, in order to clarify the mechanism of genotoxicity.	
(6)	Vol. 3, B.6.5.1 Long-term toxicity and carcinogenicity studies	UK: The incidences of uterine tumours seen in the rat study are not considered to be treatment-related. There is no evidence of carcinogenicity in this study.	
(7)	Vol. 3, B.6.5.1 Long-term toxicity and carcinogenicity studies	UK: The RMS should justify the NOAEL proposed for this study (300 ppm), when elevated bone fluoride was seen at 60 ppm.	

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section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(8)	Vol. 3, B.6.5.3 Long-term toxicity and carcinogenicity studies	UK: Survival to 18 months in the mouse study should be reported to enable an assessment of the adequacy of this study.	
(9)	Vol. 3, B.6.5.3 Long-term toxicity and carcinogenicity studies	UK: The RMS should justify the NOAEL proposed for this study (60 ppm), when elevated bone fluoride was seen in males at 60 ppm.	
(10)	Vol. 3, B.6.10.4 Proposed ADI	UK: The ADI derivation is not agreed. The RMS' proposal to base the ADI on a NOAEL from a chronic toxicity study is agreed, as the overall NOAEL from the reproductive toxicity studies is shown to be 23 mg/kg bw/d. However the NOAEL of 15 mg/kg bw/d from the mouse study should be used to derive the ADI, leading to a value of 0.15 mg/kg bw/d.	
(11)	Vol. 3, B.6.12.4 Dermal absorption	UK: The predicted dermal absorption values for human skin *in vivo* should be calculated using the available comparative *in vitro* data, according to current EU guidance. The relevant figures from the rat study *in vivo* to use in this calculation are those from the 168 hour measurement. These figures clearly show that residual skin radioactivity following an 8-hour exposure is bioavailable.	

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(12)		UK: The minimum purity of the manufactured material is 960 g/kg, whereas the genotoxicity studies were performed with material of higher purity (98-100%). The RMS is therefore requested to clarify whether all impurities associated with the manufactured material have been adequately tested for genotoxicity.	
(13)	Vol. 3, B.6.14.1.Operator exposure and comparison to the AOEL. (Annex IIIA.7.2)	UK:Exposure estimates for this WG formulation have been predicted using UK POEM. As UK POEM does not have the appropriate data to estimate the level of exposure arising during mixing and loading a WG formulation these calculations may be unreliable. In these situations a combination of the German and UK POEM models may be used; the German model to obtain a figure for exposure during mixing and loading and POEM to derive an estimate for application exposure.	The POEM data for mixing and loading are based on pouring data for liquid formulations.
(14)	Vol. 3, B.6.14.1.Operator exposure and comparison to the AOEL. (Annex IIIA.7.2)	UK:For measurement of operator exposure, only limited details of three operator exposure studies are provided. Greater detail in terms of study design, methodology and results are required for this section to be transparent. It is also unclear whether these data have been generated in accordance with GLP principles.	The studies referenced were conducted in the Netherlands, Belgium, and Germany.

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(15)	Vol. 3, B.6.14.2. Conclusions on operator exposure. (Annex IIIA.7.2)	UK: This section concludes 'in greenhouse applications a re-entry interval of 12 hours is recommended'. It is unclear from the exposure assessment what this recommendation is based on.	
(16)	Vol. 3, B.6.14.4 Re-entry exposure (Annex IIIA.7.2)	UK: The worker exposure assessment considers only exposure from crops treated with a single application of 'Euparen M 50 WG'. As crops may be treated with up to 7 applications of this product, systemic exposure for workers harvesting treated crops could be higher than that which has been predicted. The potential accumulation of DFR should be considered.	
(17)	Vol. 3, B.6.14.4 Re-entry exposure (Annex IIIA.7.2)	UK: In accordance with good hygiene standards, workers should not re-enter treated crops until spray deposits are dry. Workers exposed to dislodgeable foliar residues would therefore be expected to be exposed to a dry foliar deposit. The dermal absorption value which has been assumed for the worker exposure assessment (13%) relates to the spray dilution. This value may therefore be high.	

