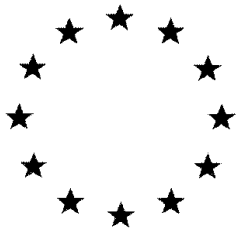
# European Commission

## Peer Review Programme



## ECCO Peer Review Meetings

# Full Report on Tritosulfuron

- Reports of the meetings
- Comments on the draft assessment report
- Other documents considered at the meetings

ECCO-Team, at: Pesticides Safety Directorate (PSD), York

17.10.2003

ECCO PEER REVIEW PROGRAMME

FULL REPORT ON **TRITOSULFURON**

CONTENTS

**PART 1: REPORTS**



**PART 2: COMMENTS AND OTHER DOCUMENTS**

## ANNEX 4 TO CONCISE OUTLINE REPORT OF ECCO 140 PEER REVIEW MEETING

Specific comments from the **Overview Meeting** on the active substances are listed below. The conclusions of the meeting were as follows:

## TRITOSULFURON

Rapporteur Member State: Germany

1a. Comments received and discussed:

| Date | Supplier | File Name |
|---|---|---|
| August 2003 | Germany | tritosulfuron_140_com01_DE |

1b. Comments received but not discussed (because deadline of submission was not met):

| Date | Supplier | File Name |
|---|---|---|
| | | |

1c. Documents tabled at the meeting:

| Date | Supplier | Content | File Name |
|---|---|---|---|
| | | | |

1d. Addenda:

| Date | Supplier | File Name |
|---|---|---|
| August 2003 | RMS/ Germany | tritosulfuron_140_3eval_table_0-2_Aug03 |
| August 2003 | RMS/ Germany | tritosulfuron_140_addendum1_vol4_Aug03 |
| Sept 2003 | RMS/ Germany | tritosulfuron_140_addendum2_vol4_Sept03 |

1e. Miscellaneous:

| Date | Supplier | Content | File Name |
|---|---|---|---|
| | | | |

### 1 Physical and chemical properties, Methods of analysis section

- The meeting noted that batches of the technical material could not be used if the impurity AMTT occurred at greater levels than 0.02% of the technical material because of toxicological concerns over this impurity. The meeting agreed that batches that were unacceptable should be purified before they were used. The applicant offered to provide more information on the manufacturing process if this would help resolve the issues regarding the presence of this impurity.

- The ECCO Chair requested whether there had been any degradation occurring during the shelf life study. The RMS reported that they would consult internally to determine if there was any degradation.

- Additional requirements were set for methods of analysis and validation data for AMTT and M02 because of toxicological concerns over these metabolites. These data are essential for Annex I inclusion.

**2 Environmental fate and behaviour section**

- Further information on the field dissipation trials is to be provided by the applicant in November 2003. These data are considered essential for Annex I inclusion.

- Further FOCUS modelling and PELMO calculations are to be provided by the applicant to address a number of concerns relating to groundwater exposure. The calculations will be considered by the RMS.

**3 Ecotoxicology section**

- The applicant confirmed that they had submitted the wrong data to address the risk to mammals from AMTT. They will provide a risk assessment to address this data requirement which must be addressed prior to Annex I inclusion.

- The RMS is to evaluate data to address the long-term risk to earthworms from a number of metabolites. The data requirement must be satisfactorily addressed before the active substance can be considered for Annex I inclusion.

- The RMS confirmed that the end point table with regard to *T. pyri* was correct and so the requirement for the table to be updated was incorrect.

**4 Mammalian toxicology section**

- A number of toxicological studies still need to be submitted by the applicant. Once these have been evaluated, the RMS will produce an addendum to the DAR detailing their evaluation.

- The meeting noted concerns over the relevance of genotoxicity data from mice to address tumour formation in rats. The ECCO Chairperson confirmed that genotoxicity data are required to show that tritosulfuron is not involved in tumour formation in rats. It was noted that a comet assay could be helpful.

- The meeting agreed that work to address the possibility of the formation of AMTT in tank-mixes must be carried out under field, and not laboratory, conditions. The applicant believes that this work has already been performed and which shows that there is no increase in levels of AMTT. The applicant will submit a protocol for an appropriate study to the RMS to consider if it will be acceptable.

- The applicant informed the meeting that range-finding developmental one generation study is ongoing and will be ready for submission in August 2004. The applicant was asked to discuss with the RMS whether this study is necessary, as if it is not required, a decision on the Annex I inclusion of the active substance may be taken earlier.

**5 Residues section**

- An ongoing metabolism study in wheat is still to be submitted and will be available by April 2004. Preliminary results indicate that the data will be similar to the metabolism study on maize. The data are considered essential for Annex I inclusion.

- The meeting discussed the toxicity of metabolite 635M02 and the effect this could have on the residue definition and the consumer exposure risk assessment. The RMS was asked to consider the concerns with regard to this metabolite. It was noted that further information on the metabolite would be available when the wheat metabolism study was submitted and that these issues should be considered once this study has been evaluated. The RMS was also to take into account information that the applicant offered to provide on this metabolite.

## 6 Recommendations

Within one week, the applicant should provide an estimate as to when the data will be available to address the outstanding data requirements. The RMS are to evaluate the additional data as soon as possible, and produce the final addenda, so that further consideration of the active substance can take place in the Working Groups (Evaluation) in September or December 2004.

Appendix 1: Revised evaluation table rev. 0-3 (including complete list of data requirements): tritosulfuron

Classification criteria for data requirements were discussed at the meeting. The group agreed on having three criteria:

- Data requirements essential for unconditional Annex I inclusion;
- Data requirements to be dealt with at Member State level; and
- Data requirements fulfilled.

Appendix 2: Complete list of end points: tritosulfuron

Appendix 3: List of studies which were submitted during the evaluation process and were not cited in the draft assessment report: tritosulfuron

Appendix 4: Suggested classification and labelling: tritosulfuron

# Evaluation table Tritosulfuron (Hb)



**WORKING DOCUMENT – DOES NOT NECESSARILY REPRESENT THE VIEWS OF THE COMMISSION SERVICES**

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

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|---|---|---|---|---|
| | | | | Section 1<br>Data requirements: 4<br>Open points: 0 |
| 1.1 | Applicant to provide 5 batch analysis data. (AIIA-1.11)<br>**A** | July 11, 2003:<br>Analysis data of 7 batches have been submitted to RMS (and to PSD (UK) under national submission):<br>BASF DocID 2002/1014014 | 21. July 2003<br>Data requirement fulfilled. The result will be reported in the addendum.<br><br>04. August 2003<br>Data were evaluated in an addendum to volume C.<br><br>03. September 2003<br>It is correct that in the batch CHPHNP005 (one of seven) the single values for AMTT are a little higher than 0.02% (0.0248, 0.0251, 0.0244, 0.0249). However, the meaning of a maximum content is, that those batches cannot be used for the preparations. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled.<br><br>A discussion followed on whether levels of 0.025% were acceptable, as the cut-off point for the impurity AMTT that was set to 0.020% at the Tox meeting.<br><br>The proposal of the RMS was accepted that if the maximum of 0.020% is exceeded, the batches could not be used for preparation. |

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|---|---|---|---|---|
| 1.2 | Applicant to provide data on the stability of technical material with regard to formation of AMTT. (AIIIA-2.7.3)<br>**A** | July 11, 2003:<br>The storage stability of tritosulforon (BAS 635 H) technical material has been checked in the study PCF 01541 (BASF DocID 1997/11359). The study has shown, that the material is stable at 20 °C and 30 °C over a period of two years. Since tritosulfuron TGAI is stable no additional GLP shelf life study for AMTT has been carried out with TGAI, but studies with separate AMTT determination were done for the formulated product BAS 635 00 H, because the auxiliaries of the formulation can destabilise the active.<br>In study PCF02098 (BASF DocID 2002/1004730 [subm. to RMS and PSD (UK)]) and PCF02096 (BASF Doc ID 2002/1004731 [subm. to RMS and PSD (UK)]) for the formulated product BAS 635 00 H a very minor increase of AMTT content (0.05 to 0.08 % ) over two years has been observed. | 21. July 2003<br>The increase of AMTT is negligible. Data requirement fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 1.3 | Applicant to provide validated methods and nitrosamine quantification as part of 5 batch analysis. (AIIA-4.1)<br>**A** | July 11, 2003:<br>The report “Determination of total N-Nitrosoamine content in "BAS 635 H CHPHNP0001-0007" was submitted to RMS (and to PSD (UK) under national submission):<br>BASF DocID 2002/1014559<br><br>The report contains in chapter 3 the validation of the analysis method for determination of nitrosoamine. | 21. July 2003<br>The report was submitted and the validation data will be reported in the addendum. Data requirement fulfilled.<br><br>2003-09-05<br>Data were evaluated in the addendum 2 to vol. 4 (05.09.2003). | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |
| | The RMS confirmed that methods used to quantify water and chloride ions were well established and the meeting agreed that further validation of these methods was not required. (AIIA-4.1) | | | Overview Meeting (16.09.2003):<br>Fulfilled |

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|---|---|---|---|---|
| 1.4 | Applicant to justify technical specification against 5 batch analysis. (AIIA-1.11) | July 11, 2003:<br>The current specification was drafted according to the results of the old batch analysis and tox batch results. These batches are listed in BASF DocID 2001/1003808 [EU Dossier J II 1.9 / 1]<br>A new specification according the new batch analysis is currently under discussion. | 04.08.03<br>see 1.1 | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion. |
| | Open point 1.0:<br>RMS to include actual values and amend the endpoint sheets (AIIA-2.3.1) | | 04.08.03<br>The end points are updated. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |
| | Open point 1.1:<br>RMS to include actual values and amend the endpoint sheets (AIIA-2.7) | | 04.08.03<br>The end points are updated. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |
| | Open point 1.2:<br>RMS to amend end point sheets in line with section B2. (AIIA-2.9.3) | | 04.08.03<br>The end points are updated. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |

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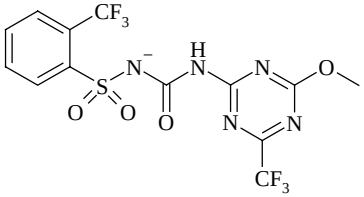
|---|---|---|---|---|
| | Open point 1.3:<br>RMS to liaise with Fate colleagues to check for inclusion of the ionic species in the reporting table. (AIIA-2.9.4) | | 22.08.03<br>The ionic species is:<br>  | Overview Meeting (16.09.2003):<br>Open point fulfilled. |
| | Open point 1.4:<br>RMS to check whether ASTM E 1518-93 test method addresses physical properties with the adjuvant when in dilution then no further data will be needed. If it does not then this will be a data gap to be addressed at MS level (AIIIA-2) | | 21. July 2003<br>ASTM E 1518-93 is a dynamic method which reports physical properties of the tank mixtures as particle size, foam, etc.<br>Open point fulfilled. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |

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|---|---|---|---|---|
| 1.5 | Applicant to supply data to address the attrition potential of the preparation at MS level. (AIIIA-2.8.6.3)<br>**MS** | July 11, 2003:<br>Data on attrition of the formulated product BAS 635 00 H have been included into the dossier Annex III A 2.8.6/1:<br>BASF Doc ID 1997/10398 | 21. July 2003<br>Method FK81/2 corresponds with CIPAC MT 178.2. The differences between both methods are the attrition time (3 times longer for FK81/2) and the mesh size of the sieves (MT 178.2 and FK81/2, 125 µm and 50 µm, respectively).<br>The result of the test according to FK81/2 was 99.4 % attrition resistance.<br>Data requirement fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |
| 1.6 | Applicant to supply shelf life data with indication of AMTT formation. Study must be GLP compliant. (AIIIA-2.7.3)<br>**A** | July 11, 2003:<br>Shelf life data have been submitted to RMS (and to PSD (UK) under national submission):<br>BASF DocID 2002/1004730<br>BASF DocID 2002/1004731 | 21. July 2003<br>See point 1.2. Data requirement fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |
| 1.7 | Applicant to address when the buffer should be used, i.e. to identify those matrices which could give low recoveries and hence would require the addition of buffer prior to extraction. (AIIA-4.2.1)<br>**A** | July 11, 2003:<br>For unknown samples, the addition of Tris(hydroxymethyl)-aminomethane puffer solution S9 (e.g. 5 g) is recommended prior to macerisation. | 2003-07-21<br>Requirement fulfilled | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 1.8 | Validation data for high water and acid crops to be provided at MS level, because this is a sulphonylurea and the nature of the risk assessment. (AIIA-4.2.1)<br>**MS** | July 11, 2003:<br>See attached document BASF DocID 2003/1001356 | 2003-07-21<br>To be evaluated on member state level. | Overview Meeting (16.09.2003):<br>Data requirement to be dealt with at Member State level. |
| | ~~Open point 1.5:~~<br>Message to ECCO 138 (residues):<br>for residue meeting to note that monitoring methods for parent and AMTT are available. (AIIA-4.2.1) | July 11, 2003:<br>Suitable and fully validated data generation methods for plants are available for the parent molecule BAS 635 H and AMTT. Both methods allow the exact and accurate quantitation of the residue after BAS 635 H application. The data obtained can be used as basis for consumer dietary risk assessments.<br>Since BAS 635 H is regarded as the only relevant residue by the notifier for MRL enforcement purposes, the parent method was additionally validated in an independent laboratory according to the EU guidelines. | 2003-07-21<br>Methods are available for parent and for AMTT. No method is available for the metabolite M02.<br><br>In case AMTT will be included in the residue definition for monitoring purposes an ILV will be required for determination of AMTT in foodstuff of plant and/or of animal origin.<br><br>In case metabolite M02 will be included in the residue definition for monitoring purposes a method and an ILV will be required for determination of M02 in foodstuff of plant and/or of animal origin. | Overview Meeting (16.09.2003):<br>No action needed<br><br>Two new data requirements were proposed (1.9 and 1.10). |

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|---|---|---|---|---|
| 1.9 | Notifier to supply analytical methods and an ILV for AMTT<br>(Data requirement inserted during the Overview Meeting) | | | |
| 1.10 | Notifier to supply analytical methods and an ILV for MO2<br>(Data requirement inserted during the Overview Meeting) | | | |
| | Open point ~~1.6~~ 1.5:<br>RMS to identify the analytes in the appropriate sections of the end point sheets. (AIIA-4.2) | | 2003-07-21<br>List of end points is updated. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |
| | Open point ~~1.7~~ 1.6:<br>RMS to update end point sheets with appropriate end points for all the analytes. (AIIA-4.2.3) | July 11, 2003:<br>The LOQ for parent and all metabolites included in the water method are 0.05 µg/kg and therefore meet the requirements. | 2003-07-21<br>List of end points is updated.<br>For the metabolite M02 the mean recovery at the 0.05 µg/L level in surface water is lower than the required range. The recovery at the 0.5 µg/L level is within the range and therefore the limit of quantification.<br>If the metabolite M02 is relevant to the environment than further validation may be needed according to the relevant concentrations with impact on non target organisms. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |

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# Evaluation table Tritosulfuron (Hb)



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## 2. Environmental fate and behaviour

| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | | Section 2<br>Data requirements: 6<br>Open points: 1 |

## Evaluation table Tritosulfuron (Hb)



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|---|---|---|---|---|
| 2.1 | Metabolite 635M19 was major under anaerobic conditions. For Annex I inclusion, anaerobic conditions are only considered relevant for autumn uses and this proposed use is for application in the spring. Although not required for Annex I inclusion, some MSs may wish to further consider the relevance of 635M19.<br>(IIA 7.1.1.1.2) **MS** | July 18, 2003:<br>Metabolite 635M19 was a major metabolite in the anaerobic soil metabolism studies. In the reports it was discussed that the compound was unstable and attempts failed to isolate the compound by fractionation of HPLC peaks. The same compound was also found in the aqueous hydrolysis study at pH 9. It was suggested to be the product of a nucleophilic displacement of methoxy group by a hydroxyl group. It decomposed readily to 635M01 (BH 635-4). Attempts to synthesize 635M19 were not successful because the compound was unstable. In summary, 635M19 is an intermediate and unstable metabolite that decomposes readily to 635M01. Synthesis and in depth investigations are therefore neither needed nor possible. Additionally, anaerobic conditions are not expected for spring uses. | 24.07.2003<br>Comment of the notifier is accepted. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 2.2 | The RMS is to discuss with the applicant including more transparent information on the field dissipation trials, the standardisation approach taken for the field DT50 values and their acceptability for use in the groundwater risk assessment, before considering whether more data should be requested.<br>(IIA 7.1.1.2.2) **A** | July 18, 2003:<br>To be discussed on meeting on 22 Jul 2003 at UBA..<br><br>July 28, 2003:<br>An expert meeting with the UBA has taken place on 22 July 2003: BASF will provide more transparent information on the standardization approach and the parameter selection for groundwater risk assessment to the RMS to enable the RMS to prepare an amendment/change of the monograph after the ECCO overview meeting. A manageable submission date would be November 2003 (see no. 2.6). | 24.07.2003<br>The notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Further information will be submitted in November 2003. |

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|---|---|---|---|---|
| 2.3 | Applicant is to recalculate the PECsoil values using worst case field DT50 values, instead of DT50 values normalised to 15°C.<br>(IIIA 9.1.3) **A** | July 18, 2003:<br>In the course of the national submission in Germany PECsoil calculations with uncorrected worst case field DT50 (BAS 635 H, 635M02), uncorrected worst case laboratory DT50 (635M04) and worst case assumptions (635M03, 635M01) were conducted (BASF DocID 2002/1000216). Since reliable estimations of uncorrected field DT50 could not be provided for all metabolites in the original studies the chosen approach is reasonable. Together with the assumed crop interception of 0% and assumed formation fraction of 100% for all metabolites this provides a worst case estimation of the PECsoil for BAS 635 H and its soil metabolites. | 24.07.2003<br>PEC values still need to be recalculated. If no reliable DT50s from field studies were available, data from laboratory studies should taken into account. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Some information was submitted by the notifier but further information is still needed. |
| 2.4 | Applicant is to recalculate the PECsed values using the standard EU assumptions of 5 cm sediment depth and 1.3 g/cm$^3$ bulk density.<br><br>(IIA 9.2.3) **A** | July 18, 2003:<br>New PECsed values for a sediment thickness of 5 cm were calculated in an amendment (BASF DocID 2003/1009268) to the original report, which is provided. The bulk density of 1.3 g/cm3 had already been used in the original report. | 24.07.2003<br>Accepted. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 2.5 | The applicant should repeat FOCUS groundwater modelling using scenarios representative of neutral and alkaline soils and associated sorption values to reflect the possible effect of pH on adsorption in the PECgw calculations.<br><br>Dependent on the outcome of this, consideration would also be given to requesting a lysimeter study using a soil of higher pH, using methodology appropriate to include detection of the metabolite 635M04, either dual radiolabelling or a specific cold analytical method.<br>(IIIA 9.2.1) A | July 18, 2003:<br>Detailed statistical analyses showed that a "postulated" dependence of the $K_{f,oc}$-values of tritosulfuron from the pH-values was not a "true" correlation in a scientific sense (plausible cause - effect relation) but is caused by a cross correlation between the $K_{f,oc}$ and the organic carbon content on the one hand and the organic carbon content and the pH-values on the other hand. This statement is supported by the fact that after an inclusion of newly measured sorption data for tritosulfuron in soils with high pH-values the previously postulated dependency between $K_{f,oc}$ of tritosulfuron and soil pH can not be identified anymore.<br>It can be concluded that the sorption parameters of BAS 635 H (tritosulfuron) and metabolites BH 635-2, BH 635-3, BH 635-4 and BH 635-5 are not depending on the pH-values. The lysimeter studies are therefore reliable higher tier leaching experiments independent of soil pH.<br>(see BASF DocID 2003/1005456) | 24.07.2003<br>Comment concerning the pH-dependence of the $K_{OC}$ is valide. According to that, the lysimeter is representing a realistic worst case szenario, at least for German conditions.<br>However, to assess the leaching for the different European environmental conditions, the notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group for all relevant szenarios. | Overview Meeting (16.09.2003):<br>Data requirement to be dealt with at Member State level.<br><br>A new data requirement (2.9) was proposed during the Overview Meeting. |

**Evaluation table Tritosulfuron (Hb)** *EU RESTRICTED* Doc. SANCO/10397/2002 rev. 0-3 (16.09.03)
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|---|---|---|---|---|
| 2.6 | The RMS is to discuss with the applicant the comments made by ECCO 137 (Fate) on the acceptability of the standardised field DT50 values used in the FOCUS groundwater model and to consider the appropriate degradation parameters to be used in the model. Transparent information is to be provided on the degradation parameters used in the repeated FOCUS calculations.<br>(IIIA 9.2.1) **A** | July 18, 2003:<br>To be discussed on meeting on 22 Jul 2003 at UBA.<br><br>July 28, 2003:<br>An expert meeting with the UBA has taken place on 22 July 2003: BASF will provide more transparent information on the standardization approach and the parameter selection for groundwater risk assessment to the RMS to enable the RMS to prepare an amendment/change of the monograph after the ECCO overview meeting. A manageable submission date would be November 2003 (see no. 2.2). | 24.07.2003<br>The notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Data will be submitted in November 2003. |

## Evaluation table Tritosulfuron (Hb)

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| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| 2.7 | The applicant is to address the potential of the soil metabolites 635M01, 635M02, 635M03, and 635M04 to contaminate groundwater at > 0.1 µg/l and their relevance in accordance with the latest guidance on relevant metabolites.<br><br>(IIIA 9.2.1) | July 18, 2003:<br>635M01, 635M02 and 635M03 showed in the lysimeter studies yearly average concentrations >0.1 µg/l. In the PECGW calculations 635M01 and 635M02 also showed values >0.1 µg/l in some scenarios. The assessment on the relevance of 635M01 and 635M02 is currently pending, awaiting the results of ongoing toxicity studies. 635M03 has been checked for relevance according to the Relevant Metabolite Guidance document rev.10 and is defined to be not relevant. 635M04 is relevant from the toxicological point of view, but the concentrations in ground water determined in lysimeter studies and estimated by PEC calculations were below 0.1µg/l | 24.07.2003<br>The notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group and address the relevance of the metabolites that might exceed the 0.1 µg/L limit. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion. |

## Evaluation table Tritosulfuron (Hb)



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|---|---|---|---|---|
| 2.8 | The applicant should also address the relevance of the plant metabolite 635M17, detected in the lysimeter leachate (using acidic soil), at concentrations >0.1 µg/l in individual samples.<br>(IIIA 9.2.1) **A** | July 11, 2003:<br>635M17 was detected in individual leachate samples in concentrations >0.1µg/l (< 0.75 µg/l), but the highest yearly average concentration was never greater than 0.08 µg/l. The leaching behaviour of BAS 635 H and metabolites is not pH dependent, as discussed above. Therefore the sandy lysimeter soil with low organic carbon content represents a worst case scenario. | 24.07.2003<br>Comment of the notifier is reliable and accepted. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |
| | Open point 2.1:<br>RMS is to consider whether the aerobic DT50 of 96 days estimated for metabolite 635M02 using TopFit modelling is reliable, given the lack of degradation seen in the laboratory (aerobic) degradation study.<br>(IIA 7.1.1.2.1) | July 18, 2003:<br>The aerobic DT50 of 635M02 as determined by the chosen fitting procedure with Topfit (BASF DocID 1998/10662 [EU Dossier II A 7.1.1.2.1/10]) is not very reliable, a refinement of the estimation might improve the reliability. Nonetheless, the DT50 of 96 days from this study was not used in PECgw (BASF DocID 2000/1018546 [EU Dossier III A 9.2.1/1]) or PECsoil (BASF DocID 2002/1000216 []) calculations. Instead the DT field values were used. | 24.07.2003<br>List of end points will be amended.<br>In addition to that, the Notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group. | Overview Meeting (16.09.2003):<br>Open point still open.<br><br>This open point is linked to data requirement 2.1.<br><br>A new data requirement (2.9) was proposed during the Overview Meeting. |

## Evaluation table Tritosulfuron (Hb)



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|---|---|---|---|---|
| 2.9 | Notifier is requested to submit a revised PELMO calculation according to the recommendations of the FOCUS groundwater group<br><br>(This data requirement was inserted during the Overview Meeting) | | | |

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|---|---|---|---|---|
| | Open point 2.2:<br>RMS is to provide more information on the number of chromatographic peaks and the concentration of the biggest peak for the non-identified radioactivity (NIR) detected in the lysimeter leachate.<br>(IIA 7.1.3.3.) | July 18, 2003:<br>The total number and maximum concentration of individual chromatographic peaks of the non-identified radioactivity (NIR) in the leachate of lysimeters treated with BAS 635 H was re-investigated exemplary with lysimeter 18 of study 37537. This was the double-treated BAS 635 H lysimeter and it showed the highest concentration of NIR of all lysimeters treated with BAS 635 H.<br>The non-indentified radioactivity can be attributed to very minor individual peaks and to a couple of inhomogeneous chromatographic regions, in which very polar compounds of low molecular weight are to be expected (s.a. BASF DocID 2003/1009267) | 24.07.2003<br>Comment of the notifier is accepted. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |

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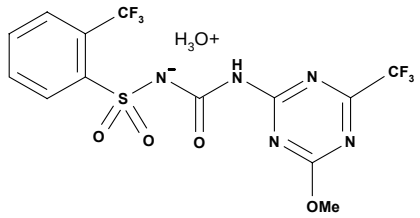
|---|---|---|---|---|
| | Message from ECCO 137 (Fate) to ECCO 139 (Ecotox) and to ECCO 140 (Overview):<br>The ecotoxicological and toxicological relevance of metabolite, 635M01, which was still increasing in water and sediment phases at the end of the water-sediment study, needs to be considered.<br>(IIA 7.2.1.3.2) | July 18, 2003:<br>s. eval. 139: conclusion by ECCO 139 (Ecotox):<br>Ecotoxicology of M01 not relevant. | 24.07.2003<br>The risk for benthic and sediment-dwelling organisms arising from metabolite M01 (BAS 635-4) is covered by the risk assessment for tritosulfuron, because in the submitted tests with aquatic organisms M01 was less toxic than tritosulfuron. | Overview Meeting (16.09.2003):<br>Fulfilled |
| | ECCO 137 (Fate) experts noted that at ECCO 135 (Chemistry) a requirement was set for the applicant to address the ionic species of dissociated tritosulfuron. | July 18, 2003:<br>Tritosulfuron dissociates into single charged anionic form and hydrated Proton:<br>  <br> | 24.07.2003<br>Comment is acceptable. | Overview Meeting (16.09.2003):<br>Fulfilled |

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## 3. Ecotoxicology

| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | | Section 3<br>Data requirements: 5<br>Open points: 3 |

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|---|---|---|---|---|
| 3.1 | The applicant to define the risk to mammals from AMTT using toxicology end points.<br>(IIIA 10.3)<br>~~Open point 3.1:~~<br>~~RMS to convert toxicity values into daily dose values.~~ | July 11, 2003:<br>For consumer dietary risk assessment, a 100 % conversion from BAS 635 H into AMTT and 635M02 is assumed (see point 5.1).<br>Metabolites have been tested on N-transformation in two field soils. This test system is considered in the scientific community as the more susceptible one compared to that of C-transformation. Turnover rates deviated from those in the untreated control by only +4.2% to -6.5% after 28 days (OECD trigger: +/- 25%).<br>FURTHERMORE, THE TERRESTRIAL GUIDANCE DOCUMENT (SANCO/10329/2002 REV.2 FINAL) READS THAT STUDIES WITH METABOLITES ON MICROFLORA ARE NO LONGER REQUIRED AND FOCUS IS ONLY PUT ON EARTHWORMS.<br><br>It is concluded that additional tests on C-transformation should be waived. | 24.07.2003<br>This comment might address point 3.4, but not this point.<br>We propose the Notifier to recalculate the risk to mammals (and birds) according to the actual Guidance Document for birds and mammals taking into account the risk that might arise from AMTT. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>The notifier will amend the information in Column B. Risk assessment has been done and will be submitted to RMS. |

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| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | Open point 3.1:<br>RMS to convert toxicity values into daily dose values.<br>(IIIA 10.1) | September 1, 2003<br>The daily doses for the short-term dietary and reproduction studies in birds have been calculated based on the study data on food consumption and body weight:<br>BASF DocID 1997/10355, quail:<br>LC50 > 5000 mg/kg diet (> 981 mg/kg b.w./day)<br>BASF DocID 1997/11137, mallard:<br>LC50 > 5000 mg/kg diet (> 1504 mg/kg b.w./day)<br>BASF DocID 1999/11108, mallard:<br>NOAEL = 300 mg/kg diet (42.4 mg/kg b.w./day)<br>BASF DocID 1998/10621, quail:<br>NOAEL = 1000 mg/kg diet (90 mg/kg b.w./day) | 24.07.2003<br>We propose the Notifier to recalculate the risk to mammals (and birds) according to the actual Guidance Document for birds and mammals taking into account the risk that might arise from AMTT. | Overview Meeting (16.09.2003):<br>Open point still open.<br><br>This open point is linked to data requirement 3.1. |

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|---|---|---|---|---|
| | Open point 3.2:<br>RMS to clarify if nominal or mean measured concentrations were used in the aquatic studies.<br>(IIA 8.2, IIIA 10.2)<br>~~Message from ECCO 137 (Fate):~~<br>~~Additional data for MO1 were not considered necessary.~~ | July 11, 2003:<br>As a general principal, the results are based on nominal concentrations if those are confirmed by analytical measurements (i.e. ± 20 % of theoretical values); else results are based on mean measured concentrations.<br>In this case the analytical investigations showed very good fit of the nominal concentrations in all studies with the as (usually ± 5 - 10 % of nominal). Therefore the respective results were based on nominal concentrations. Only in some studies with metabolites, there was some further degradation during the course of the study. In these cases mean measured concentrations were used. | 24.07.2003<br>Comment accepted. End points will be verified taking the ECCO comments into account. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |
| | Message from ECCO 137 (Fate) to ECCO 140 (Overview):<br>Additional data for MO1 were not considered necessary. | | | Overview Meeting (16.09.2003):<br>Fulfilled |

## Evaluation table Tritosulfuron (Hb)



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|---|---|---|---|---|
| | Open point 3.3:<br>RMS to update end point table with respect to ESCORT I value for *T. pyri*.<br>(IIIA 10.5) | | 24.07.2003<br>List of end points will be amended. | Overview Meeting (16.09.2003):<br>Open point fulfilled.<br><br>RMS informed the meeting that the comment in Column C was incorrect. |

## Evaluation table Tritosulfuron (Hb)



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|---|---|---|---|---|
| 3.2 | The long-term risk to earthworms for MO1, MO2, MO3 and MO4 (AMTT) metabolites to be addressed. The plateau concentration in the environment must be covered.<br>(IIA 10.6)<br><br>rapporteur DE | July 11, 2003:<br>3.2 Meanwhile 4 studies on earthworm reproduction are available. NOEC-values are equivalent to the highest concentrations tested. Based on the assumptions made (application rate: 50 g as/ha; other parameters see below) trigger of 5 is met, thus long-term risk to earthworm is highly unlikely.<br>**635M02**: NOEC = 0.05 mg /kg soil<br>(PECini = 0.01 mg/kg; 25 % transformation;<br>mol factor included ; log pow = 1.02 ;<br>study: Lührs, BASF DocID 2002/1012746)<br>**635M03**: NOEC = 0.035 mg /kg soil<br>($PEC_{ini}$ = 0.007 mg/kg; 15 % transformation;<br>mol factor included ; log pow = 0.75 ;<br>study: Lührs, BASF DocID 2002/1012745<br>**635M01**: NOEC = 0.16 mg /kg soil<br>(PECini = 0.032 mg/kg; 60 % transformation;<br>mol factor included ; log pow = 2.59 ;<br>study: Lührs, BASF DocID 2002/1012744)<br>**635M04**: NOEC = 0.015 mg /kg soil<br>(PECini = 0.003 mg/kg; 10 % transformation;<br>mol factor included ; log pow = 1.18 ;<br>study: Lührs, BASF DocID 2002/1012743) | 24.07.2003<br>Studies were not submitted so far, will be evaluated when received. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Studies were submitted to the RMS and will be evaluated. |

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|---|---|---|---|---|
| 3.2 | *continued*<br>The long-term risk to earthworms for MO1, MO2, MO3 and MO4 (AMTT) metabolites to be addressed. The plateau concentration in the environment must be covered. | Updated modelling is to be performed in order to confirm that PECs (plateau) are addressed with 1x test concentrations tested. Data will be submitted in e-fate section. Further, the accumulative potential of the metabolites will be discussed in detail.<br><br>See document BASF DocID 2003/1009263<br>which is going to be submitted in context with BASF` response to the evaluation tables considering e-fate (ECCO 137). | | |
| 3.3 | Regarding the MO4 study, the residues in earthworms should be determined to aid the vertebrate risk assessment<br>(NB This part of the DR is dependent upon the outcome of the results of 3.2).<br>(IIIA 10.1, IIIA 10.3) | July 11, 2003:<br>3.3. Data on 635M04 available did not show any adverse effects on earthworms. Hence residue determination in earthworms is not needed. | 24.07.2003<br>Comment was misinterpreted by Notifier. The possibility of accumulation of the metabolite M04 (AMTT) in earthworms needs to be considered when assessing the risk for birds and other vertebrates. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion. |

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|---|---|---|---|---|
| 3.4 | Data are required to address the risk posed to soil macro-organisms.<br>(IIIA 10.6.2) | July 11, 2003:<br>3.4 Earthworms as an outstanding important representative group of soil dwelling macro-organisms will not be at risk following an application with BAS 635 H and successive formation of metabolites. Additionally, further studies are available on soil arthropod species (Poecilus, Aleochara, Pardosa) showing no adverse effects. Furthermore, major metabolite have been tested on soil microflora (N-transformation) which contribute to organic matter decomposition (OMD) at a considerable extent. Metabolites did not exhibit any adverse influence.<br>It is concluded that single species and functional tests available prove that soil functions such as OMD will not be at risk; hence field study on OMD should be waived. | 24.07.2003<br>Only in some of the studies the metabolites were degraded with a DT90 > 365 days. From laboratory studies and most of the field degradation studies the DT90 values calculated were < 365 days.<br>Depending on the outcome of the long-term risk assessment for earthworms and the results of the tests with soil microorganisms additional tests for effects on organic matter decomposition with the metabolites were not needed. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>This data requirement could be partially dependent on data requirement 3.2. |

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| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| 3.5 | Data are required to address the address risk posed from metabolites to carbon mineralisation<br>(IIIA 10.7)<br>~~Open point 3.4:~~<br>~~RMS to update list of end points.~~ | July 11, 2003:<br>Metabolites have been tested on N-transformation in two field soils. This test system is considered in the scientific community as the more susceptible one compared to that of C-transformation. Turnover rates deviated from those in the untreated control by only +4.2 % to -6.5 % after 28 days (OECD trigger: +/- 25 %).<br>Furthermore, the terrestrial Guidance Document (SANCO/10329/2002 rev. 2 final) reads that studies with metabolites on microflora are no longer required and focus is only put on earthworms.<br><br>It is concluded that additional tests on C-transformation should be waived. | 24.07.2003<br>Comment of the notifier is not accepted. Taking into account the results of the soil degradation studies the effects of the metabolites on soil macroorganisms need to be addressed. It is not comprehensible why the notifier only addressed the effects on N-turnover. The tests on C-mineralisation are still needed to address the effects of the metabolites on soil microflora. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion. |
| | Open point 3.4:<br>RMS to update list of end points concerning carbon mineralisation.<br>(IIIA 10.7) | | 21.08.2003<br>List of end points will be amended when data package is complete. | Overview Meeting (16.09.2003):<br>Open point still open. |

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|---|---|---|---|---|
| | Open point 3.5:<br>RMS to amend reference to field studies in end point table.<br>(IIIA 10.8) | | 24.07.2003<br>List of end points will be amended. | Overview Meeting (16.09.2003):<br>Open point fulfilled.<br><br>RMS informed the meeting that the comment in column C was incorrect. |

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## 4. Mammalian Toxicology

| No. | Column A<br>Conclusions of the ECCO-Peer Review Meeting | Column B<br>Comments from the main data submitter / applicant on the ECCO-Review conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations ECCO-Overview Meeting / Conclusions of the evaluation group |
|---|---|---|---|---|
| | | | | Section 4<br>Data requirements: 5<br>Open points: 2 |
| 4.1 | ~~Open Point 4.1:~~<br>The Notifier to comment on the differences in absorption, distribution and excretion leading to the biphasic and monophasic patterns at the low and high dose levels, respectively.<br>(IIA 5.1) | July 11, 2003:<br>The higher increase than expected in AUC from the low to the high dose level is possibly due to a rapid distribution of the radioactivity into one or more compartments other than plasma which are saturated at the high dose level but not at the low dose level. | July 25, 2003<br>Open point fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |
| | ~~Open Point 4.2:~~<br>Message from ECCO 136 (Mamtox) to ECCO 137 (Fate) and 138 (residues):<br>ECCO residues/Fate and Behaviour Meetings to consider the formation of the metabolites (AMTT, 635 M02, AHTT) in plant and the environment. | | | Overview Meeting (16.09.2003):<br>Fulfilled |