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.3 Residues definition	UK: Volume 3, page 269 The residues definition in plants for consumer risk assessment is parent plus the metabolite DMST. However the text indicates that the identified metabolites were not of toxicological significance, DMST was identified in the rat metabolism study and the majority of the residue in the crops samples from the residue trials is parent tolylfluanid. Therefore, consideration should be given to amending the residue definition to parent only.	
(2)	Vol. 3, B.7.3 Residues definition	UK: Volume 3, page 269 In line with (1) above the residue definition for consumer risk assessment, should be amended to parent only. Neither of the 2 and 4-hydroxy metabolites were identified in the rat metabolism study, however the metabolic pathway indicates that the major metabolite 4-hydroxy is likely to have been present in the rat.	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	Vol. 3, B.7.3 Residues definition	UK: Volume 3, page 269 A residues definition for animal products does not need to be set at this stage, as none of the crops for which continuing approval is sought, are fed to animals. If a residues definition is set, a method of analysis of determination residues in animal products will be required, analysing the products for the components of the residue definition (method of analysis for animal products is currently not available). The proposed residue definition is parent and its metabolites, this could be refined to the metabolites DMST (only included to the levels in hen fat, however it is a rat metabolite), 4-(Dimethylaminosulfonylamino) hippuric acid and 4-(Dimethylaminosulfonylamino) benzoic acid, which are the three main components analysed in the animal products	
(4)	Vol. 3, B.7.10	UK: Volume 3 on page 326 The case for none submission of rotational crop data needs to be expanded quoting the DT90's for tolylfluanid and its primary metabolite DMST.	
(5)	Vol. 3, B.7.10	UK: Volume 3 on page 326 The MRL for grapes needs to be amended from 5 to 10 mg/kg (one of the trials gave a residue of 5.1 mg/kg)	

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section 4 - Environmental fate and behaviour (B.8)

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol 3, B.8.2.1.1, adsorption/desorption of active substance (Sommer 2000)	UK: Chemicals used as reference standards do not have similar characteristics to active substance. Suggest RMS adds comment to endpoints explaining that result from study is likely to be a rough estimate.	
(2)	Vol 3, B.8.2.2.2, aged residue column leaching study (Scholz 1987a)	UK: Ageing periods used significantly in excess of one half-life. Suggest RMS clarifies by stating this, or by repeating half-life value, in endpoints for this study.	
(3)	Vol 3, B.8.3, predicted environmental concentration in soil (Schad 2001a, Schäfer 2001a)	UK: PECs not calculated in accordance with Commission doc 7617/VI/96 (FOCUS soil persistence guidance). Approach used may underestimate worst case PECs, particularly for mobile metabolite DMST. UK considers that PECs for endpoints should be recalculated in accordance with 7617/VI/96.	
(4)	Vol 3, B.8.4.1 and B.8.4.2, hydrolytic degradation and photochemical degradation (Wilmes 1982, Suzuki and Yoshida 1994, Hellpointer 1992 and 2000)	UK: Procedural recoveries for these cold studies were not stated. UK considers that levels (or acceptability) of recoveries should be stated.	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3 General point	UK: The use scenarios (max application rate/max number of treatments) used in the risk assessment sections of Vol 3 do not appear to reflect the GAPs proposed in section 1.5.3.1 of Vol 1 Level 1.	If the use scenarios used in the risk assessments do not reflect the maximum rates and numbers of applications proposed by the Notifier then **all** areas of the risk assessment will need to be revised. (The following comments are therefore in addition to this general comment)
(2)	Vol. 3, B.9.1.4 page 433-450. Long term risk to herbivorous birds	UK: UK agrees that further refinement of TERlt is necessary. However, the proposed refinement of residue levels using median 50% values requires further justification. Justification for the extrapolation from the DT50 of 3.1 days based on lettuce heads to outdoor short grasses must also be provided.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	Vol. 3, B.9.3.3 page 507-524. Long term risk to herbivorous mammals	UK: UK agrees that further refinement of TERlt is necessary. However, proposed refinement of residue levels using median 50% values requires further justification. Justification for the extrapolation from the DT50 of 3.1 days for lettuce heads to outdoor short grasses must also be provided. Further justification for not using the 2-gen rat NOEC (100 ppm = 9 mg a.s./kg bw/day) must be provided. The proposed use of the teratogenicity NOAEL (100 mg a.s./kg bw/day) is questionable given that frequent exposure may occur in certain use scenarios (i.e. apples/pears 15 applications @ 7 day intervals). It is important to consider in more detail the effects reported in the 2–gen rat study at the 700 ppm dose (= 70 mg a.s./kg bw/day), which appear to be related to maternal toxicity and which are otherwise not accounted for in the proposed refinement.	
(4)	Vol 3, B.9.2.9 page 480-482	UK: The detail provided on the effects observed in Study 4 is insufficient to allow MSs to reach any conclusion as to the validity of the proposed endpoint from this study.	Information on the species present and on the magnitude of any observed impacts should normally be included together with appropriate statistical analyses. In this case the UK is prepared to accept the RMS opinion that fish are the most sensitive group of aquatic organisms.
(5)	Vol 1 Appendix 3 Listing of Endpoints Effects on Non-Target species	UK: It is implied that the recommendations in HARAP and ESCORT 2 are Annex VI triggers. Unless and until they are formally incorporated into Annex VI they should be treated only as guidance for the possible refinement of first tier uncertainty triggers.	