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|---|---|---|---|---|
| rapporteur DE | ~~Open Point 4.3:~~<br>Message from ECCO 136 (Mamtox) to ECCO 137 (Fate) and 138 (residues):<br>For the residues/Fate and Behaviour Meetings to consider, how robust are the methods for determining AMTT in plants and the environment. | July 11, 2003:<br>Suitable and fully validated data generation methods for plants are available for the parent molecule BAS 635 H and AMTT. Both methods allow the exact and accurate quantitation of the residue after BAS 635 H application. The data obtained can be used as basis for consumer dietary risk assessments.<br>Since BAS 635 H is regarded as the only relevant residue by the notifier for MRL enforcement purposes, the parent method was additionally validated in an independent laboratory according to the EU guidelines.<br><br>The robustness of an analyte determined within an analytical method can be expressed with its mean recovery value (accuracy) and the relative standard deviation (precision) obtained in a set of fortified samples. For fortification samples of soil and water, mean values of AMTT between 70 and 110 % and relative standard deviations < 20 % are obtained in several studies. This meets the European guideline requests on accuracy and precision of analytical methods. | July 25, 2003<br>Additionally, to be discussed on meeting on 13 Aug 2003 at BfR.<br><br>August 28, 2003<br>The ECCO meeting 135 noted that methods of analysis are available for AMTT in plant materials. These methods can be considered as suitable, validated and robust methods for determining AMTT.<br>Methods for determination of AMTT in soil and water are not presented yet.<br>Open point not fulfilled. | Overview Meeting (16.09.2003):<br>Message still to be considered.<br><br>Awaiting outcome of RMS discussions. |

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|---|---|---|---|---|
| 4.2 | ~~Open Point 4.4:~~<br>The Notifier to comment on the relevance of exposure to AMTT, and 635MO2 to man (paying special attention to potential for reproductive toxicity).<br>(IIA 5.9) | July 11, 2003:<br>AMTT and 635M02 are considered to represent toxicologically relevant impurities/metabolites. Exposure to AMTT and 635 M02 is expected to be very low based on the proposed specification limits and GAP's. Since both AMTT and 635 M02 were co-tested in studies with tritosulfuron at considerable percentages, all relevant end points including reproduction toxicity are covered and therefore the available toxicological database is considered sufficient for risk assessment.<br><br>**September 1, 2003:**<br>**No agreement to ECCO's assessment of 635 M02's clastogenic potential in vitro ("positive with activation", see endpoint list), s.a. statement of the Study Director (BASF Dioc ID 2003/1014003)]**<br><br>July 11, 2003:<br>**$NOAEL_{AMTT}$ (Reproduction toxicity studies with tritosulfuron batches):**<br>(2gen rat, batch N24) = 0.06 mg/kg bw/dd | July 25, 2003<br>AMTT and 635M02 are considered to represent toxicologically relevant impurities/metabolites.<br>Two 28-day studies were submitted with metabolite 635M02, the results will be reported in the addendum.<br>Data on metabolite 635M01 are still missing, the results will be reported in the addendum.<br>One-generation study with metabolite 635M02 was not required by ECCO and RMS since in the 28-day studies effects on reproductive organs were seen. The results will then be reported in the addendum.<br><br>August 28, 2003:<br>A preliminary chronic risk assessment for consumers has been performed for AMTT and TBSA (see 5.1). For AMTT, a NOAEL of 0.06 mg/kg bw/d has been used, based on the 2-generation study in rats with tritosulfuron (batch N24). With the German intake model, the margin of safety (MOS) was estimated to be about 1600 for raw agricultural commodities and about 300 for | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Awaiting submission of study (ies) to RMS and production of an addendum. |

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|---|---|---|---|---|
| 4.2 | *continued*<br>The Notifier to comment on the relevance of exposure to AMTT, and 635MO2 to man (paying special attention to potential for reproductive toxicity).<br>(IIA 5.9) | (prenatal rat, N12) = 0.29 mg/kg bw/d<br>(prenatal rabbit, N14) = 0.08 mg/kg bw/d<br>**$NOAEL_{TBSA}$ (Reproduction toxicity studies with tritosulfuron batches):**<br>(2gen rat, batch N34) = 0.85 mg/kg bw/d<br>(prenatal rat, N12) = 1.37 mg/kg bw/d<br>(prenatal rabbit, N14) = 2.99 mg/kg bw/d<br>(For details on risk assessment with proposed ADI, AOEL, ARfD see Appendix).<br>Since effects on reproductive organs were noted in a 28-d rat study with TBSA, two one-generation range-finding studies have been started to investigate the potential of TBSA to affect fertility (data considered necessary to address relevance of TBSA as metabolite in groundwater) | processed products. For TBSA a NOAEL of 150 ppm (ca. 15 mg/kg bw/d; based on the 28-day studies with TBSA) has been used. With the German intake model, the margin of safety (MOS) was estimated to be about 40000 for raw agricultural commodities and about 25000 for processed products. Since additional studies with TBSA have been announced by the main data submitter BASF (e.g. a 1-generation study), a revised toxicological evaluation and risk assessment will be presented in an addendum after submission of the data. | |

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|---|---|---|---|---|
| 4.3 | ~~Open Point 4.5:~~<br>The Notifier to comment on the increase of AMTT content in the dosing solution in the bile experiment (Vol. 3, Table B.6.1-16)<br>(IIA 5.1) | July 11, 2003:<br>The increase of AMTT is assumed to have resulted from radiolysis, a phenomenon known to occur with $^{14}C$-radiolabelled molecules. The stability of non-radiolabelled tritosulfuron has been demonstrated in a range of studies which have been summarised in the dossier [Annex III A 2.7.1/1, 2.7.3/1 and 2.7.3/2]. Recent analytical data on shelf-life of the formulation BAS 63500H (Doc ID 2002/1004730 and 2002/1004731[subm. to RMS and PSD (UK)]) show that AMTT is formed only to a very limited degree after 2-yr storage of the formulated product. The tritosulfuron (hydrolytic) stability in spray dilutions of formulated products at different pH levels has also been demonstrated (Doc ID 1999/10894) | July 25, 2003<br>In the DAR there are indications that under acidic conditions and high temperatures the AMTT content is increasing (Vol. 3, pp 425).<br>At the Residues Meeting (ECCO 138) it was stated " *AMTT, however, was also present in rotational crops (see iii) and it was possible that it may also be formed on mixing in the spray tank, especially under* ***alkaline*** *conditions ».*<br>These controversies must additionally be discussed on meeting on 13 Aug 2003 at BfR | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>The main concern is over formation of in the spray tank AMTT giving high levels of AMTT exposure to the operator and as a plant residue. |

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|---|---|---|---|---|
| 4.4 | ~~Open Point 4.6:~~<br>The Notifier to explain why it was not possible to generate a smaller particle size distribution with the as given that it could be done with the formulation.<br>(IIA 5.2.3; IIA 7.1.3) | July 11, 2003:<br>The active substance is ground as part of the formulating process using kaolin and silica gel as inert components, which results in a small MMAD of the formulation aerosol particles. In comparison, the MMAD for the technical active substance (no grinding inerts present) is larger. Otherwise both active substance and the formulation were assessed under the same experimental conditions with all measures taken to achieve as small particle sizes as possible. | July 25, 2003<br>Open point fulfilled.<br>Rat inhalation LC50: 5.4 mg/L air (dust aerosol, 4 h , MMAD: 9.2 µm) | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 4.5 | ~~Data requirement 4.1:~~<br>An a *in vitro* cytogenetics assay with AMTT is required.<br>(IIA 5.8.2) | July 11, 2003:<br>An in-vitro cytogenitic assay with AMTT will be initiated, although BASF feels this data requirement is not justified.<br>(1) No concern from 3 genotoxicity studies with AMTT (Ames test, HPRT test and mouse micronucleus test) and further 5 genotoxicity studies with as batch N24 (2.45 % AMTT)<br>(2) The low specification limit for AMTT (0.02 %) should not trigger any data requirements<br>(3) no evidence of carcinogenicity was found for the as (with low AMTT content) up to 7,000 ppm.<br>(4) A clear NOAEL for AMTT carcinogenicity can be obtained from studies conducted with tritosulfuron batch including 2.45 % AMTT | 25. July 2003<br>The result will be reported in the addendum. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>The main concern is over formation of in the spray tank AMTT giving high levels of AMTT exposure to the operator and as a plant residue. |

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|---|---|---|---|---|
| | Open Point ~~4.7~~ 4.1:<br>RMS to consider additional genotoxicity study with tritosulfuron (*in vivo* assay in rats, comet assay on mammary cells)<br>(IIA 5.4) | July 11, 2003:<br>An additional genotoxicity study with tritosulfuron is considered not necessary, because no evidence of genotoxicity was established for tritosulfuron in a full battery of tests and no evidence of carcinogenicity or effects on the mammary gland were found for tritosulfuron with low AMTT contents at dose levels of up to 7,000 ppm. | 25. July 2003<br>With respect to mammary gland tumour formation rats seem to be more sensitive than mice. The *in vivo* micronucleus assay was conducted in mice.<br>Genotoxicity studies were all performed with the batch containing high amounts of AMTT.<br>Open point still needs to be considered. | Overview Meeting (16.09.2003):<br>Open point still open. |

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|---|---|---|---|---|
| 4.6 | ~~Open Point 4.8:~~<br>The Notifier to comment on the toxicological significance of the increased water consumption seen down to the lowest dose levels (50 and 100 ppm) in the chronic rat studies.<br><br>(IIA 5.5) | July 11, 2003:<br>Increased water consumption at 50 and 100 ppm observed in the supplemental chronic toxicity study (Doc ID 2001/1006061) was slight, transient, not dose-dependent and not reproducible in other chronic toxicity studies at 100 ppm (Doc ID 2001/1006059 and 2001/1006062) or 250 ppm (2001/1006060 and 2001/1006064). Moreover, the urinary volume is not increased up to dose levels of 1,000 ppm (Doc ID 2001/1006061, 2001/1006059 and 2001/1006060). Adverse kidney effects are first observed at feed concentrations of 7,000 ppm tritosulfuron with low AMTT content, and at 3,500 ppm tritosulfuron with high AMTT content. In conclusion, the slightly increased water consumption at 50 and 100 ppm is not considered to be biologically significant. | 25. July 2003<br>Increased water consumption at 50 and 100 ppm did not occur at all investigation points and was not dose-dependent. Therefore, no biological significance is attributed to this finding.<br>Open point fulfilled | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| 4.7 | ~~Open Point 4.9:~~<br>The Notifier to give the rationale for the premature termination of the top dose groups in the chronic rat (BASF doc 2001/1006060 and 2001/1006064) and mouse (BASF doc 2001/1006084) studies<br>(IIA 5.5) | July 11, 2003:<br>The chronic rat and mouse studies were each performed with the N24 batch (high AMTT content) using four dose groups instead of three to ensure the MTD would be included. Marked reductions in body weight gain were observed after 16 months treatment with both 3,500 ppm and 7,000 ppm, which indicated that the MTD would be reached at 3,500 ppm and be most certainly exceeded at 7,000 ppm. It was expected that continuation of treatment would have resulted in further body weight gain reductions, in unnecessary animal suffering, and ultimately in increased mortality without having gained additional, useful information. Given that the OECD test guideline requirements are met by using three dose groups, and that the MTD was clearly reached at 3,500 ppm, there was no point in continuing treatment at 7,000 ppm. | July 25, 2003<br>Comment from the notifier accepted.<br>Open point fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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| 4.8 | ~~Open point 4.10:~~<br>The Notifier to give comment on the use of 3 and 4 different batches during the 12- and 24-month rat studies (BASF doc 2001/1006059; BASF doc 2001/1006062; BASF doc 2001/1006063).<br>(IIA 5.5) | July 11, 2003:<br>When it was decided to repeat the rat long-term studies using tritosulfuron with low AMTT-content, not enough test substance from a single batch was available to last thoughout the 2y study period considering the high dose levels to be tested. Therefore, while new test substance was synthesized, the studies were nevertheless started using available "left-over" amounts of test substance from appropriate batches with low AMTT-content. This procedure was considered not to have compromised the validity of the study results. The possible alternative approach to postpone the experimental part of the study until sufficient amounts of test substance were synthesized would have caused a considerable delay of the registration process and was therefore not pursued. | July 25, 2003<br>Comment from the notifier accepted.<br>Open point fulfilled. | Overview Meeting (16.09.2003):<br>Data requirement fulfilled. |

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|---|---|---|---|---|
| | Open Point ~~4.11~~ 4.2:<br>RMS to provide details of the 28- day studies on 635 M01 and 635 M02 in the new addendum<br>(IIA 5.8) | | July 25, 2003<br>The reports of two 28-day studies on metabolite 635M02 were submitted. Results on the study with 635M01 are still missing. All results will be reported in the addendum. | Overview Meeting (16.09.2003):<br>Open point still open. |
| 4.9 | ~~Data requirement 4.2:~~<br>Repeat-dose oral toxicity study with metabolite 635 M01 in rats of at least 28 days of duration each and at least 10 animals/sex/group (investigation parameters according to a 90-day oral toxicity study in rodents / revised OECD guideline 408). Dose levels selected should be based on the dose levels tested in the most relevant short-term studies with the parent compound.<br>(IIA 5.8) | July 11, 2003:<br>The 635 M01 28-d rat study is ongoing (current status: in-life part completed, histopathological examination ongoing; preliminary results (clinical signs, clinicochemistry, haematology, necroscopy, organ weight determinations) indicate no evidence of toxicity up to 3900 ppm (the highest dose tested). The study report is expected to be available at the end of 2004.<br><br>The 28-day studies on 635 M02 have already been submitted (Doc ID 2003/1004048 and 2003/1004049) | July 25, 2003<br>see open point 4.2<br><br>**Input from ECCO 137:** The soil metabolites 635M01, 635M02 and 635M03 all showed potential to contaminate groundwater ≥0.1 µg/l. Plant metabolite 635M17 also appeared in the lysimeter leachate at high concentrations. Therefore, the relevance of these metabolites needed to be addressed. Metabolite 635M04 (AMTT) was toxicologically relevant and was possibly a major metabolite in field soil. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Data and addendum on some metabolites are awaited. Necessity to address M03 and M17 needs to be considered. |

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|---|---|---|---|---|
| 4.10 | ~~Data requirement 4.3:~~<br>The Notifier must address the possibility of the formation of AMTT and it's metabolites in tank mix (including the effect of adding the specified adjuvant). | July 11, 2003:<br>The tritosulfuron (hydrolytic) stability in spray dilutions of formulated products at different pH levels has also been demonstrated (Doc ID 1999/10894) | July 25, 2003<br>Additionally, to be discussed on meeting on 13 Aug 2003 at BfR<br><br>August 28, 2003:<br>Technical tritosulfuron (BAS 635 H) contains up to 0.02 % AMTT. In the formulated product BAS 635 00 H a very minor increase of AMTT content over 2 years has been observed (from 0.05 % to 0.08 % at 20 °C). In spray dilutions of the formulated product the AMTT content increased from 0.026 % to 0.11 % within 48 h at temperatures <25 °C and pH > 4. The formation of AMTT in spray dilutions may, however, increase considerably at temperatures above 25 °C and/or pH < 4. | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>Work should be carried out under field conditions rather than laboratory conditions. A protocol needs to be established in collaboration with the RMS. |

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**5. Residues**

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|---|---|---|---|---|
| | | | | Section 5<br>Data requirement: 1<br>Open points: 1 |
| 5.1 | There is concern that a number of toxic metabolites (eg. AMTT and 635M02) are found for which there is insufficient information on their source (eg. impurities, formed during tank mixing, formed in plant metabolism).<br>Further information is required, including details of the effects of the proposed adjuvant on the amount and nature of the residue.<br>(IIA, 6.1 and 6.7) **A** | July 5, 2003:<br>The amount of AMTT formed during tank mixing is under simulated worst case conditions of acidic pH of 5.5 of the spray broth not larger than 0.1 % of parent BAS 635 H in 48 hours (see BASF Doc ID 1999/10894). Since BAS 635 H is hydrolytically cleaved to equal amounts, a conclusion on the levels of 635M02 is also possible. The amounts of 635M02 are comparable to the levels of AMTT (< 0.1 %):<br><br>In the maize metabolism study, no AMTT and 635M02 was found in any matrix. Key degradation steps are hydroxylation of the phenyl ring system followed by glucosidation and cleavage of the triazine ring system resulting in the metabolite 635M01. | July 23, 2003:<br>The corresponding document (BASF Doc ID 1999/10894) has been submitted. This contains information only on the formation of the hydrolysis product AMTT. The conclusion of the notifier concerning the content and formation of both metabolites AMTT and 635M02 in the spray tank is accepted.<br><br>The ongoing study on metabolism of tritosulfuron in wheat plants has not been submitted yet. However, the results reported in advance seem to be plausible to answer the question of a possibly different metabolism pathway in maize or wheat. No significant differences have been found based on the new study on wheat including the adjuvant "Dash HC" instead of BAS | Overview Meeting (16.09.2003):<br>Data essential for unconditional Annex I inclusion.<br><br>The results will be available in April 2004. |

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|---|---|---|---|---|
| 5.1 | *continued*<br>There is concern that a number of toxic metabolites (eg. AMTT and 635M02) are found for which there is insufficient information on their source (eg. impurities, formed during tank mixing, formed in plant metabolism).<br>Further information is required, including details of the effects of the proposed adjuvant on the amount and nature of the residue.<br>(IIA, 6.1 and 6.7) **A** | A wheat metabolism study with BAS 635 H was initiated in fall 2003. The application was performed in December 2003. The test substance BAS 635 H (two treatment groups: phenyl and triazine label) was applied in form of a WG formulation to wheat plants (BBCH GS 37-39) at the intended use rate of 50 g as/ha. As adjuvant Dash HC was added to the spray solution. Due to the properties and its ingredients (phosphoric acid), Dash HC can be regarded as reasonable worst case.<br><br>According to the preliminary results available, the metabolism of BAS 635 H in wheat is comparable to the metabolism in maize. The TRR levels of both labels were in the same range for all matrices.<br>In wheat grain, the TRRs were very low (0.005 mg/kg). In all matrices investigated up to now, the metabolite patterns were almost identical indicating that the direct cleavage of the sulfonyl urea bridge is not key degradation step in wheat. The parent molecule BAS 635 H formed the major | 152 00 S (contained in the commercial product BAS 635 00 H) compared to the results on maize plants.<br>Provided these results are confirmed after submission of the expected document the requirements are considered fulfilled. | |

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| | | part of the MeOH extractable radioactivity. Second most ambundant peak is the glucoside 635M13.<br><br>In the supervised residue trials no BAS 635 H and AMTT was found in the edible parts (kernels) of maize and cereals. In the feed items (green matter and straw), the residue levels of both compounds were significantly below 0.050 mg/kg. In cereal straw, maximum 0.023 mg/kg BAS 635 H was found whereas the AMTT levels were at maximum 0.013 mg/kg. The levels of both compounds detected in maize straw were even lower.<br>According to the notifier's opinion sufficient information is available on the formation and the amount of the residues. | | |
| | Open point 5.1:<br>RMS to provide a new risk assessment, to include metabolite AMTT (and 635MO2 if toxicologically relevant).<br>(IIA, 6.1 and 6.7) | July 5, 2003:<br>Chronic dietary risk assessments were performed for BAS 635 H (ADI: 0.06 mg kg bw), AMTT (ADI: 0.0003 mg/kg) and TBSA (synonym: 623M02, 0.0046 mg/kg bw).<br>In a first approach, the dietary risk was assessed taking the supported crops | August 28, 2003:<br>Refering to point 4.2 metabolite 635M02 is considered to represent a toxicologically relevant impurity/metabolite. The chronic consumer risk assessement estimations based on the German and the WHO intake models, the given | Overview Meeting (16.09.2003):<br>Open point still open. |

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| | | plus animal matrices into account. For BAS 635 H and TBSA, residue levels of 0.010 mg/kg were assumed whereas for AMTT, the LOQ of the data generation method (0.001 mg/kg) was used. The assessment for the infant (UK diet) reflects the worst case:<br>BAS 635 H: 2 % ADI (see M-II; 6.9)<br>AMTT: 38 % ADI<br>TBSA: 24 % ADI<br>A sufficient margin of safety exists for all three compounds.<br>The inclusion of potentially present residues from succeeding crops (annually planted vegetable crops, same levels as above) does not have any major impact on the total exposure. The calculation resulted in only slightly higher values.<br>AMTT: 42 % ADI<br>TBSA: 27 % ADI<br>The TMDI calculations using several worst case estimates (see also 5.2) clearly indicate that the consumer is not at risk | residue levels and an ADI value of 0.06 mg/kg bw for tritosulfuron, NOAEL values of 0.06 mg/kg bw/d for AMTT and 15 mg/kg bw/d for 635M02 [see point 4.2] lead to the following results :<br>German model:<br>for RAC:<br>Tritosulfuron (0.01 mg/kg): 0.6 % ADI<br>AMTT (0.001 mg/kg): 0.06 % NOAEL → margin of safety approx. 1600<br>635M02 (0.01 mg/kg): 0.002 % NOAEL → margin of safety approx. 40 000<br><br>for processed products, 100% conversion from tritosulfuron into AMTT and 635M02 assumed:<br><br>AMTT (0.005 mg/kg): 0.3 % NOAEL → margin of safety approx. 300<br>635M02 (0.015 mg/kg): 0.004 % NOAEL → margin of safety approx. 25 000<br><br>WHO model:<br>for RAC:<br>Tritosulfuron (0.01 mg/kg): 0.4 % ADI | |
| | *continued*<br>Open point 5.1:<br>RMS to provide a new risk assessment, to include | | | |

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|---|---|---|---|---|
| | metabolite AMTT (and 635MO2 if toxicologically relevant).<br>(IIA, 6.1 and 6.7) | | AMTT (0.001 mg/kg): 0.04 % NOAEL → margin of safety approx. 2500<br>635M02 (0.01 mg/kg): 0.001 % NOAEL → margin of safety approx. 70 000<br><br>for processed products, 100% conversion from tritosulfuron into AMTT and 635M02 assumed:<br>AMTT (0.005 mg/kg): 0.2 % NOAEL → margin of safety approx. 500<br>635M02 (0.015 mg/kg): 0.002 % NOAEL →margin of safety approx. 47 000<br><br>These worst case assessments show very low contributions of the intake of residues of parent compound based on expected maximum residue levels of 0.01 mg/kg in food of plant origin. For AMTT and 635M02 a preliminary risk assessment was conducted, a further refinement needs confirmation by required toxicological studies with the metabolites. At this time, one could conclude that there might be a sufficient safety margin for the residue intake by consumers of all analytes of | |

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| | | | concern. | |
| | Message from ECCO 138 (Residues) to ECCO 140 (overview meeting):<br>A statement on the toxicity of metabolite 635M02 is required. | July 11, 2003:<br>A statement on the toxicity of 635M02 is given in the attachment (BASF Doc ID 2003/1013468) | August 28, 2003:<br>Refering to point 4.2 metabolite 635M02 is considered to represent a toxicologically relevant impurity/metabolite. Therefore it is concluded that this metabolite has to be included in the residue definition for risk assessment for food of plant origin. | Overview Meeting (16.09.2003):<br>If the metabolites are of concern they need to be included in the residue definition. |
| ~~5.2~~ | Open point 5.2<br>Given the significance of processing in consumption of cereal products, the RMS should establish a NEDI value (possibly including 635M02, pending confirmation of toxicological relevance)<br>(IIA, 6.9) | July 5, 2003:<br>For consumer dietary risk assessment, a 100 % conversion from BAS 635 H into AMTT and 635M02 is assumed (see point 5.1). | July 23, 2003:<br>It is referred to the given statements under open point 5.1. Based on the sufficient safety margin derived from the preliminary TMDI calculation there is no requirement at this point of time to establish a NEDI value. | Overview Meeting (16.09.2003):<br>Open point fulfilled. |

**Areas of concern**:

Section 1: Impact of impurity on other areas of the risk assessment (note impurity is also a metabolite).

Section 2: Potential for contamination of groundwater at concentrations $\geq$ 0.1 µg/l and relevance of the metabolites, 635M01, 635M02, 635M03, 635M04 and 635M17 needs to be addressed.

Section 3: Possible risk to soil organisms from metabolites.

rapporteur DE

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Section 4: The main area of concern was the possible formation of AMTT and/or it's metabolite's in treated crops, the environment and in solution in the spray tank.

Section 5: General concern expressed over the amount, nature and unknown source(s) of toxic metabolites in plant metabolism. Further information required.

Overview Meeting (16.09.2003):

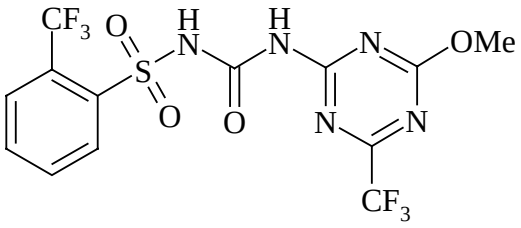
- There is no provisional authorisation until now.
- The latest study (wheat metabolism study) will be available by April 2004, if no range-finding study is needed. If a range-finding study is necessary, it will be submitted by August 2004. Its necessity will be discussed between the RMS and the notifier.
- Two confidential addenda (Annex C) have been prepared. All information will be included in one final addendum, which will be prepared as soon as the outstanding information has been submitted to the RMS. The addendum will be discussed in the Working Group (evaluation) either in September 2004 or at the end of 2004, depending on when the studies will be available.

# COMPLETE LIST OF ENDPOINTS: TRITOSULFURON

## 1 Physical chemical properties section

| | |
|---|---|
| Active substance (ISO Common Name) | Tritosulfuron (ISO) |
| Function (*e.g.* fungicide) | Herbicide |
| Rapporteur Member State | Federal Republic of Germany |

**Identity** (Annex IIA, point 1)

| | |
|---|---|
| Chemical name (IUPAC) | 1-(4-methoxy-6-trifluoromethyl-1,3,5-triazin-2-yl)-3-(2-trifluoromethyl-benzenesulfonyl)urea |
| Chemical name (CA) | N-[[[4-methoxy-6-(trifluoromethyl)-1,3,5-triazin-2-yl]amino]carbonyl]-2-(trifluoromethyl)benzene-sulfonamide |
| CIPAC No | 735 |
| CAS No | 142469-14-5 |
| EEC No (EINECS or ELINCS) | not assigned |
| FAO Specification (including year of publication) | n. a. (new active substance) |
| Minimum purity of the active substance as manufactured (g/kg) | 950 (based on a pilot plant) |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg) | AMTT: 0.2 g/kg (max. content) |
| Molecular formula | $C_{13}H_9F_6N_5O_4S$ |
| Molecular mass | 445.3 |
| Structural formula |  |

**Physical-chemical properties** (Annex IIA, point 2)

| | | |
|---|---|---|
| Melting point (state purity) | 166.5 – 169.4 °C (99.8 %) | |
| Boiling point (state purity) | – | |
| Temperature of decomposition | approx. 340 °C | |
| Appearance (state purity) | white crystalline solid, odourless (99.8 %) | |
| Relative density (state purity) | $d_4^{20}$ = 1.7 (99.8 %) | |
| Surface tension | 64.6 mN/m 1.0 % (w/w) (93.8 %, at 20 °C)<br>71.3 mN/m 0.5 % (w/w) and<br>71.0 mN/m 2.0 % (w/w) (99.8 %, both at 20 °C) | |
| Vapour pressure (in Pa, state temperature) | < 1.0 x $10^{-5}$ (20 °C), 99.8 % | |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) | < 1 x $10^{-4}$ (20 °C) | |
| Solubility in water (g/L or mg/L, state temperature) | 38.6 mg/L pH 4.7 (deionised water)<br>78.3 mg/L pH 10.2<br>0.94 mg/L pH 1.7 | <br><br>all at 20 °C |
| Solubility in organic solvents (in g/L or mg/L, all at 20 °C). | Toluene<br>Dichloromethane<br>Methanol<br>Aceton<br>Ethyl acetate<br>Acetonitrile<br>1-Octanol<br>2-Propanol<br>olive oil | < 10 g/L<br>25 g/L<br>23 g/L<br>250 - 300 g/L<br>83 - 86 g/L<br>90 - 94 g/L<br>13 g/L<br>< 10 g/L<br>< 10 g/L |
| Partition co-efficient (log $P_{OW}$) (state pH and temperature) | 2.93 non ionised form<br>2.93 pH 2.7, 2.85 pH 4, 0.62 pH 7, -2.38 pH 10<br>all at 20 °C | |
| Hydrolytic stability ($DT_{50}$) (state pH and temperature) | pH 4: 39 - 56 d (25 °C), pH 5: > 62 d (25 °C)<br>pH 7: > 62 d (25 °C)<br>pH 9: 17 - 20 d (25 °C) | |
| Dissociation constant | $pK_a$ 4.69 (20 °C), 99.7 % | |
| UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) | pH 0.5:<br>202 nm (ε 24440), 212 nm (ε 21412), 226 nm (ε 25172), 254 nm (ε 7037), 300 nm (ε 212)<br>pH 6.7:<br>202 nm (ε 18331), 215 nm (ε 18515), 237 nm (ε 21494), 260 nm (ε 13021), 300 nm (ε 144)<br>pH 13.3:<br>219 nm (ε 18151), 235 nm (ε 15825), 260 nm (ε 11908), 300 nm (ε 1890) | |
| Photostability ($DT_{50}$) (aqueous, sunlight, state pH) | stable over 15 days at pH 5 and pH 7 | |
| Quantum yield of direct phototransformation in water at λ > 290 nm | < 1.05 x $10^{-4}$ (pH 5)<br>< 2.23 x $10^{-4}$ (pH 7) | |
| Flammability | not highly flammable | |

| | |
|---|---|
| Explosive properties | none |

## List of uses evaluated for Annex I inclusion

| Crop and/ or situation (a) | Member State or Country | Product name | F G or I (b) | Pests or Group of pests Controlled (c) | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks: (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Type (d-f) | Conc. of g as/kg (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | interval between applications (min) | kg as/hL min max | water L/ha min max | kg as/ha min max | | |
| Maize | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 12-18 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |
| Maize | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 12-18 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |
| Cereals, winter | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 21-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |
| Cereals, winter | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 21-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |
| Cereals, summer | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 13-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |
| Cereals, summer | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 13-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | pending finalisation of the assessment |

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/L
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions/supported by available data or not

**Classification and proposed labelling** (Annex IIA, point 10)

| | |
|---|---|
| with regard to physical/chemical data | none |
| with regard to toxicological data | R43 |
| with regard to fate and behaviour data | none |
| with regard to ecotoxicological data | R50, R53 |

### 1.1.1.1 Appendix III.2: Chapter 2 (methods of analysis)

**Analytical methods for the active substance** (Annex IIA, point 4.1)

| | |
|---|---|
| Technical as (principle of method) | HPLC-UV |
| Impurities in technical as (principle of method) | HPLC-UV |
| Plant protection product (principle of method) | HPLC-UV |

**Analytical methods for residues** (Annex IIA, point 4.2)

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | Tritosulfuron:<br>HPLC-UV 0.01 mg/kg (wheat: grain, plant, straw; maize: grain, plant, straw)<br>LC-MS/MS 0.001 mg/kg (wheat: grain, middlings; maize: grain)<br>Metabolite AMTT:<br>GC-MS 0.001 mg/kg (wheat: grain, forage, hay straw; maize: grain) |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | Tritosulfuroan:<br>HPLC-UV 0.01 mg/kg (milk, muscle, fat, egg, kidney, liver)<br>Metabolite AMTT:<br>GC-MS 0.001 mg/kg (milk, muscle, fat, kidney, liver) |
| Soil (principle of method and LOQ) | Tritosulfurron, M01, M02, M03, AMTT:<br>LC-MS/MS 0.001 mg/kg<br>Tritosulfuron:<br>GC-ECD 0.001 mg/kg<br>Metabolites M01, M02, M03<br>GC-ECD 0.01 mg/kg |
| Water (principle of method and LOQ) | Tritosulfuron, M01, M03<br>LC-MS/MS 0.05 µg/L (surface / drinking water)<br>GC-MS 0.05 mg/kg (drinking water)<br>Metabolite M02<br>GC-MS 0.5 µg/L (surface / drinking water)<br>0.05 µg/L (drinking water)<br>Metabolite AMTT:<br>GC-MS 0.05 µg/L (surface / drinking water) |
| Air (principle of method and LOQ) | HPLC-UV 2.8 µg/m³ |
| Body fluids and tissues (principle of method and LOQ) | not relevant |

rapporteur DE

## 2 Environmental Fate and behaviour

**Route of degradation (aerobic) in soil** (Annex IIA, point 7.1.1.1.1)

| | |
|---|---|
| Mineralisation after 100 days | 5 % after 90 d, (21 % after 358 d), triazine label<br>0 % after 91 d (< 3 % after 358 d), phenyl label<br>0 % after 122 d, phenyl label |
| Non-extractable residues after 100 days | 17-25 % after 90 d (both labels)<br>43 % after 358 d (phenyl label)<br>28 % after 358 d (triazine label) |
| Relevant metabolites - name and/or code, % of applied (range and maximum) | 635M01 max. 56 % after 60 d (n = 5)<br>635M03 max. 15 % after 120 d (n = 5)<br>635M02 max. 23 % after 118 d (n = 5)<br>635M04 (AMTT) max 6 % after 90 d (n = 1) |

**Route of degradation in soil - Supplemental studies** (Annex IIA, point 7.1.1.1.2)

| | |
|---|---|
| Anaerobic degradation | tritosulfuron: 33 % (phenyl) and 24 % (triazine) remained after 120 d, bound residues 6 %<br>major metabolites:<br>635M01 max. 53 % after 120 d<br>635M19 max. 16 % after 28 d |
| Soil photolysis | after 15 d: 78 - 81 % tritosulfuron remained, 3 - 5 % bound residues, < 1 % $CO_2$, no major metabolites (> 10 %) |

**Rate of degradation in soil** (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

| | |
|---|---|
| Method of calculation | ModelMaker 3.0.3/3.0.4 (Cherwell Scientific Publishing Limited); TOPFIT pharmacokinetic analysis; Timme and Frehse, 1st order kinetics, $DT_{50}$ of metabolites calculated from studies with tritosulfuron |
| Laboratory studies (range or median, with n value, with $r^2$ value) | $DT_{50lab}$ (20 °C, aerobic) in days: |

| soil | as | 635M01 | 635M02 | 635M03 | 635M04 |
|---|---|---|---|---|---|
| Li35b | 31/32 | 110/184 | 96 | 347/737 | 98 |
| Lufa2.2 | 16 | 65 | 37 | 203 | nc |
| US-soil | 19 | 59 | 44 | 32 | nc |
| Bruch | 38 | 23 | 28 | nc | nc |
| Canad. | (124) | 44 | nc | nc | nc |
| Speyer | 20 | 115 | nc | nc | nc |
| mean | 26 | 86 | 51 | 330 | - |
| $r^2$ (low) | 0.970 | 0.886 | 0.900 | 0.893 | 0.962 |
| $r^2$ (high) | 0.997 | 0.979 | 0.951 | 0.977 | - |

| |
|---|
| tritosulfuron: $DT_{90lab}$ (20 °C, aerobic): 53 - 125 d (409 d) |
| tritosulfuron: $DT_{50lab}$ (10 °C, aerobic, calc.): 42 - 271 d |
| tritosulfuron: $DT_{50lab}$ (20 °C, anaerobic): 61 - 82 d |
| degradation in the saturated zone: not relevant |

| | |
|---|---|
| Field studies (state location, range or median with n value) | $DT_{50f}$: 10 locations (3 Germany, 2 Spain, Sweden, California, South Dakota, Indiana, Texas )<br>method of calculation: EU: 1st order, USA: non-linear<br>tritosulfuron: EU: 11 - 21 d, USA: 3 - 15 d<br>635M01: EU: 30 - 336 d, USA: 65 - > 621 d<br>635M02: EU: 36 - 216 d, USA: 76 - > 614 d<br>635M03: EU: nc, USA: 53 - > 417 d<br>635M04 (AMTT): EU: 11 - 133 d, USA: 5 - 69 d |
| | tritosulfuron $DT_{90f}$: EU: 37 - 77 d |
| Soil accumulation and plateau concentration | based on degradation studies, no accumulation is expected |

**Soil adsorption/desorption** (Annex IIA, point 7.1.2)

| | |
|---|---|
| $K_f$ /$K_{oc}$<br>$K_d$ | soils: 5 German, 2 US |

| | Koc | (mean) | $K_F$ | 1/n |
|---|---|---|---|---|
| tritosulfuron | 4 - 11 | (7) | 0.04 – 0.16 | 0.76 - 0.98 |
| 635M01 | 18 – 184 | (89) | 0.32 – 1.47 | 0.90 - 0.96 |
| 635M02 | 16 – 79 | (40) | 0.18 – 0.52 | 0.92 - 0.98 |
| 635M03 | 18 – 51 | (30) | 0.11 – 0.42 | 0.85 - 0.97 |
| 635M04 | 8 – 57 | (21) | 0.1 – 0.29 | 0.90 - 0.98 |

| | |
|---|---|
| pH dependence (yes / no) (if yes type of dependence) | yes, decreasing sorption with increasing pH |