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		BAYER CROP SCIENCE AG: No comment	

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section 2 - Mammalian toxicology (B.6)

2. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
		BAYER CROP SCIENCE AG: No comment	

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.3.2 Definition of residues of animal origin Vol. 3, B.7.17 Summary and evaluation of residue behaviour Vol. 1, Appendix 3, List of endpoints	BAYER CROP SCIENCE AG: The definition of residues of animal origin is given as parent compound in Vol. 3, B.7.3.2, and as parent compound and metabolites under Vol. 3, B.7.17. In Vol. 1, Appendix 3, List of endpoints a distinction is made with respect to the purpose of the definition. For MRL enforcement (and control of misuse) parent compound only was proposed and for refined estimations of dietary intake parent compound and metabolites (4-dimethylaminosulfonylamino) benzoic acid, and 4-(dimethyl-aminosulfonylamino) hippuric acid.	Is this consistent?

section 4 – Environmental fate and behaviour (B.8)

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
		BAYER CROP SCIENCE AG: No comment	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 1, Appendix 3, List of endpoints	BAYER CROPSCIENCE AG: The list of endpoints, Page 102-103, AQUATICS, has to be revised in such a manner, that the list of endpoints reflects the results of the two outdoor-microcosm studies as well as the newly calculated TER and crop dependent buffer zones	
(2)	Vol. 3, B.9.2.4, Acute toxicity to aquatic invertebrates	BAYER CROPSCIENCE AG: It is stated to the acute static study with aquatic invertebrates (Page 468), that "…in principle, the results of the test should not be considered valid for the risk assessment or measured concentrations should be used for the calculation of LC_{50}. In contrast, is stated to the corresponding acute static study with fish, that "… results of the test can be considered valid for the risk assessment, as an appropriate risk assessment for substances being highly instable in water should be conducted by comparing the initial environmental concentrations after the application in the field versus the initial concentrations in the laboratory test system..."	Are these two statements compatible?

section 5 – Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(3)	Vol. 3, B.9.2.10, Summary and risk assessment to aquatic organisms	BAYER CROPSCIENCE AG: It is stated ahead of the TER calculation - acute static (Page 488), that "…the evaluator agrees to these statements but would like to use the results of static acute studies with caution because the nominal concentrations were used in calculations… " In view of the conclusions given by FIN to the acute static study with fish (see above), the two statement are not compatible	
(4)	Vol. 3, B.9.2.10, Summary and risk assessment to aquatic organisms	BAYER CROPSCIENCE AG: It is stated (Page 497), that "the assessment factor of 1.5… as proposed by the applicant… is considered not to be protective enough …as pH-values in surface water of lower than 6 are quite common in Northern Europe " However, according to the "Guidance Document on Aquatic Ecotoxicology, SANCO/3268/2001 rev. 4", the relevant pH range for Europe is 6-9	
(5)	Vol. 3, B.9.2.10, Summary and risk assessment to aquatic organisms	BAYER CROPSCIENCE AG: In the diagram on page 498: (i) row strawberries (Northern Europe), column "30 m buffer strip": the stated value of 200 is incorrect, as the correct value is 72.3; (ii) according to the assessments of FIN, the TER has to be > 3, however, in the row apples/pears (Northern Europe, reduced buffer zone scenario), column 10m, the value of 2.88 is considered to be still safe (which is inconsistent)	