**Mobility in soil** (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

| | |
|---|---|
| Column leaching | guideline: BBA IV, 4-2<br>precipitation: 200 mm in 2 days<br>86 % in leachate (all unchanged tritosulfuron) |
| Aged residues leaching | guideline: BBA IV, 4-2<br>precipitation: 200 mm in 2 days, aeging 30 d<br>40 % in leachate (mostly unchanged tritosulfuron) |
| Lysimeter/ field leaching studies | 5 lysimeters, location: Limburgerhof, RP, Germany<br>application: 50 g ($^{14}$C-phenyl) as/ha in spring, 1$^{st}$ year (lys 5, 6, 16, 17), 1$^{st}$ + 2$^{nd}$ year (lys 18)<br>annual rainfall incl. add. irrigation (mm): 802 - 836<br>annual leachate volume (l): 200 - 487<br>annual average concentrations (highest concentration during the study) [µg/L]: |

| | lys 5 | lys 6 | lys 16 | lys 17 | lys 18 |
|---|---|---|---|---|---|
| tritosulfuron | 0.04 | 0.02 | 0.02 | 0.02 | 0.04 |
| 635M01 | 0.54 | 0.39 | 0.1 | 0.36 | 1.04 |
| 635M02 | 0.09 | 0.09 | 0.02 | 0.06 | 0.11 |
| 635M03 | 0.26 | 0.20 | 0.07 | 0.22 | 0.57 |
| 635M04* | < 0.05 | < 0.05 | < 0.1 | < 0.05 | < 0.05 |
| 635M17 | 0.05 | 0.02 | 0.05 | 0.03 | 0.08 |
| NIR | 0.42 | 0.32 | 0.59 | 0.64 | 0.68 |
| $^{14}$C (as-eq.) | 1.44 | 1.22 | 0.75 | 1.13 | 2.50 |

| |
|---|
| * analysed by GC/MS, not possible to detect as $^{14}$C, because of the labeling position |

**PEC (soil)** (Annex IIIA, point 9.1.3)

| | |
|---|---|
| Method of calculation | First order kinetics (with the worst case field half-life standardised to 15° C): tritosulfuron: 49 d, 635M01: 133 d, 635M02: 171 d, 635M03: 187 d, 635M04: 34 d<br>Maximum amounts of metabolites formed in field studies (% of as): 635M01: 30 %, 635M02: 27 %, 635M03: 16 %, 635M04: 19 %<br>5 cm soil layer, bulk density of 1.5 kg/L |
| Application rate | Single application to maize and cereals<br>tritosulfuron: 0.05 kg as/ha (no interception) |

| **PEC$_{(s)}$** (mg/kg) | | Single application Actual | Single application twa | Single application Actual | Single application twa | Single application Actual | Single application twa |
|---|---|---|---|---|---|---|---|
| | | **tritosulfuron** | | **635M01** | | **635M02** | |
| Initial | | 0.067 | 0.067 | 0.020 | 0.020 | 0.018 | 0.018 |
| Short term | 24 h | 0.066 | 0.066 | 0.020 | 0.020 | 0.018 | 0.018 |
| | 2 d | 0.065 | 0.066 | 0.020 | 0.020 | 0.018 | 0.018 |
| | 4 d | 0.063 | 0.065 | 0.020 | 0.020 | 0.018 | 0.018 |
| Long term | 7 d | 0.060 | 0.063 | 0.019 | 0.020 | 0.017 | 0.018 |
| | 28 d | 0.045 | 0.055 | 0.017 | 0.019 | 0.016 | 0.017 |
| | 50 d | 0.033 | 0.048 | 0.015 | 0.018 | 0.015 | 0.016 |
| | 100 d | 0.016 | 0.036 | 0.012 | 0.016 | 0.012 | 0.015 |

| **PEC$_{(s)}$** (mg/kg) | | Single application Actual | Single application twa | Single application Actual | Single application twa |
|---|---|---|---|---|---|
| | | **635M03** | | **635M04 (AMTT)** | |
| Initial | | 0.011 | 0.011 | 0.013 | 0.013 |
| Short term | 24 h | 0.011 | 0.011 | 0.012 | 0.013 |
| | 2 d | 0.011 | 0.011 | 0.012 | 0.012 |
| | 4 d | 0.011 | 0.011 | 0.012 | 0.012 |
| Long term | 7 d | 0.010 | 0.011 | 0.011 | 0.012 |
| | 28 d | 0.010 | 0.010 | 0.007 | 0.010 |
| | 50 d | 0.009 | 0.010 | 0.005 | 0.008 |
| | 100 d | 0.007 | 0.009 | 0.002 | 0.005 |

**Route and rate of degradation in water** (Annex IIA, point 7.2.1)

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) (state pH and temperature) | pH 4 (25 °C):<br>tritosulfuron: 56 d (phenyl), 39 d (triazine)<br>635M01 (11 % after 35 d)<br>635M02 (26 % after 35 d)<br>635M04 (22 % after 31 d) |
| | pH 7 (25 °C):<br>tritosulfuron : > 62 d<br>635M04 : no hydrolysis in sterile buffer at pH 6.5 and 7.5 and in natural water pH 8.1 |
| | pH 9 (25 °C):<br>tritosulfuron: 20 d (phenyl), 17 d (triazine)<br>635M01 (34 % after 31 d)<br>635M19 (28 % after 23 d) |

| | | |
|---|---|---|
| Photolytic degradation of active substance and relevant metabolites | | Suntest apparatus, 15 days continuous irradiation<br>tritosulfuron: stable (15 d, 22 °C, pH 5 and 7)<br>635M01: sensitised water : $DT_{50}$ = 3.6 d |
| Readily biodegradable (yes/no) | | no |
| Degradation in water/sediment | - $DT_{50}$ water | 32 - 67 d |
| | - $DT_{90}$ water | 107 - n.c. |
| | - $DT_{50}$ whole system | 36 - 77 d |
| | - $DT_{90}$ whole system | n.c. |
| Mineralization | | ≤ 5 % after 100 d |
| Non-extractable residues | | < 5 % - 10 % after 100 d |
| Distribution in water / sediment systems (active substance) | | sediment: max. 14 % after 14 d, max. 13 % after 28 d |
| Distribution in water / sediment systems (metabolites) | water: 635M01 | max. 28.1 % after 100 d |
| | 635M02 | max. 15 % after 14 d |
| | 635M03 | max. 3.8 % after 100 d |
| | sediment: 635M01 | max. 35 % after 100 d |
| | 635M02 | max. 0.9 % after 100 d |
| | 635M03 | max. 4.8 % after 100 d |

**PEC (surface water)** (Annex IIIA, point 9.2.3)

| | |
|---|---|
| Method of calculation | static water body, depth: 30 cm<br>tritosulfuron: 1st order kinetics (67 d), metabolites: no degradation<br>Maximum amounts of metabolites formed (% as):<br>in water-sediment study (drift-entry): 635M01: 28 %, 635M02: 15 %, 635M04: not formed in w/s-study.<br>Mean of maximum amounts of metabolites formed in field soil (runoff entry): 635M01: 14 %, 635M02: 15 %, 635M04: 12 %<br>The $PEC_{actual}$ are based on the worst case of the $PEC_{initial}$ calculated for spray drift and runoff events |
| Application rate | Single application of 0.050 kg as/ha to maize and cereals |
| Main routes of entry | **Spray Drift:**<br>2.77 % of the applied as (90th percentiles for field crops with 1 m buffer)<br>**Runoff:**<br>0.5 % of the concentration (as) in soil at day 3 after application or 0.5 % of the max. concentrations of metabolites observed reach the water body with a volume of 130000 l.<br>Interception of 25 % of the applic. rate and a dilution factor of 0.5 are considered for calculation. |

| **PEC**$_{(sw)}$ | Single application Actual | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| | **tritosulfuron (drift entry)** | | **635M01 (drift entry)** | |
| Initial | 0.46 | 0.46 | 0.103 | 0.103 |
| Short term 24 h | 0.46 | 0.46 | 0.103 | 0.103 |
| 2 d | 0.45 | 0.46 | 0.103 | 0.103 |
| 4 d | 0.44 | 0.45 | 0.103 | 0.103 |
| Long term 7 d | 0.43 | 0.45 | 0.103 | 0.103 |
| 14 d | 0.40 | 0.43 | 0.103 | 0.103 |
| 21 d | 0.37 | 0.41 | 0.103 | 0.103 |
| 28 d | 0.35 | 0.40 | 0.103 | 0.103 |
| 42 d | 0.30 | 0.37 | 0.103 | 0.103 |

| **PEC**$_{(sw)}$ | Single application Time weighted average | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| | **635M02 (runoff)** | **635M02 (drift)** | **635M04 (runoff)** | |
| Initial | 0.055 | 0.034 | 0.039 | 0.039 |
| Short term 24 h | 0.055 | 0.034 | 0.039 | 0.039 |
| 2 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 4 d | 0.055 | 0.034 | 0.039 | 0.039 |
| Long term 7 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 14 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 21 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 28 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 42 d | 0.055 | 0.034 | 0.039 | 0.039 |

**PEC (sediment)**

| | |
|---|---|
| Method of calculation | sediment: 2 cm layer, 1.3 kg/L bulk density (wet sediment), entry route as for surface water (drift and runoff), pattern of decline reflecting that measured in the water sediment study. |
| Application rate | Single application of 0.050 kg as/ha to maize and cereals |

| **PEC**$_{(sed)}$ [mg/kg] | tritosulfuron drift (1 m buffer) | 635M01 drift (1 m buffer) |
|---|---|---|

| | | |
|---|---|---|
| maximum $PEC_{sed}$ | 0.00066 at day 28 | 0.00042 at day 100 |

**PEC (ground water)** (Annex IIIA, point 9.2.1)

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter ) | lysimeter studies and modelling using FOCUS-PELMO v.1.1.1 (all locations) and MACRO FOCUS v1.2.1 (Chateaudun) |
| Application rate | 0.05 kg as/ha |
| **$PEC_{(gw)}$** | |
| Maximum concentration | lysimeter: tritosulfuron: 0.07 µg/L<br>635M01: 1.24 µg/L<br>635M02: 0.18 µg/L<br>635M03: 0.91 µg/L<br>635M04: 0.09 µg/L<br>635M17 0.17 µg/L<br>modelling: not calculated |
| Average annual concentration | lysimeter: tritosulfuron: 0.04 µg/L<br>635M01: 1.04 µg/L<br>635M02: 0.11 µg/L<br>635M03: 0.57 µg/L<br>635M04: < 0.1 µg/L<br>635M17: 0.08 µg/L<br>modelling: see below |

| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v.1.1.1 |
| Application rate | 0.05 kg as/ha to winter cereals in early spring with 50 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/L) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun | 01/04 | 0.008 | 0.01 | 0.156 | 0.097 | 0.001 |
| Hamburg | 01/04 | 0.066 | 0.040 | 0.218 | 0.166 | 0.008 |
| Jokionen | 01/06 | 0.082 | 0.018 | 0.216 | 0.129 | 0.008 |
| Kremsmünster | 01/04 | 0.079 | 0.059 | 0.207 | 0.153 | 0.014 |
| Okehampton | 01/04 | 0.089 | 0.067 | 0.189 | 0.152 | 0.014 |
| Piacenza | 01/04 | 0.074 | 0.071 | 0.232 | 0.178 | 0.009 |
| Porto | 10/03 | 0.006 | 0.002 | 0.058 | 0.032 | 0.001 |
| Sevilla | 10/03 | 0.000 | 0.000 | 0.007 | 0.002 | 0.000 |
| Thiva | 10/03 | 0.000 | 0.001 | 0.105 | 0.053 | 0.000 |

| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v1.1.1 |
| Application rate | 0.05 kg as/ha to spring cereals 3 weeks after emergence with 25 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/L) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun | 31/03 | 0.004 | 0.006 | 0.179 | 0.097 | 0.001 |
| Hamburg | 22/04 | 0.063 | 0.046 | 0.324 | 0.237 | 0.009 |
| Jokionen | 01/06 | 0.143 | 0.018 | 0.296 | 0.166 | 0.009 |
| Kremsmünster | 22/04 | 0.075 | 0.065 | 0.305 | 0.213 | 0.011 |
| Okehampton | 22/04 | 0.099 | 0.064 | 0.309 | 0.224 | 0.017 |
| Porto | 31/03 | 0.002 | 0.001 | 0.060 | 0.025 | 0.000 |

| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v1.1.1 |
| Application rate | 0.05 kg as/ha to maize 3 weeks after emergence with 25 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/L) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun* | 22/05 | 0.015 | 0.012 | 0.212 | 0.124 | 0.002 |
| Hamburg | 26/05 | 0.084 | 0.048 | 0.347 | 0.240 | 0.013 |
| Kremsmünster | 26/05 | 0.050 | 0.033 | 0.273 | 0.183 | 0.006 |
| Okehampton | 15/06 | 0.083 | 0.050 | 0.298 | 0.223 | 0.011 |
| Piacenza* | 05/06 | 0.062 | 0.091 | 0.254 | 0.218 | 0.010 |
| Porto | 22/05 | 0.001 | 0.000 | 0.036 | 0.010 | 0.000 |
| Sevilla* | 28/03 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Thiva* | 11/05 | 0.000 | 0.000 | 0.060 | 0.023 | 0.000 |

*Scenarios with irrigation

| | |
|---|---|
| Method of calculation and type of study | Modelling using MACRO FOCUS v1.2.1<br>Location: Chateaudun |
| Application rate | 0.05 kg as/ha to winter cereals in early spring (50 % interception), spring cereals 3 weeks after emergence (25 % interception), to maize 3 weeks after emergence (25 % interception) |

| Crop | Application time (julian days) | Predicted 80th percentile concentration (µg/L) | |
|---|---|---|---|
| | | tritosulfuron | 635M04 (AMTT) |
| Winter cereals | 91 | 0.012 | 0.002 |
| Spring cereals | 90 | 0.017 | 0.003 |
| Maize | 144 | 0.064 | 0.009 |

**Fate and behaviour in air** (Annex IIA, point 7.2.2, Annex III, point 9.3)

| | |
|---|---|
| Direct photolysis in air | no data, not required |
| Quantum yield of direct phototransformation | < 1.05 x 10-4 (pH 5)<br>< 2.23 x $10^{-4}$ (pH 7) |
| Photochemical oxidative degradation in air | calculation according to Atkinson (AOP, ver 1.51, Syracuse), $DT_{50}$: 5.2 h (12 h-day) |
| Volatilization | from plant surfaces: 3 % (24 h) |
| | from soil: 2 % (24 h) |

**PEC (air)**

| | |
|---|---|
| Method of calculation | not calculated due to low volatility and rapid photochemical oxidative degradation |

**$PEC_{(a)}$**

| | |
|---|---|
| Maximum concentration | not calculated |

**Definition of the residue** (Annex IIA, point 7.3)

| | |
|---|---|
| Relevant to the environment | tritosulfuron and metabolites 635M01, 635M02 and 635M03<br>Metabolites 635M01, 635M02 and 635M03 show no biological activity. The ecotoxicological risk assessment 635M01, 635M02 and 635M03 is not yet finished. The toxicological relevance of 635M01 and 635M02 is open. |

**Monitoring data, if available** (Annex IIA, point 7.4)

| | |
|---|---|
| Soil (indicate location and type of study) | none |
| Surface water (indicate location and type of study) | none |
| Ground water (indicate location and type of study) | none |
| Air (indicate location and type of study) | none |

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

| | | |
|---|---|---|
| Hazard symbol | | Not discussed |
| Risk phrase | | Not discussed |
| Safety phrase | | Not discussed |

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## 3 Ecotoxicology section

**Effects on terrestrial vertebrates** (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

| | |
|---|---|
| Acute toxicity to mammals | $LD_{50}$ = 4700 mg as/kg bw/d (rat) (batch no. N12) |
| Reproduction toxicity to mammals | NOAEL 600 mg as/kg diet (two-generation-test, rat) (batch no. N34) |
| Acute toxicity to birds | $LD_{50}$ > 2000 mg as/kg bw/d (mallard duck, bobwhite quail) (batch no. N24) |
| Dietary toxicity to birds | $LC_{50}$ > 5000 mg as/kg diet (mallard duck, bobwhite quail) (batch no. N24) |
| Reproductive toxicity to birds | NOAEL = 300 mg as/kg diet (one-generation-test, mallard duck) (batch no. N24) |

**Toxicity/exposure ratios for terrestrial vertebrates** (Annex IIIA, points 10.1 and 10.3)

| Application rate (kg as/ha) | Crop | Category (*e.g.* insectivorous bird) | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|---|
| 0.05 kg as/ha | maize/cereals | herbivorous bird | acute | > 1429 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous bird | subacute | 111 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous bird | long-term/ reproduction (one-generation-study) | 53 | 5 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | acute | > 3448 | 10 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | short-term | 431 | 10 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | long-term / reproduction (one-generation-study) | 207 | 5 |
| 0.05 kg as/ha | maize/cereals | herbivorous mammal | acute | 3357 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous mammal | long-term/ reproduction (two-generation-study, rat) | 107 | 5 |

| **Toxicity data for aquatic species (most sensitive species of each group)** (Annex IIA, point 8.2, Annex IIIA, point 10.2) | | | | |
|---|---|---|---|---|
| Group | Test substance | Time-scale | Endpoint | Toxicity (mg/L)* |
| Laboratory tests | | | | |
| *O. mykiss* | as | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *O. mykiss* | as | chronic, 28 d flow-through | Mortality NOEC | 21.5 |
| | as | acute, 48 h, static | Immobilisation $EC_{50}$ | > 100 |
| *D. magna* | as | chronic, 21 d static renewal | Growth NOEC | 56 |
| *A. flos-aquae* | as | chronic 96 h static | Biomass $EC_{50}$ | 0.58 |
| *P. subcapitata* | as | chronic, 72 h static | Biomass $EC_{50}$ | 0.23 |
| *L. gibba* | as | chronic, 7 d static renewal | Fronds $EC_{50}$ | 0.0255 |
| *P. putida* | as | acute | Growth $EC_{50}$ | > 10000 |
| *O. mykiss* | 635M02 (BH 635-2 Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic | Biomass $EC_{50}$ | > 100 |
| *O. mykiss* | 635M03 (BH 635-3, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 48 (m) |
| *D. magna* | " | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | > 100 |
| *O. mykiss* | 635M01 (BH 635-4, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 54 (m) |
| *D. magna* | " | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | > 100 |
| *B. rerio* | 635M04 (BH 635-5, AMTT, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | 170 |
| *D. magna* | ” | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic | Biomass $EC_{50}$ | > 100 |

| | | | | |
|---|---|---|---|---|
| *O. mykiss* | BAS 635 00 H | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | 0.42 |
| *O. mykiss* | 70 g BAS 635 00 H + 1.5 L BAS 15200S | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilisation $EC_{50}$ | > 100 |
| *L. gibba* | " | chronic, 7 d static | Fronds $EC_{50}$ | 0.0355 |
| Microcosm or mesocosm tests | | | | |
| | | | | |

***: with exception of the concentrations signed with (m), all concentrations were given as nominal**

**Toxicity/exposure ratios for the most sensitive aquatic organisms** (Annex IIIA, point 10.2)

| Application Rate (kg as/ha) | Crop | Organism | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|
| 0.05 | field crop | *L. gibba* | chronic | 1 | 54 | 10 |

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) | not relevant; logPow < 3 |
| Annex VI Trigger for the bioconcentration factor | |
| Clearance time ($CT_{50}$)<br>($CT_{90}$) | |
| Level of residues (%) in organisms after the 14 day depuration phase | |

**Effects on honeybees** (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

| | |
|---|---|
| Acute oral toxicity | $LD_{50}$ = 200 µg/bee (active substance)<br>$LD_{50}$ = 121.62 µg/bee (formulation: BAS 63500 H + BAS 15200 S) |
| Acute contact toxicity | $LD_{50}$ = 200 µg/bee (active substance)<br>$LD_{50}$ = > 100 µg/bee (formulation: BAS 63500 H + BAS 15200 S) |

**Hazard quotients for honey bees** (Annex IIIA, point 10.4)

| Application rate (kg as/ha) | Crop | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|---|
| Laboratory tests (active substance) | | | | |
| 0.05 | maize, cereals | oral | 0.25 | 50 |
| 0.05 | maize, cereals | contact | 0.25 | 50 |
| Laboratory tests (formulation: BAS 635 00 H + BAS 15200 S) | | | | |
| 0.05 | maize, cereals | oral | 0.41 | 50 |
| 0.05 | maize, cereals | contact | 0.5 | 50 |

| Field or semi-field tests |
|---|
| Not required |

**Effects on other arthropod species** (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

| Species | Stage | Test Substance | Dose (kg as/ha) | Endpoint | Effect (%) | Annex VI Trigger |
|---|---|---|---|---|---|---|
| Laboratory tests | | | | | | |
| *T. pyri* | protonymphs | BAS 635 00 H + BAS 152 00 S | 0.05<br>0.002 - 0.05 | mortality<br>fertility | 74<br>($LR_{50}$: 28.6 g as/ha) | 30 |
| *T. pyri* (natural substrate) | protonymphs | ” | 0.05 | mortality<br>fertility | 0<br>3.6 | 30 |
| *A. rhopalos.* | imagines | ” | 0.150 | mortality<br>parasitation capacity | 10<br>30 | 30 |
| *C. carnea* | larvae | ” | 0.05 | mortality<br>fertility | 0<br>0 (+ 11) | 30 |
| *P. cupreus* | imagines | ” | 0.05 | mortality<br>food uptake | 0<br>0 | 30 |
| *A. bilineata* | imagines | ” | 0.05 | parasitation capacity | 14 | 30 |
| *Pardosa sp.* | adult | ” | 0.05 | mortality<br>food uptake | 0<br>0 (+ 23) | 30 |

| Field or semi-field tests |
|---|
| Not required |

**Effects on earthworms** (Annex IIA, point 8.4, Annex IIIA, point 10.6)

| | |
|---|---|
| Acute toxicity | $LC_{50}$ > 1000 mg as/kg (technical tritosulfuron)<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M02 (BH 635-2)<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M03 (BH 635-3))<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M01 (BH 635-4))<br>$LC_{50}$ = 671 mg/kg (metabolite 635M04 (BH 635-5))<br>$LC_{50}$ > 34.2 mg as/kg (formulation BAS 635 00 H + BAS 152 00 S) |
| Reproductive toxicity | - |

**Toxicity/exposure ratios for earthworms** (Annex IIIA, point 10.6)

| Application rate (kg as/ha) | Crop | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|
| 0.05 | maize, cereals | Acute | > 510 | 10 |
| 0.05 | maize, cereals | chronic | | 5 |

**Effects on soil micro-organisms** (Annex IIA, point 8.5, Annex IIIA, point 10.7)

| | |
|---|---|
| Nitrogen mineralisation | No effects > 25 % up to 0.35 kg BAS 635 00 H + 6.25 L BAS 152 00 S |
| Carbon mineralisation | No effects > 25 % up to 0.35 kg BAS 635 00 H + 6.25 L BAS 152 00 S |

**Effects on terrestrial non-target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)**

| | |
|---|---|
| Greenhouse test | *Brassica napus* (most sensitive species):<br>$ED_{50}$ 4.3 g BAS 635 00 H + 76.4 ml BAS 152 00 S |
| Extended study, plants moved in the field | *Brassica napus* (most sensitive species):<br>$ED_{50}$ 8.7 g BAS 635 00 H + 126 ml BAS 152 00 S |

**Toxicity/exposure ratios for terrestrial non-target plants (Annex IIIA, point 10.8)**

| Distance from treated area (m) | Drift (%) | Amount of drift (g product/ha) | TER ($ED_{50}$ 4.3 g/ha) | TER ($ED_{50}$ 8.7 g/ha) |
|---|---|---|---|---|
| 1 | 2.77 | 1.94 | 2.2 | 4.5 |
| 5 | 0.57 | 0.399 | 10.8 | 21.8 |

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

| | | |
|---|---|---|
| Hazard symbol | **N** | Dangerous for the environment |
| Risk phrase | **R 50** | Very toxic to aquatic organisms |
| | **R 53** | May cause long-term adverse effects in the aquatic environment |

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## 4 Mammalian toxicology section

NOTEs: FIGURES IN PARENTHESIS INDICATE BATCH NUMBER OF TRITOSULFURON USED IN STUDY (N24 contained 2.4% AMTT other batches contained AMTT ranging from 0.006 – 0.16% w/w)

### 1.2 ENDPOINTS APPLY TO TRITOSULFURON CONTAINING 0.02% AMTT

**Absorption, distribution, excretion and metabolism in mammals** (Annex IIA, point 5.1)

| | |
|---|---|
| Rate and extent of absorption | Rapid (Tmax 0.5h) and complete (> 90 % based on urinary and bile excretion (10 – 27 %) over 48 h)-rats 50 and 500 mg/kg bw |
| Distribution | Widely distributed |
| Potential for accumulation | No potential for accumulation |
| Rate and extent of excretion | Rapid (approx. 80 % via urine and 12 % via feces over 48 h) |
| Metabolism in animals | Limited (hydroxylation at the 4-position of the phenyl ring followed by conjugation; cleavage of the triazine ring and degradation to sulfonamide and sulfonate) |
| Toxicologically significant compounds (animals, plants and environment) | Parent compound and metabolites (especially AMTT (2-amino-4-trifluoromethyl-6-methoxy-1,3,5-triazine and 635 M02) possibly AHTT (major metabolite of AMTT) and 635M02. To be clarified at the residues/Fate and Behaviour Meetings). Data on metabolite 635M01 still outstanding (July 25, 2003) |

**Acute toxicity** (Annex IIA, point 5.2)

| | | |
|---|---|---|
| Rat $LD_{50}$ oral | (N12) | 4700 mg/kg bw |
| Rat $LD_{50}$ dermal | (N12) | > 2000 mg/kg bw |
| Rat $LC_{50}$ inhalation | (N12) | 5.4 mg/L air (dust aerosol, 4 h , MMAD: 9.2 µm) |
| Skin irritation | (N12) | Not irritating |
| Eye irritation | (N12) | Not irritating |
| Skin sensitisation (test method used and result) N12) | | Sensitising (M&K test) R43 |

**Short term toxicity** (Annex IIA, point 5.3)

| | |
|---|---|
| Target / critical effect | Liver, kidney/centrilobular hypertrophy, nephropathy (rat and dog). Urinary bladder and kidney (mouse) |
| Lowest relevant oral overall NOAEL/NOEL* | 12-month, dog (N24): 200 ppm (6 mg/kg bw/d) [calculated level of AMTT: 0.15 mg/kg bw/day] |
| Lowest relevant dermal NOAEL/NOEL* | 28-day (20 exposure), rat (N24): 1000 mg/kg bw no systemic effects |
| Lowest relevant inhalation NOAEL / NOEL | No data - not necessary |

**Genotoxicity*** (Annex IIA, point 5.4)

| | |
|---|---|
| (N24) | No evidence of genotoxic potential in vivo based on a mouse micronucleus assay; clastogenic effect under in vitro conditions. |

**Long term toxicity and carcinogenicity** (Annex IIA, point 5.5)

| | |
|---|---|
| Target / critical effect | Kidney (interstitial nephritis), Liver (pericholangitis) |
| Lowest relevant NOAEL / NOEL* | 2-yr, rat (N24): 100 ppm (5 mg/kg bw/d)<br>[calculated level of AMTT: 0.123 mg/kg bw/day]<br>2-year rat (N59): 1000 ppm<br>18-month mouse: LOAEL 250 ppm (36 mg/kg bw/day) |
| Carcinogenicity* | Mammary gland tumours in female rats at 1000ppm (N24). NOAEL (tumours 250 ppm, 16 mg/kg bw/day)<br>**R 40** |

**Reproductive toxicity** (Annex IIA, point 5.6)

| | |
|---|---|
| Reproduction target / critical effect* | Pup mortality in absence of parental toxicity |
| Lowest relevant reproductive NOAEL / NOEL* | 2-gen. rat: 25 ppm (N24) (2.4 mg/kg bw/d)<br>[calculated level of AMTT: 0.06 mg/kg bw/d]<br>**R61**<br>2-gen. rat: 600 ppm (N34) (40 mg/kg bw/d)<br>[calculated level of AMTT: 0.01 mg/kg bw/d] |
| Developmental target / critical effect | 2-gen. rat: cleft palate in 2 F1a and in 1 F1b pups, agenesia of kidney in F2 pups at 3500/2100 ppm (N24)<br>Developmental rat (N12): Hydrourethers, renal pelves dilatation<br>Developmental rabbit (N14): accessory 13th rib(s) (rabbits). |
| Lowest relevant developmental NOAEL / NOEL | 120 mg/kg bw/d (rat) |

**Neurotoxicity / Delayed neurotoxicity** (Annex IIA, point 5.7)

| | |
|---|---|
| Acute oral and 90-day neurotoxicity* | No signs of neurotoxicity in the presence of general toxicity (rat)<br>NOAELs Acute (N24): 2000 mg/kg, 90 day (N24) 3500 ppm (243 mg/kg bw/d)<br>**(NOAEL General toxicity, 90-d, rat: 100 ppm (7 mg/kg bw/d))** |
| Developmental neurotoxicity | No developmental neurotoxicity (N59) |
| Lowest relevant NOAEL for neurotoxicity* | 90-d, rat: 3500 ppm (243 mg/kg bw/d) |

**Other toxicological studies** (Annex IIA, point 5.8)

| | |
|---|---|
| Supplementary studies with metabolites: | 635M01: $LD_{50}$ oral rat: > 5000 mg/kg bw; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative<br><br>635M02: $LD_{50}$ oral rat: 1000 mg/kg bw; Ames test, CHO-HPRT test: negative, in vitro chromosome aberration test: **positive** (with activation)<br><br>635M03: $LD_{50}$ oral rat: > 5000 mg/kg bw; subchronic study in rats: no effects; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative<br><br>635M17: $LD_{50}$ oral rat: > 2000 mg/kg bw; Ames test, CHO-HPRT test, in vivo mouse micronucleus test: negative<br>Supplementary studies with AMTT (635M04): Toxicokinetic, rats: rapid excretion, major metabolite AHTT (635M11); $LD_{50}$ oral rat: > 200 < 2000 mg/kg bw (ulcer in glandular stomach); no changes in estrus cycle and hormone analysis parameters; Ames test, CHO-HPRT test, mouse micronucleus test: negative; developmental toxicity < 20 mg/kg bw/d; low bonding capacity of tritosulfuron and AMTT to the estrogen receptor in the presence of endogenous estrogens |

**Medical data** (Annex IIA, point 5.9)

| |
|---|
| Limited data (new compound); no human health problems reported |

**Summary** (Annex IIA, point 5.10) **Proposal**

| | Value | Study | Safety factor |
|---|---|---|---|
| ADI (temporary) | 0.06 mg/kg bw | 12-mo dog | 100 |
| AOEL systemic (temporary) | 0.15 mg/kg bw/d | 90-day dog | 100 |
| ARfD | Not allocated | Not necessary | |

**These reference values relate to tritosulfuron containing < 0.02 % AMTT.**

**Dermal absorption** (Annex IIIA, point 7.3)

| |
|---|
| 1 % (concentrate), 2 % (in-use dilution) based on in vitro (rat/human) and in vivo (rat) studies conducted using the commercial formulation |

**Acceptable exposure scenarios** (including method of calculation)

| | |
|---|---|
| Operator<br>Workers<br>Bystanders | The possible formation of AMTT and/or it's metabolite's in the spray tank must be considered.<br>Exposures to be recalculated, as required. |

SUGGESTED CLASSIFICATION AND LABELLING: TRITOSULFURON

**Classification and proposed labelling** (Annex IIA, point 10)

**ATTENTION**. Tritosulfuron (**≤** 0.02% AMTT): Xi, R43

| | |
|---|---|
| with regard to toxicological data | Tritosulfuron (≤ 0.02 % AMTT): Xi, R43<br>AMTT : T, R40, R 48/22, R61 (R64) |

* batch no. N24 is containing 2.45 % AMTT

** AMTT

## 5 Residues section

Appendix III.4: Chapter 4 (residues)

**Metabolism in plants** (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Plant groups covered | maize |
| Rotational crops | lettuce, wheat, carrots, beans |
| Plant residue definition for monitoring | tritosulfuron |
| Plant residue definition for risk assessment | tritosulfuron, AMTT, 635M02 expressed as tritosulfuron (depending on results of new wheat metabolism study) |
| Conversion factor (monitoring to risk assessment) | open |

**Metabolism in livestock** (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Animals covered | goat, hen |
| Animal residue definition for monitoring | tritosulfuron, AMTT expressed as tritosulfuron |
| Animal residue definition for risk assessment | tritosulfuron, AMTT expressed as tritosulfuron |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | Yes |
| Fat soluble residue: (yes/no) | no |

**Residues in succeeding crops** (Annex IIA, point 6.6, Annex IIIA, point 8.5)

| |
|---|
| 30, 120, 365 days plant back interval after application of 60 g as/ha to soil.<br>The total radioactive residues were low for carrot root (≤ 0.011 mg/kg / parent: ≤ 0.001 mg/kg), green beans (≤ 0.005 mg/kg), lettuce head (≤ 0.022 mg/kg/ parent: ≤ 0.006 mg/kg) and wheat grain (≤ 0.019 mg/kg / parent: < 0.001 mg/kg)) after all 3 plant back intervals.<br>In carrot foliage and bean plants only few samples showed residues of tritosulfuron slightly above 0.01 mg/kg.<br>The metabolite AMTT (635M04) was detected in almost all samples of the triazine label but mostly at low absolute concentrations (< 0.01 mg/kg). Only after plant back intervals of 30 days in early samplings of bean plant and wheat forage and in wheat straw amounts in the range of 0.011 - 0.029 mg/kg were found. |

**Stability of residues** (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

| |
|---|
| Food of plant origin (maize grain, maize forage, wheat grain, wheat straw, radish root): tritosulfuron was stable over a period of 3 years. |

**Residues from livestock feeding studies** (Annex IIA, point 6.4, Annex IIIA, point 8.3)

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: yes/no | Poultry: yes/no | Pig: yes/no |
|---|---|---|---|
| Muscle | No ruminant feeding study conducted | No hen feeding study conducted | No pig feeding study conducted. Metabolism in rat and ruminant similar |
| Liver | | | |
| Kidney | | | |
| Fat | | | |
| Milk | | | |
| Eggs | | | |

**Summary of critical residues data** (Annex IIA, point 6.3, Annex IIIA, point 8.2)

| Crop | Northern or Mediterranean Region | Trials results relevant to the critical GAP (a) | Recommendation/comments | MRL | STMR (b) |
|---|---|---|---|---|---|
| Summer barley | N | 7 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 5 x < 0.01 mg/kg | | | |
| Winter barley | N | 11 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 8 x < 0.01 mg/kg | | | |
| Summer wheat | N | 3 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Winter wheat | N | 15 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 10 x < 0.01 mg/kg | | | |
| Durum wheat | S | 6 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Winter rye | N | 1 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Maize | N | 15 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 21 x < 0.01 mg/kg | | | |

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x < 0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

**Consumer risk assessment** (Annex IIA, point 6.9, Annex IIIA, point 8.8)

| | |
|---|---|
| ADI | 0.06 mg/kg bw/d for tritosulfuron with max 0.02 % AMTT |
| TMDI (European Diet) (% ADI) | tritosulfuron 0.61 % (German diet) / 0.35 % (WHO diet)<br>AMTT open, preliminary assessment of MOS<br>635M02 open, preliminary assessment of MOS |
| NEDI (% ADI) | not calculated |
| Factors included in NEDI | - |
| ARfD | Not assigned |
| Acute exposure (% ARfD) | Not applicable |

**Only a preliminary risk assessment for AMTT and 635M02 could be carried out because of lacking data bases.**

**Processing factors** (Annex IIA, point 6.5, Annex IIIA, point 8.4)

| Crop/processed crop | Number of studies | Transfer factor | % Transference * |
|---|---|---|---|
| Not conducted | | | |

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

**Proposed MRLs** (Annex IIA, point 6.7, Annex IIIA, point 8.6)

| | |
|---|---|
| barley, oats, maize, rye, triticale, wheat | 0.01 mg/kg |
| | |

LIST OF STUDIES WHICH WERE SUBMITTED DURING THE EVALUATION PROCESS AND WERE NOT SITED IN THE DRAFT ASSESSMENT REPORT: TRITOSULFURON

**APPENDIX III**

## B.1 Identity B.2 Physical and chemical properties B.3 Data on application and further information B.4 Proposals for the classification and labelling B.5 Methods of analysis

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[1],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| | | | |
| AIIA-1.11 | Foerster, R. | 2002 | Analytical characterization of seven batches tritosulfuron TGAI.<br>BAS,BBA<br>2002/1014014<br>GLP, unpublished<br>CHE2003-222 |
| AIIA-1.11 | Güntner, A. | 2002 | Determination of chloride in "BAS 635 H CHPHNP0001-0007".<br>BAS,BBA<br>2002/1014066<br>not GLP, unpublished<br>CHE2003-224 |
| AIIA-1.11 | Güntner, A. | 2002 | Determination of total N-Nitrosoamine content in "BAS 635 H CHPHNP0001-0007".<br>BAS,BBA<br>2002/1014559<br>not GLP, unpublished<br>CHE2003-223 |
| AIIA-4.2.1 | Bross, M. and Mackenroth, Ch. | 2003 | Validation of the analytical method 405/1: Determination of BAS 635 H (LAB 271 272) in plant matrices.<br>BAS<br>2003/1001356; 130141<br>GLP, unpublished<br>MET2003-330 |
| AIIIA-2.7.3 | König, W. | 2002 | Shelf life in original container at 20°C of the formulation BAS 635 00 H 24 month storage - analytical results.<br>BAS<br>2002/1004731<br>GLP, unpublished<br>PHY2003-458 |