section 5 – Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, B.9.2.10, Summary and risk assessment to aquatic organisms	BAYER CROPSCIENCE AG: In the diagram on page 500: (i) row strawberries (Northern Europe), column "30 m buffer strip": the stated value of 330 is incorrect, as the correct value is 119	
(7)	Vol. 3, B.9.5, Risk assessment non-target arthropods	BAYER CROPSCIENCE AG: FIN stated to the lab. study with *C. 7-punctata* (Page 530), that "the reproductive output determined in the above mentioned laboratory study is well within the historical database for control beetles and hence this parameter is considered as not impacted by the treatment… as about trice the number of fertile eggs per viable female per day were observed with regard to the lower threshold stated for this testing endpoint…the residue levels resulting from applications up to 2.5 kg a.i./ha tolylfluanid can be regarded as safe when used as a single application". Why does FIN considers then the residues caused by to 2.5 kg a.i./ha tolylfluanid "to be in borderline of a safe residue level" in the risk assessment (Page 562)?	

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.2.1.14, hydrolysis	NL: the purity of the active substance is missing	
(2)	Vol. 3, B2.1.21, explosive properties	NL: is this determined or by statement? If statement please give statement.	
(3)	Vol. 3, B.2.2.32, chemical compatibility	NL: If there is no evidence that the product is compatible I suggest to remove this text and leave it open	
(4)	Vol. 3, B5.2.1, residue methods	NL: Not all the methods are acceptable as monitoring methods (e.g. Vogeler 1967). For all those methods no data protection can be claimed. RMS is asked to see which methods are acceptable and to remove all the data protection form the other methods.	
(5)	Vol. 3, B5.2.1, residue methods plants	NL: the residue definition for monitoring in plants is not clear. Is it only the parent (as in the list of endpoints) or with the metabolite DMST (and for grapes with the glycoside adducts)? In the end points no conversion factor is proposed, and still only the parent is proposed. Propose to use the parent and DMST as the residue definition for monitoring.	

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(6)	Vol. 3, B5.2.1, residue methods animal products	NL: the residue definition for monitoring in animal products is not clear. Is it only the parent (as in the list of endpoints) or with the metabolite DMST? In the end points no conversion factor is proposed, and still only the parent is proposed. It is strange to measure only the parent if the parent was not found in the residue trials! Propose to use the parent and DMST as the residue definition for monitoring.	
(7)	Vol. 3, B5.3.1, residue method soil	NL: The method proposed is not sufficient validated and therefore not acceptable. Additional validation is required, for the parent as well as for DMST. The individual results cannot be pulled together because there are different detectors used, and also different extraction solvents are used.	
(8)	Vol. 3, B5.3.2, residue method water	NL: I don not agree that the method is validate for drinking water because there is validation for surface water. From experience it is seen that this compound behaves very different if a matrix is present, and in drinking water almost no matrix is present. Validation in drinking water is required.	
(9)	Vol. 4, C1.2, batch profile	NL: The batches are from 1995. This is 8 years ago, and maybe they are no longer representative for the current production. Are there also new batches to confirm that the production still is the same?	
(10)	Vol. 4, C1.2, specifications a.s.	NL: Please fill the complete table C2. with all the specifications. The specification for impurity 1, 2, 4 and 5 are to high compared to the content in the batches and should be lowered.	

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(11)	Vol. 4, C1.4, analytical methods impurities	NL: How is the accuracy determined? If this was not done by standard addition additional validation is required.	
(12)	Vol. 4, C1.4, analytical methods impurities	NL: There is no indication that the identity of the impurities are confirmed. Also there is no confirmatory method submitted. Or the identity should be confirmed (using HPL-MSMS with the same eluent and column) or a confirmatory method should be submitted.	

section 2 - Mammalian toxicology (B.6)

2. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.4.1, Proposals for the classification and labelling of the active substance	NL: Based on the results of the 28-day dermal toxicity study in rabbits tolylfluanid should be labeled with R66. Based on the results of the 2-generation reproduction studies, labeling of tolyfluanide with R63 should be considered.	
(2)	Vol. 3, B.6.3.2.1, Oral 90-day toxicity, feeding 3 months	NL: The NOAEL was based on increased organ weights in the absence of histopathological findings or changes in clinical biochemistry. A higher NOAEL might be considered, but cannot be established based on the present summary due to the absence of quantitative data on organ weight changes.	
(3)	Vol. 3, B.6.3.2.2, Oral 90-day toxicity, 13– weeks diet and 4 weeks recovery	NL: The NOAEL was based on a decrease in AP and calcium. No futher changes were noted. The establishement of a higher NOAEL might be considered.	
(4)	Vol. 3, B.6.3.3.3, Percutaneous 28-day toxicity study	NL: Based on the observed moderate-to-severe skin irritation, tolylfluanid should be labelled with R66.	

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(5)	Vol 3, B.6.6.1, Two generation reproduction toxicity in the rat	NL: Based on the decreased lactation and/or viability index at doses at which very slight maternal toxicity was noted, labeling of tolylfluanide with R63 should be considered.	
(6)	Vol 3, B.6.8, Further toxicological studies	NL: Studies with several metabolites were performed. Studies included acute toxicity data and genotoxicity data. One should establish which of these metabolites are considered relevant in terms of exposure, e.g. exposure to plant metabolites during re-entry activities, exposure through drinking water, exposure through food, etc. For relevant metabolites additional data on repeated dose toxicity should be provided.	
(7)	Vol 3, B.6.10.4, AOEL	No A rather large range of urinary excretion was given in the summary of toxicokinetics: 60-90% (B.6.1.9.). Furthermore, it is not clear whether the excreted radioactivity in bile had been systemically available. Therefore, one should consider correction for systemic availability for the derivation of the AOEL.	

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(8)	Vol 3, B.6.10.4, AOEL	NL: The AOEL should be based on the overall NOAEL of approximately 20 mg/kg bw/day from the 2-generation reproduction studies. The NOAEL of 9 mg/kg bw/day is the lowest NOAEL from the 2-generation reproduction studies, but comparison of NOAELs and LOAELs results in an overall NOAEL of approximately 20 mg/kg bw/day. Application of a safetyfactor 100 results in an AOEL of 0.2 mg/kg bw/day.	
(9)	Vol 3, B.6.10.4, AOEL	NL: Tolylfluanide is labeled with R26 (very toxic by inhalation). Although in most studies local effects were noted, one repeated dose inhalation study (B.6.3.3.1..3) showed systemic effects (increased thyroid weight) at 0.05 mg/L. Based on these findings, the derivation of a respiratory AOEL, based on inhalation data should be considered.	

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(10)	Vol 3, B.6.12.4, Summary of dermal absorption	NL: The percentage absorbed after 8 hours dermal exposure were selected. However, based on the 168 h. data from the in vivo dermal absorption study it should be noted that part of the amount remaining in the skin after washing becomes systemically available. Therefore, the amount potentially absorbed (absorbed dose and amount remaining in the skin) should be taken to established the percentage dermal absorption. This results in dermal absorption percentages of 8, 7 and 27% for the dose levels of 0.75, 0.075 and 0.0075 mg/cm^2, respectively.	
(11)	Vol 3, B.6.14, Exposure data	NL: The use of dermal absorption values of 8 and 27% for the undiluted and diluted formulation, respectively, for the calculation of internal exposure values should be considered.	

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 1, level 2, 2.4.2, residues relevant for consumer safety	Netherlands: It is questioned if the extrapolation from residue levels form the goat metabolism study performed at 45X to 1X is reliable. According to the Netherlands, it is quite uncertain that the LOQ will not be exceeded for liver and kidney tissue which are already *calculated* to be 0.03 mg/kg which is near to the LOQ. Furthermore it is questioned what happens if in future the MRL will be set at 0.01 mg/kg ('zero') after implementation of the new MRL regulation which is now under discussion, with respect to the calculated levels which are up to 0.03 mg/kg for liver. Therefore, it is proposed that a ruminant feeding study is needed to set MRLs for animal products.	
(2)	B5.4. analysis method for plant and animal products	Netherlands: As a consequence of the need for providing a ruminant feeding study and deducing MRLs for animal products (Vol 1, Level 2, 2.4.2), an analysis method (enforcement) for animal products is required for parent compound, 4-(dimethylaminosulfonyl amino) benzoic acid and 4-(dimethylaminosulfonyl) hypuric acid.	