[1] Only notifier listed

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[1],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| AIIIA-2.7.3 | König, W. | 1997 | Storage Stability of PS 271 272: Two year study analytical resul.<br>BAS<br>1997/11359; PCF01541<br>GLP, unpublished<br>PHY2003-475 |
| AIIIA-2.7.3 | König, W. | 2002 | Shelf life in original container at 20°C of the formulation BAS 635 00 H 24 month storage - analytical results.<br>BAS<br>2002/1004730<br>GLP, unpublished<br>PHY2003-457 |
| AIIIA-2.9.2 | Hassink, J. | 1999 | Determination of Reg. No. 231700 (AMTT) in the spray volume of BAS 635 H formulations.<br>BAS<br>99/10894<br>not GLP, unpublished<br>PHY2003-459 |

**Codes of company**

BAS: BASF Aktiengesellschaft
BBA: Biologische Bundesanstalt für Land-und Forstwirtschaft

## B.6 Toxicology and metabolism

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[2],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| | | | |
| AIIA-5.8.2 | Kaspers, U., Deckardt, K., Gembardt, C. and van Ravenzwaay, B. | 2003 | TBSA - Repeated dose oral toxicity study in Wistar rats Administration in the diet for 4 weeks.<br>BAS<br>2003/1004049<br>GLP, unpublished<br>TOX2003-1462 |
| AIIA-5.8.2 | Kaspers, U., Deckardt, K., Gembardt, C. and van Ravenzwaay, B. | 2003 | TBSA - Subacute toxicity study in Wistar rats Administration in the diet for 4 weeks.<br>BAS<br>2003/1004048<br>GLP, unpublished<br>TOX2003-1461 |
| AIIA-5.8.2 | Engelhardt | 2003 | In vitro chromosome aberration assay<br>Comments from the „Pesticide safety directorate“ (PSD), UK.<br>BAS<br>2003/1014003 |
| AIIA-5.10 | Stinchcombe, S.; | 2003 | Tritosulfuron Ecco Evaluation - Position Paper on Open points and Data requirements Related to Mammalian Toxicology.<br>BAS<br>2003/1013468<br>not GLP, unpublished<br>TOX2003-1463 |
| AIIIA-7.2.1.1 | Lungershausen, R.; | 2002 | Risk Assessment for AMTT (Reg No 231700) as an impurity in the active substance BAS 635 H.<br>BAS<br>2002/1004227<br>not GLP, unpublished<br>TOX2003-1474 |

**Codes of company**

BAS: BASF Aktiengesellschaft

[2] Only notifier listed

## B.7 Residue data

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[3],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| | | | |
| AIIIA-8.9 | Westphalen, K.-O. | 2002 | Dossier for the evaluation of the plant protection product - Document M-III, Tier II summaries and assessments of individual tests and studies and groups of tests and studies.<br>BAS<br>BASF DocID 2002/1010460<br>not GLP, unpublished<br>RIP2002-2258 |

**Codes of company**

BAS: BASF Aktiengesellschaft

[3] Only notifier listed

## B.8 Environmental fate and behaviour

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[4],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| | | | |
| AIIA-2.9.1<br>AIIA-7.2.11 | Singh, M. | 2002 | Comments on the question raised by Dr. Aden, BBA re 14C Hydrolysis studies<br>BAS<br>2003/1007842 |
| AIIA-7.1.2 | Gottesbüren, B. | 2003 | Evaluation of the sorption of BAS 635 H - Tritosulfuron and metabolites BH 635-2, BH 635-3, BH 635-4 and BH 635-5 considering the dependency of sorption to soil parameters and sorption kinetics.<br>BAS<br>2003/1005456<br>GLP, unpublished<br>BOD2003-300 |
| AIIA-7.1.2 | Gottesbüren, B. | 2003 | Kinetic evaluation of the adsorption behaviour of the metabolites of BAS 635 H (tritosulfuron): BH 635-2, BH 635-3, BH 635-4 and BH 635-5.<br>BAS,BAS<br>2003/1000991<br>GLP, unpublished<br>BOD2003-171 |
| AIIA-7.1.2 | Gottesbüren, B. | 2003 | Evaluation of the sorption of BAS 635 H - Tritosulfuron and metabolites BH 635-2, BH 635-3, BH-635-4 and BH 635-5 considering the dependency of sorption to soil parameter and sorption kinetics.<br>BAS,BAS<br>2003/1005456; CALC-407<br>GLP, unpublished<br>BOD2003-169 |
| AIIA-7.1.2 | Jene, B. | 2002 | Estimation of effective relevant sorption values of BAS 635 H in soils; study CALC-299.<br>BAS,BAS<br>2001/1015001<br>GLP, unpublished<br>BOD2003-170 |
| AIIA-7.1.2 | Staudenmaier, H. | 2003 | Non-identified radioactivity in Iysimeter leachates of Iysimeters treated with BAS 635 H.<br>BAS<br>2003/1009267; Li 740<br>not GLP, unpublished<br>BOD2003-301 |

[4] Only notifier listed

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[4],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| AIIIA-9.1.3 | Dressel, J. | 2003 | Second Amendment to final report: Calculatio of predicted evironmental concentrations for BAS 635 H and metabolites BH 635-2, BH 635-4 and BH 635-5 in static surface waters (PECsw) and sediment (PECsed) after dift enttry<br>(PECsed) after drift entry.<br>BAS<br>2003-1001039; CALC315<br>not GLP, unpublished<br>BOD2003-304 |
| AIIIA-9.1.3 | Dressel, J. | 2003 | Predicted long term concentrations of the soil metabolites of BAS 635 H (635M01, 635M02, 635M03, 635M04) in soil.<br>BAS<br>2003-1009263; CALC-452<br>not GLP, unpublished<br>BOD2003-306 |
| AIIIA-9.1.3 | Dressel, J. | 2003 | Third Amendment to Final Report: Calculation of Predicted Environmental Concentrations for BAS 635 H and metabolites BH 635-2, BH 635-4 and BH 635-5 in static surface waters (PECsw) and sediment (PECsed) after drift entry.<br>BAS<br>2003/1009268; CALC-315<br>not GLP, unpublished<br>BOD2003-303 |
| AIIIA-9.1.3 | Hauck, T. | 2002 | Calculation of predicted environmental concentratios for BAS 635 H (Tritosulfuron) and metabolites BH 635-2, BH 635-3, BH 635-4 and BH 635-5 in soil using worst case half-lives.<br>BAS<br>2002-1000216; CALC-316<br>not GLP, unpublished<br>BOD2003-302 |
| AIIIA-9.2.1 | Gottesbüren, B. | 2002 | Calculation of predicted environmental concentrations in groundwater (PECgw) of BAS 635 H and its metabolites for UK under special considering of sorption dependencies; study CALC-365.<br>BAS,BAS<br>2002/1011916<br>GLP, unpublished<br>WAS2003-115 |

**Codes of company**

BAS: BASF Aktiengesellschaft

## B.9 Ecotoxicology

| Annex point/ reference number | Author(s) | Year | Title<br>source (where different from company)<br>Company[5],<br>report no.<br>GLP or GEP status (where relevant),<br>published or not<br>BBA registration number |
|---|---|---|---|
| | | | |
| AIIA-8.4.2 | Lührs, U. | 2002 | Effects of BH 635-4 on Reproduction and Growth of Earthworms Eisenia fetida in Artificial Soil.<br>BAS<br>2002/1012744<br>GLP, unpublished<br>ARW2003-148 |
| AIIA-8.4.2 | Lührs, U. | 2002 | Effects of BH 635-2 on Reproduction and Growth of Earthworms Eisenia fetida in Artificial Soil.<br>BAS<br>2002/1012746<br>GLP, unpublished<br>ARW2003-150 |
| AIIA-8.4.2 | Lührs, U. | 2002 | Effects of BH 635-3 on Reproduction and Growth of Earthworms Eisenia fetida in Artificial Soil.<br>BAS<br>2002/1012745<br>GLP, unpublished<br>ARW2003-149 |
| AIIA-8.4.2 | Lührs, U. | 2002 | Effects of BH 635-5 on Reproduction and Growth of Earthworms Eisenia fetida in Artificial Soil.<br>BAS<br>2002/1012743<br>GLP, unpublished<br>ARW2003-147 |
| AIIIA-10.3 | Welter, K. | 2002 | Risk assessment for terrestrial vertebrates other than birds<br>BAS<br>2002/1011551 |

**Codes of company**

BAS: BASF Aktiengesellschaft

[5] Only notifier listed

# COMPLETE LIST OF SUGGESTED CLASSIFICATION AND LABELLING : TRITOSULFURON

ECCO Peer Review Programme, Round 14, York

## 1. Classification and labelling:

| | |
|---|---|
| Physical and Chemical properties | None |
| Fate and Behaviour | None |
| Mammalian Toxicology | R43 |
| Ecotoxicology | R50, R53 |

**ANNEX 4 TO CONCISE OUTLINE REPORT OF ECCO 135 PEER REVIEW MEETING**

TRITOSULFURON

Rapporteur Member State: GERMANY

Specific comments on the active substance in the section **Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis** are listed below. The conclusions of the meeting were as follows:

1a. Comments received and discussed:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| 14 January 2003 | United Kingdom | Tritosulfuron_135_com01_UK |
| 3 February 2003 | Belgium | Tritosulfuron_135_com02_BE |

1b. Comments received but not discussed (because deadline of submission was not met):

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |

1c. Documents tabled at the meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |

2. **Data on preparations:** The data set is incomplete.

3. **Classification and labelling:** No Comments

4. **Recommended restrictions/conditions for use:** None proposed at the meeting.

**Areas of concern:** Impact of impurity on other areas of the risk assessment (note impurity is also a metabolite) .

Appendix 1: ECCO 135 reporting table: TRITOSULFURON

Appendix 2: List of end points: TRITOSULFURON

Appendix 3: Suggested classification and labelling: TRITOSULFURON

# Appendix 1: ECCO 135 reporting table Tritosulfuron (Hb)

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

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | Section 1<br>Data requirements: 8<br>Open points: 7 |
| (i) | Batch analysis | The meeting commented that the batch analysis was carried out with just 4 batches rather than 5. The RMS replied that they were awaiting final 5 batch analysis data from the applicant. | 1.1 Applicant to provide 5 batch analysis data **A** |
| (ii) | Batch analysis | The meeting mentioned the stability of the technical material, in relation to the formation of the AMTT impurity/metabolite. | 1.2 Applicant to provide data on the stability of technical material with regard to formation of AMTT.**A** |
| (iii) | Batch analysis | The meeting agreed that the RMS and the UK had seen the same information on nitrosamine analysis, but that data on the analytical methods had not been provided. | 1.3 Applicant to provide validated methods and nitrosamine quantification as part of 5 batch analysis **A** |
| (iv) | Batch analysis | Discussion point. | The RMS confirmed that methods used to quantify water and chloride ions were well established and the meeting agreed that further validation of these methods was not required. |
| (v) | Technical specification | FR re-iterated the requirement for the levels of impurities in the technical specification should be justified by the applicant. | 1.4 Applicant to justify technical specification against 5 batch analysis. |
| (vi) | Vapour pressure | BE noted that the vp was recorded as$< 1.012 \cdot 10^{-4}$ Pa $m^3$ $mol^{-1}$ and the meeting agreed that the actual value should be recorded. | Open point (1.0) RMS to include actual values and amend the endpoint sheets |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (vii) | Solubility in organic solvents | The meeting agreed also that the actual solubility in toluene, 2-propanol and olive oil should be recorded. | Open point (1.1) RMS to include actual values and amend the endpoint sheets |
| (viii) | Quantum yield | The meeting agreed that the end point sheets should be amended in line with the section B2. | Open point (1.2) RMS to amend end point sheets in line with section B2. |
| (ix) | Dissociation constant | FR noted the pka was 4.7 and considered that the ionic species should be included | Open point (1.3) RMS to liaise with Fate colleagues to check for inclusion of the ionic species in the reporting table. |
| (x) | Annex III | BE noted that no adjuvant was included in the tests and questioned if the PPP is always to be used with an adjuvant, then this should be included in the tests. The meeting observed that the UK had seen an acceptable sprayability study with the PPP and adjuvant together and had concluded that this area had been addressed. The RMS had seen data with ASTM E 1518-93 test method which has been accepted by CIPAC and which was felt by the RMS to include foaming etc. The meeting agreed that at MS level, physical properties of the PPP with the adjuvant when in dilution must be addressed, either by direct physical chemical properties data or by sprayability study. The meeting agreed that if the ASTM method addresses these requirements then the MS requirement can be waived.. | Open point (1.4) RMS to check whether ASTM E 1518-93 test method addresses physical properties with the adjuvant when in dilution then no further data will be needed. If it does not then this will be a data gap to be addressed at MS level |
| (xi) | Attrition | The RMS had advised that there is no internationally agreed method, but BE considered that this area should be addressed, using perhaps the new provisional method MT 178-2. The meeting considered the possibility of using MT 171 data, but BE pointed out that this would not assess the effect of transport. | 1.5 Applicant to supply data to address the attrition potential of the preparation at MS level. **MS** |
| (xii) | Shelf life data | It was drawn to the attention of the meeting of concerns for the stability of the active substance and the potential for formation of AMTT. Meeting agreed that this must be addressed and given the concerns over the toxicological profile of AMTT this must be to GLP and required for Annex I listing | 1.6 Applicant to supply shelf life data with indication of AMTT formation. Study must be GLP compliant **A** |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (xiii) | Methods of analysis (plant material) | The meeting noted that on page 60, there is a statement that if low recoveries are found, then 5 mls of buffer should be added prior to extraction. AT noted that this is not helpful as there was no indication for monitoring which matrices could cause problems. the meeting agreed that as this was a sulphonylurea, the risk was perhaps low, but this could affect the LOQ for monitoring | 1.7 Applicant to address when the buffer should be used, i.e. to identify those matrices which could give low recoveries and hence would require the addition of buffer prior to extraction. **A** |
| (xiv) | Methods of analysis (ILV) | During ILV cleanup, the solvents were changed; iso-octane or ethyl acetate was used and because of the different polarities, this change was questioned as an important issue. It was noted that validation data were available for dry and oil crops, but none were available for high water or acid crops. There was much discussion on whether the validation data for high water or acid crops should be Annex I or MS level requirement and some of these discussion raised important general points not restricted to this active substance. | 1.8 Validation data for high water and acid crops to be provided at MS level, because this is a sulphonylurea and the nature of the risk assessment **MS** |
| (xv | Methods of analysis | The meeting noted for the residue group that methods of analysis are available for parent and AMTT if needed | Open point (1.5) for residue meeting to note that monitoring methods for parent and AMTT are available. |
| (xvi) | Endpoint table | The meeting agreed that the endpoint sheets should indicate the analytes as for other active substances | Open point (1.6) RMS to identify the analytes in the appropriate sections of the end point sheets. |
| (xvii) | Methods of analysis - water | BE noted that the LOQ for metabolite M02 should be 0.5µg/l rather than 0.05µg/l. The meeting agreed that if this metabolite was considered relevant, then this level is too high (needs to be 0.1µg/l) | Open point (1.7)RMS to update end point sheets with appropriate endpoints for all the analytes. |
| | | | |

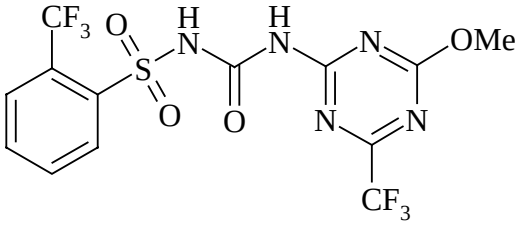
Appendix 2

LIST OF END POINTS: **TRITOSULFURON**

## 1 Physical chemical properties section

| | |
|---|---|
| Active substance (ISO Common Name) | Tritosulfuron (ISO) |
| Function (*e.g.* fungicide) | Herbicide |
| Rapporteur Member State | Federal Republic of Germany |

**Identity** (Annex IIA, point 1)

| | |
|---|---|
| Chemical name (IUPAC) | 1-(4-methoxy-6-trifluoromethyl-1,3,5-triazin-2-yl)-3-(2-trifluoromethyl-benzenesulfonyl)urea |
| Chemical name (CA) | N-[[[4-methoxy-6-(trifluoromethyl)-1,3,5-triazin-2-yl]amino]carbonyl]-2-(trifluoromethyl)benzene-sulfonamide |
| CIPAC No | 735 |
| CAS No | 142469-14-5 |
| EEC No (EINECS or ELINCS) | not assigned |
| FAO Specification (including year of publication) | n. a. (new active substance) |
| Minimum purity of the active substance as manufactured (g/kg) | 950 (based on a pilot plant) |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg) | AMTT: 0.2 g/kg (max. content) |
| Molecular formula | $C_{13}H_9F_6N_5O_4S$ |
| Molecular mass | 445.3 |
| Structural formula |  |