section 3 - Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	B7.6 (residue trials)	Netherlands: In table 7.6.4 for trial 8202-87, 8203-87, 0210-88, 0211-88, 0212-88 and 0213-88 the wrong PHI was selected (at the right PHI higher residues were found).	
		Netherlands: In table 7.6.13 (strawberry) residue trials with PHI 3 days in stead of PHI 7 days were selected	
		Netherlands: In table 7.6.17 (tomatoes) residue trials with PHI 3 days in stead of PHI 7 days were selected	
		Netherlands: In table 7.6.22 residue trials (pepper) with a application rate of 1.0 kg ai/ha were selected while this is outsite the acceptable range of 1.5 ± 25% (1.11-1.88) kg ai/ha	
		Netherlands: In table 7.6.24 residue trials (cucumber) with a application rate of 1.0 kg ai/ha were selected while this is outsite the acceptable range of 1.5 ± 25% (1.11-1.88) kg ai/ha	
(4)	B7.7 (storage stability data)	Netherlands: As a consequence of the need for providing a ruminant feeding study and deducing MRLs for animal products (Vol 1, Level 2, 2.4.2), storage stability data for animal products of parent compound, 4-(dimethylaminosulfonyl amino) benzoic acid and 4-(dimethylaminosulfonyl) hypuric acid are needed.	

section 4 - Environmental fate and behaviour (B.8)

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.8.1.1, Route of degradation in soil	NL: The analytical method used is not validated and not comparable to the method supposed in chapter B.5. Because of the low recovery of the parent on t=0 and the values for DMST serious doubts about the validity of the used method arise.	
(2)	Vol 3, B.8.1.3, Summary of degradation in soil.	NL: As just for one of the soils the data showed a good fit there is only 1 reliable DT_{50} value for the parent compound available instead of 4 required.	For the parent 3 additional DT_{50} values in soil should be available unless the parent can be seen as a precursor. Data requirement to be added in volume 1, level 4.
(3)	Vol 3, B.8.2.1, Adsorption	NL: The determined Koc with HPLC-method is just an estimation. According to the SCP opinion (Opinion of the scientific committee on plants on methods for the determination of the organic carbon adsorption coefficient (Koc) for a plant protection product active substance, SCP/KOC/002-final, 18 July 2002) the result of the method is not a reliable value.	Because of fast hydrolysis of the parent no batch method is possible. A column study as described in the SCP opinion is considered a better study method and required.
(4)	Vol 3, B.8.3.1, PEC_s	NL: PEC_{soil} calculations should be performed with worst-case DT_{50} values.	This should than also be corrected in Volume 1.
(5)	Vol. 3, B.8.4.3.2, Water/sediment studies	NL: The DT_{50} value for DMST in sediment is much much longer than in the 1st experiment and seem urealistic.	in the 3rd experiment sampling was performend until 7 days after application. There was only one sample point after the maximum was reached in the water and it is not clear that the maximum in the sediment has been reached. The extrapolation of DT_{50} in the sediment has led to unrealistic high values.
(6)	Vol.3, B.8.6.1, PEC_{SW}	NL: temperature correction of the DT_{50} to 15ºC is not common in Tier 1 evaluation.	PEC_{sw} should, to our opinion, be recalculated using the DT_{50} at 20ºC.

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section 4 - Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(7)	Vol 3, B.8.6.1, PEC_{sw}	NL: Does the model EXAMS proovide the same data as standard input calculatations?	It looks like the same dimensions are used as in the standard calculations, we would like a conformation on this.
(8)	Vol 1, level 2, 2.5.3.3	NL: Why is the high value for DT_{50} sediment DMST used for the calculations	Because of the short incubation time of the test, the extrapolated value for DT_{50} sediment can not be guarded as reliable.
(9)	Vol 1, Appendix 3, list of endpoints	NL: Koc; change text 'determined by HPLC-method' to 'estimated using HPLC-method'.	The HPLC method provides only an estimated value (see SCP opinion).

section 5 - Ecotoxicology (B.9)

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.9.1.4, risk assessment to birds	NL: It is recommended to base the risk assessment for birds on the Guidance Document on Risk Assessment for Birds and Mammals. For orchards and grapes only an insectivorous bird should be taken into account. According to the Guidance Document the averaging time for calculating a TWA should not be longer than the interval between two applications. So, in the case of tolylfluanide, an averaging time of 7 days must be taken instead of 21 days.	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(2)	Vol. 3, B.9.2.10, risk assessment to aquatic oganisms	NL: Why the TER calculation starts with a distance of 5 m? The standard situation in orchards and grapes is 3 m and in strawberries 1 m. NL: There is an outdoor microcosm study with algae and invertebrates available. The RMS has concluded that the NOEAEC of this study is 99 µg/L. This study has also been evaluated in NL and the conclusion was that the NOEAEC should be 46 µg/L, because at this concentration there is fast recovery. At 99 µg/L there is also recovery, but the duration of the effects is longer and more species are showing effects. Besides that the frequency of application in the test is only 4 times, while in practice 8 applications are possible. If an assessment factor of 3 is applied to the value of 46 µg/L the norm will be 15.3 µg/L. This is lower than the value which is based on the higher tier studies with fish (including an assessment factor of 3).	

section 5 - Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	Vol. 3, B.9.1.4, risk assessment to mammals	NL: It is recommended to base the risk assessment for mammals on the Guidance Document on Risk Assessment for Birds and Mammals. According to the Guidance Document the averaging time for calculating a TWA should not be longer than the interval between two applications. So, in the case of tolylfluanide, an averaging time of 7 days must be taken instead of 21 days.	
(4)	Vol. 3, B.9.5.4, Risk assessment to non-target terrestrial arthropods	NL: The risk assessment for parasitoids and predatory mites is based on extended lab tests with indicator species. To account for the range of species which could be expected in off-field habitats, a 5-fold correction (uncertainty) factor must be included. This is according to the Escort 2 Guidance Document.	
(5)	Vol. 3, B.9.9, Effects on other non-target organisms (flora and fauna)	NL: For estimating the exposure of non-target terrestrial plants to tolylfluanide the drift percentage at 1 m (strawberries) or 3 m (orchards and grapes) must be taken into account. For the risk assessment an assessment factor of 5 must be applied to the lowest EC50-value.	
(6)	Vol. 1, level 2	NL: The comments mentioned above regarding Volume 3, Annex B, are also relevant for volume 1, level 2.	

Comments 2 of UK on the draft assessment report on tolylfluanid

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca.10 lines)	Column 3 Further explanations
(1)	Vol. 4, C.1.3.11 Technical specification	UK: Volume 4, page 9 The technical specification for the following impurities are slightly higher than required, when comparing them to the results of the five batch analysis. Therefore, consideration should be given to the amendment of the specification as outlined below or further batch data submitted to support the proposed specification. CONFIDENTIAL INFORMATION REMOVED!	Confidential information - faxed to RMS/EFSA

section 1 - Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis (B.1-B.5)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)		DE: no comment.	

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2. Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.3 (Short term toxicity / Inhalation)	DE: Amend the box "Lowest relevant inhalation NOAEC / NOEC as follows: 0.001 mg/L (0.27 mg/kg bw/d, not micronised dust), 4-wk rat ≥ 0.004 mg/L: Irritation of respiratory tract	Species tested, study duration, and findings are missing (rat, 4-wk, irritation in the respiratory tract at 0.004 mg/L and above). Furthermore, it should be mentioned that the study was performed with not micronised dust, because the relevance "micronised" or not for practical conditions is still in discussion, most of all with respect to labelling. (Most likely micronised dust is realistic.)
(2)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.6 (Reproductive toxicity)	DE: Amend the box "Lowest relevant reproductive NOAEL / NOEL" as follows: 100 ppm (7.9 mg/kg bw/d), 2-gen. rat	As base for the NOAEL, another reproduction study is proposed: doses: 0-100-700-900 ppm, NOAEL: 7.9 mg/kg bw/d (100 ppm), based on labored breathing and reduced survival rate of the pups at 700 ppm (about 56 mg/kg bw/d). In the study chosen by the RMS, the only tested dose (180 ppm = 19 mg/kg bw/d) revealed labored breathing and reduced lactation indices in F2 pups. This LOAEL is supported by a 3rd reproduction study with a LOAEL of 23 mg/kg bw/d (decreased viability and lactation indices), the lowest dose tested. Comment on Vol. 3, Annex B, B.6: The threshold values are noted correctly by the RMS in the Summary tables 2.3.7 (Vol. 1, level 2, page 23) and 6.6.9 (Vol. 3, Annex B, B.6, page 187), whereas under Conclusions of the study B.6.6.1.2, page 178, wrongly the reproductive LOAEL of 300 ppm is noted as NOAEL. A further contradictory conclusion is drawn on the finding *labored breathing* of the pups. In the Summary tables it is not noted and in the study B.6.6.1.3, page 179, this finding at 180 ppm is regarded as toxicologically not significant, justified in view of not occurring in the other reproduction studies. However, in the reproduction study B.6.6.1.4, page 180, labored breathing of the pups is one of the findings.

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(3)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.8 (Other toxicological studies)	DE: The last sentence relating to neurotoxicity, should be transferred to point 5.7. which should be renamed in Neurotoxicity / Delayed neurotoxicity	
(4)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.10, (Summary, ADI)	DE: ADI: 0.08 mg/kg bw, 2-gen. rat, Safety factor 100	For deriving an ADI, the 2-generation study on rat with a NOAEL of 7.9 mg/kg bw/d (see comment (2)) instead of the NOAEL of the 2-yr rat study is proposed. The NOAEL (18 mg/kg bw/d) in the 2-yr rat study resembles the LOAELs (19 and 23 mg/kg bw/d) in two further reproduction studies with the effects labored breathing and reduced viability / lactation indices.
(5)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.10, (Summary, AOEL inhalative)	DE: AOEL inhalative: 0.003 mg/kg bw/d; 4-week rat inhalation (dust not micronised), Safety factor 100	With regard to the high inhalative toxicity of tolylfluanid, the derivation of an AOEL inhalative is proposed.
(6)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIA, point 5.10, (Summary, ARfD)	DE: ARfD: 0.25 mg/kg bw, teratogenicity study rabbit, Safety factor 100	The derivation of an ARfD is proposed: With regard to adverse effects (postimplantation loss and malformations) in presence of only slight maternal toxic effects, the NOAEL of the teratogenicity study on rabbit is appropriate: 25 mg/kg bw/d and a safety factor of 100 result in an ARfD of 0.25 mg/kg bw.
(7)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIIA, point 7.3, (Dermal absorption)	DE: 4.2 % for the concentrate and 7.5 % for the dilution (*in vivo* rat and *in vitro* rat and human skin, 8 h exposure = collection period for absorbed radioactivity; fraction in / on washed skin included).	Setting a dermal absorption rate on the base of the amount of radioactivity absorbed within 8 hours (1st sacrifice), the fraction in / on the washed skin should be included - as well as the relation rat / human skin. (The corresponding findings from the original reports are documented correctly in the monograph, Vol. 3, B6, page 224-228.)

section 2 - Mammalian toxicology (B.6)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(8)	Vol. 1, App. 3, Listing of endpoints, Chapter 2.3, Annex IIIA, point 7.2, (Acceptable exposure scenarios)	DE: Considering the high inhalative toxicity of tolylfluanid (see comment (5), AOEL inhalation), the inhalation exposure should be assessed separately and RPE (respiratory protection equipment) should be recommended in all cases.	

section 3 - Residues (B.7)

3. Residues (B.7)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)	Vol. 3, B.7.16.1, Chronic Exposure	DE: Due to the proposal in the toxicological section to lower the ADI a new intake assessment is necessary.	
(2)	Vol. 3, B.7.16.2, Acute Exposure	DE: Due to the proposal in the toxicological section to set an ARfD an intake assessment is necessary.	

4. Environmental fate and behaviour (B.8)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)		DE: no comment.	

5. Ecotoxicology (B.9)

No.	Column 1 Reference to draft assessment report *	Column 2 Comment * (restricted to 500 characters, ca. 10 lines)	Column 3 Further explanations
(1)		DE: no comment.	

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