**Physical-chemical properties** (Annex IIA, point 2)

| | |
|---|---|
| Melting point (state purity) | 166.5 – 169.4 °C (99.8 %) |
| Boiling point (state purity) | – |
| Temperature of decomposition | approx. 340 °C |
| Appearance (state purity) | white crystalline solid, odourless (99.8 %) |
| Relative density (state purity) | $d_4^{20}$ = 1.7 (99.8 %) |
| Surface tension | 64.6 mN/m 1.0 % (w/w) (93.8 %, at 20 °C)<br>71.3 mN/m 0.5 % (w/w) and<br>71.0 mN/m 2.0 % (w/w) (99.8 %, both at 20 °C) |
| Vapour pressure (in Pa, state temperature) | $1.0 \times 10^{-5}$ (20 °C), 99.8 % |

| | |
|---|---|
| Henry's law constant (Pa $m^3$ $mol^{-1}$) | < 1 x $10^{-4}$ (20 °C) |
| Solubility in water (g/l or mg/l, state temperature) | 38.6 mg/l pH 4.7 (deionised water)<br>78.3 mg/l pH 10.2<br>0.94 mg/l pH 1.7 all at 20 °C |
| Solubility in organic solvents (in g/l or mg/l, all at 20 °C). | Toluene < 10 g/l<br>Dichloromethane 25 g/l<br>Methanol 23 g/l<br>Aceton 250-300 g/l<br>Ethyl acetate 83-86 g/l<br>Acetonitrile 90-94 g/l<br>1-Octanol 13 g/l<br>2-Propanol < 10 g/l<br>olive oil < 10 g/l |
| Partition co-efficient (log $P_{OW}$) (state pH and temperature) | 2.93 non ionised form<br>2.93 pH 2.7, 2.85 pH 4, 0.62 pH 7, -2.38 pH 10<br>all at 20 °C |
| Hydrolytic stability ($DT_{50}$) (state pH and temperature) | pH 4: 39-56 d (25 °C), pH 5: > 62 d (25 °C)<br>pH 7: > 62 d (25 °C)<br>pH 9: 17-20 d (25 °C) |
| Dissociation constant | $pK_a$ 4.69 (20 °C), 99.7 % |
| UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) | pH 0.5:<br>202 nm (ε 24440), 212 nm (ε 21412), 226 nm (ε 25172), 254 nm (ε 7037), 300 nm (ε 212)<br>pH 6.7:<br>202 nm (ε 18331), 215 nm (ε 18515), 237 nm (ε 21494), 260 nm (ε 13021), 300 nm (ε 144)<br>pH 13.3:<br>219 nm (ε 18151), 235 nm (ε 15825), 260 nm (ε 11908), 300 nm (ε 1890) |
| Photostability ($DT_{50}$) (aqueous, sunlight, state pH) | stable over 15 days at pH 5 and pH 7 |
| Quantum yield of direct phototransformation in water at λ > 290 nm | < 1.05 x $10^{-4}$ (pH 5)<br>< 2.23 x $10^{-4}$ (pH 7) |
| Flammability | not highly flammable |
| Explosive properties | none |

## List of uses supported by available data

| Crop and/ or situation (a) | Member State or Country | Product name | F G or I (b) | Pests or Group of pests Controlled (c) | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks: (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Type (d-f) | Conc. of g as/kg (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | interval between applications (min) | kg as/hL min max | water L/ha min max | kg as/ha min max | | |
| Maize | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 12-18 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |
| Maize | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 12-18 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |
| Cereals, winter | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 21-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |
| Cereals, winter | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 21-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |
| Cereals, summer | Northern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 13-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |
| Cereals, summer | Southern Europe | BAS 635 00 H | F | Dicotyledonous weeds | WG | 714 | spraying | 13-39 | 1 | - | 0.013-0.033 | 150-400 | 0.05 | F | |

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

**Classification and proposed labelling** (Annex IIA, point 10)

| | |
|---|---|
| with regard to physical/chemical data | none |
| with regard to toxicological data | R43 |
| with regard to fate and behaviour data | none |
| with regard to ecotoxicological data | R50, R53 |

## Chapter 2: Methods of Analysis

**Analytical methods for the active substance** (Annex IIA, point 4.1)

| | |
|---|---|
| Technical as (principle of method) | HPLC-UV |
| Impurities in technical as (principle of method) | HPLC-UV |
| Plant protection product (principle of method) | HPLC-UV |

**Analytical methods for residues** (Annex IIA, point 4.2)

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | HPLC-UV 0.01 mg/kg (wheat, maize)<br>LC-MS/MS 0.001 mg/kg (wheat, maize) |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | HPLC-UV 0.01 mg/kg (milk, muscle, fat, egg, kidney, liver) |
| Soil (principle of method and LOQ) | LC-MS/MS 0.001 mg/kg<br>GC-ECD 0.001 mg/kg |
| Water (principle of method and LOQ) | LC-MS/MS 0.05 µg/l<br>GC-MS 0.05 µg/l |
| Air (principle of method and LOQ) | HPLC-UV 2.8 µg/m³ |
| Body fluids and tissues (principle of method and LOQ) | not relevant |

Appendix 3

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

## 1 Physical chemical properties section

None.

**ANNEX 4 TO CONCISE OUTLINE REPORT OF ECCO 137 PEER REVIEW MEETING**

TRITOSULFURON

Rapporteur Member State: GERMANY

Specific comments on the active substances in the section **Fate and behaviour** are listed below. The conclusions of the meeting were as follows:

1a. Comments received and discussed:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| 6 March 2003 | Denmark | Tritosulfuron_137_com01_DK |
| 7 February 2003 | France | Tritosulfuron_137_com03_FR |
| 3 March 2003 | Greece | Tritosulfuron_137_com04_GR |
| 14 March 2003 | United Kingdom | Tritosulfuron_137_com02_UK |

1b. Comments received but not discussed (because deadline of submission was not met):

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |

1c. Documents tabled at the meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |

1. **Definition of the residues relevant to the environment:** Soil and groundwater: tritosulfuron + 635M01 + 635M02 +635M03 +635M04 + [635M17 provisionally]; Surface water: tritosulfuron + 635M01 + 635M02; Sediment: tritosulfuron + 635M01; Air: not discussed.

2. **Data on preparations:** The data set for the plant protection product was considered incomplete.

3. **Classification and labelling:** Not discussed.

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

**Areas of concern:** Potential for contamination of groundwater at concentrations $\geq$ 0.1 μg/l and relevance of the metabolites, 635M01, 635M02, 635M03, 635M04 and 635M17 needs to be addressed.

Appendix 1: ECCO 137 reporting table: TRITOSULFURON

Appendix 2: List of end points: TRITOSULFURON

Appendix 3: Suggested classification and labelling: TRITOSULFURON

# Appendix 1: ECCO 137 reporting table Tritosulfuron (Hb)

## 2. Environmental Fate and behaviour

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | Section 1<br>Data requirements: 7<br>Open points: 2 |
| (i) | Route and rate of aerobic degradation in soil - laboratory. | The DT50 values presented in the end points reflected a mix of different methods and models, (although not different reaction kinetics). The meeting agreed that the RMS should include a clearer explanation in the end points as to what methods of calculation of DT50 and rate order had been used in each case.<br><br>The meeting queried whether microbial biomass was sufficiently low in the Canadian soil to consider the DT50 of 124 days as an outlier. The RMS confirmed that there was no clear justification given for this, only a statement in DAR Volume 1 that the soil was less active and given that this was not the least microbially active soil tested, the meeting did not agree to exclude this result as an outlier. It was also noted that the new FOCUS group on degradation kinetics will be considering the issue of outliers.<br><br>The experts noted that several DT50 values were presented, 2 for the first soil (1 for each radiolabel) and then 1 for each of the other soils. They discussed how should these values be averaged. The general consensus was that the average should be taken of the 2 values from the same soil, (unless environmental behaviour differs for the 2 radiolabels), and used with the other individual values to arrive at an overall average. It was noted that this was another area that was being looked at by the new FOCUS Working Group on degradation kinetics.<br><br>The meeting noted that DT50 values of 737 and 347 days (calculated with ModelMaker and TopFit, respectively), for metabolite 635M03 were uncertain due to being extrapolated beyond the study duration of a year. The RMS confirmed these had not been excluded from the mean. Metabolite 635M03 appeared to be stable in these studies and it was not clear to the experts how a reliable DT50 could be calculated. The meeting questioned the choice of these DT50 values to obtain mean values for input to groundwater modelling. The meeting also queried the DT50 of | Open point 2.1:<br>RMS is to consider whether the aerobic DT50 of 96 days estimated for metabolite 635M02 using TopFit modelling is reliable, given the lack of degradation seen in the laboratory (aerobic) degradation study. |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | 32 days for 635M03 in US soil as a possible low outlier, compared with the other much longer DT50 values obtained. They considered that it might be unreliable, given that the maximum amount formed in that study was only 2.4%AR.<br><br>Levels of the metabolite 635M02 seemed to be stable towards the end of the study, yet a DT50 of 96 days had been calculated for 635M02 from this study using the TopFit model. Without more information on the TopFit model, it was difficult for the meeting to comment on this DT50. RMS should consider these comments and whether a DT50 of 96 days is reliable for 635M02 detected in the phenyl labelled aerobic study.<br><br>The experts queried whether the extraction methods were sufficient as 9.1%AR as 635M01 was recovered from the fulvic acid, (previously non-extractable), but were satisfied with the response from the RMS that harsh extraction was required to release the radioactivity from the non-extractable residues.<br>The meeting noted that soil metabolites 635M01, 635M02, 635M03 and 635M04 under aerobic conditions were all to be assessed further. | |
| (ii) | Route and rate of anaerobic degradation in soil - laboratory | The meeting briefly discussed the situation with regards to degradation studies under anaerobic conditions. Experts were reminded that at the EU level for Annex I inclusion, anaerobic conditions were only considered relevant to investigate for autumn uses, but it was recognised that there may be some interest at a MS level for spring uses. For tritosulfuron, it was noted that the metabolite 635M19 was major metabolite under anaerobic conditions, but was assumed to occur transiently under aerobic conditions as an intermediate (not detected in aerobic study), but the meeting were content with the information supplied.<br><br>It was noted that 10.1%AR in the triazine-labelled study consisted of 'others'. The RMS confirmed that this was the sum of several chromatographic peaks. The meeting considered that unless these were individually very high amounts it was likely that they were already covered by the aerobic degradation assessment. | 2.1 Metabolite 635M19 was major under anaerobic conditions. For Annex I inclusion, anaerobic conditions are only considered relevant for autumn uses and this proposed use is for application in the spring. Although not required for Annex I inclusion, some MSs may wish to further consider the relevance of 635M19.<br>(IIA 7.1.1.1.2) **MS** |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (iii) | Standardisation of field dissipation data for use in groundwater modelling. | At least one field DT50 was excluded from the final preparation of degradation figures, due to fluctuation at day 0 sampling. One US study (Indiana site) gave very low recoveries (35%) due to mishandling, casting doubt on the acceptability of the DT50s derived from that site. If the trial was considered acceptable, then the meeting noted that metabolite 635M04 could be considered major as it reached 10%AR.<br><br>The meeting noted that the applicant had normalised the degradation rates to standard temperature (20°C) and moisture (pF 2) with ModelMaker. These normalised rates were used in the PECgw calculations, but were not reported in the end points. The experts raised some concerns about this normalisation process of field dissipation data. There was considered to be insufficient information presented to be able to evaluate this procedure. More information was needed on the climate and field history of the EU field trials sites. The experts noted that the US field trials sites did not seem comparable to EU conditions in terms of rainfall and that no direct comparison was made with the EU sites actually used. The meeting preferred to see the raw non-standardised field DT50 values presented transparently, together with step by step calculations, so that evaluators could consider the reliability of the DT50 values at each stage. Some experts also questioned the use and robustness of standardised field data over laboratory degradation data, as input to groundwater modelling.<br><br>DT50 values were estimated for the metabolites using ModelMaker and were wide-ranging 635M01 (30-336 d), 635M02 (36-216 d), 635M04 (11-133 d) and not calculated for 635M03. It was commented that the long DT90 values seen in the field for some metabolites indicated that their potential for accumulation should be addressed. The RMS is in the first instance to discuss with the applicant including more transparent information on the field dissipation trials, the standardisation approach taken for the field DT50 values and their acceptability for use in the groundwater risk assessment, before considering whether more data should be requested. | 2.2 The RMS is to discuss with the applicant including more transparent information on the field dissipation trials, the standardisation approach taken for the field DT50 values and their acceptability for use in the groundwater risk assessment, before considering whether more data should be requested.<br><br>(IIA 7.1.1.2.2) **A** |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (iv) | PECsoil | The PECsoil for tritosulfuron was calculated using degradation data derived from field dissipation DT50 values normalised to 15°C. It was commented that this assumption was too general and a more typical approach should be taken for the PECsoil calculation, such as using the worst case field DT50 value.<br><br>The meeting considered that the DT50 values from the US field trials should also be included in the same table (Table B.8.1-24) where the first-order DT50 values for the EU field trials were summarised. Clarification was also sought as to why a non-linear method of calculation was used to determine DT50 values from the US trials. | 2.3 Applicant is to recalculate the PECsoil values using worst case field DT50 values, instead of DT50 values normalised to 15°C.<br>(IIIA 9..1.3) **A** |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (v) | Mobility in soil - laboratory adsorption/ desorption studies and lysimeter studies. | The a.s. and metabolites all had low Koc values and potential for high mobility. The meeting highlighted that adsorption was possibly influenced by pH in this case, though it was not clear how strong the relationship was. Therefore, it was not appropriate to use a mean Koc in the groundwater modelling and pH dependence of soil adsorption should be taken into account in the choice of Koc used in the PECgw calculation.<br><br>It was noted that the pH range of the soil types used in all five lysimeter studies were low and mostly acidic soils which could be best case for the a.s. The RMS confirmed that a proposal had been made that the FOCUS groundwater modelling should be recalculated using scenarios representative of neutral and alkaline soils, this would be added to the DAR Volume 1. Dependent on the outcome of this, consideration would also be given to requesting a lysimeter study using a soil of higher pH. Under conditions where another lysimeter might be considered necessary, appropriate methodology should be used to ensure detection of metabolite 635M04 is included, either by dual radiolabelling or a specific cold analytical method.<br><br>The meeting noted that a plant metabolite 635M17 (not seen in soil metabolism, water or water-sediment studies) was also detected in lysimeter leachate at >0.1 µg/l (individual samples, not annual average concentration). The meeting considered that its relevance should be addressed, given its potential to leach at concentrations borderline to the >0.1 µg/l limit in an acidic soil which might be best-case and the possibility that it might be a transient soil metabolite under aerobic conditions. The non-identified radioactivity (NIR) in the leachate was also discussed and the experts asked if information was available on the number of chromatographic peaks and the concentration of the biggest peak. | See (viii) |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (vi ) | Degradation in water-sediment | RMS to correct an error in the end points; the active substance reached a maximum of 11%AR not 14%AR in sediment at 14 days.<br><br>The meeting observed that the metabolite, M1, was still increasing at the study end in both the water and sediment phases. | Message from ECCO 137 (Fate) to ECCO 139 (Ecotox) and to ECCO 140 (Overview):<br>The ecotoxicological and toxicological relevance of metabolite, 635M01, which was still increasing in water and sediment phases at the end of the water-sediment study, needs to be considered. |
| (vii) | PECsurface water | PECsw were calculated for spray drift and also for run-off. Although usual to only include values for spray drift in the end points, it was agreed that the run-off calculation should be kept in for metabolite 635M04. (No spray drift PECsw was calculated for 635M04 as it was not formed in the sediment-water study).<br><br>The meeting noted that for the PECsed calculation, assumptions were made of 2 cm sediment depth and 1.5 kg/l bulk density. The meeting considered that for consistency these should be recalculated using the current EU standard assumptions of 5 cm sediment depth and 1.3 g/cm$^3$ bulk density.<br><br>RMS is to delete the reference in the end points to columns for multiple applications under metabolite PECsw. | 2.4 Applicant is to recalculate the PECsed values using the standard EU assumptions of 5 cm sediment depth and 1.3 g/cm$^3$ bulk density.<br><br>(IIA 9.2.3) **A** |
| (viii) | PECgroundwater | The meeting concluded that the groundwater modelling submitted was inappropriate due to use of mean adsorption values when pH might have a possible effect on sorption. The lysimeter studies also used soils of low pH. The implications of pH dependence need to be taken into account in the PECgw calculation and any further lysimeter studies requested. RMS is to add a data requirement for the influence of neutral and alkaline soils and associated sorption values to be evaluated in the PECgw calculations. RMS is also to more clearly specify in the end points the details of parameters input to the modelling e.g. on sorption and degradation.<br><br>Field dissipation DT50 values were normalised to 20°C before being input into the groundwater modelling. The meeting expressed strong reluctance to agree to the standardisation of these field | 2.5 The applicant should repeat FOCUS groundwater modelling using scenarios representative of neutral and alkaline soils and associated sorption values to reflect the possible effect of pH on adsorption in the PECgw calculations.<br><br>Dependent on the outcome of this, |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | dissipation data, in preference over laboratory data. There was noted to be an order of magnitude difference between the laboratory and field DT50 results of ca. 98 versus 9.7 days, respectively, at 20°C. Whether laboratory or field data were used the meeting wished to see more transparent information on the original DT50 values and on the standardisation process, to be able to check the reliability of the values.<br><br>The experts did not agree with the field DT50 values for 635M04 and only one DT50 was available from laboratory data on this metabolite. All the laboratory degradation data on the metabolites were obtained from studies using tritosulfuron as test material and were estimated using TopFit modelling. It was suggested that the applicant could identify which metablites were potentially relevant and then generate laboratory degradation data using each metabolite as test material. (M04, also an impurity of tritosulfuron, was already classed as toxicologically relevant). However,.it was considered likely that the applicant would accept the potential risk of leaching to groundwater from 635M01, 635M02 and 635M03 and consequently opt to address their non-relevance. Metabolite 635M17, seen in the lysimeter leachate, should also be addressed. | consideration would also be given to requesting a lysimeter study using a soil of higher pH, using methodology appropriate to include detection of the metabolite 635M04, either dual radiolabelling or a specific cold analytical method. (IIIA 9.2.1) **A**<br><br>2.6 The RMS is to discuss with the applicant the comments made by ECCO 137 (Fate) on the acceptability of the standardised field DT50 values used in the FOCUS groundwater model and to consider the appropriate degradation parameters to be used in the model. Transparent information is to be provided on the degradation parameters used in the repeated FOCUS calculations. (IIIA 9.2.1) **A**<br><br>2.7 The applicant is to address the potential of the soil metabolites 635M01, 635M02, 635M03, and 635M04 to contaminate groundwater at > 0.1 µg/l and their relevance in accordance with the latest guidance on relevant metabolites. (IIIA 9.2.1) **A**<br><br>The applicant should also address |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | the relevance of the plant metabolite 635M17, detected in the lysimeter leachate (using acidic soil), at concentrations >0.1 µg/l in individual samples. (IIIA 9.2.1) **A**<br><br>Open point 2.2: RMS is to provide more information on the number of chromatographic peaks and the concentration of the biggest peak for the non-identified radioactivity (NIR) detected in the lysimeter leachate. |
| (ix) | Fate and behaviour in air | The meeting agreed with the RMS that long range transport of tritosulfuron in air is not expected due to low volatility. RMS is to delete the reference to the aqueous photolysis data in the end points under direct phototransformation in air and replace with 'no data submitted'. | |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (x) | Residue definition | The soil metabolites 635M01, 635M02 and 635M03 all showed potential to contaminate groundwater ≥0.1 µg/l. Plant metabolite 635M17 also appeared in the lysimeter leachate at high concentrations. Therefore, the relevance of these metabolites needed to be addressed. Metabolite 635M04 was toxicologically relevant and was possibly a major metabolite in field soil..<br><br>The PECsw for metabolites from run-off was currently an issue for MSs, but the meeting agreed that the residue definition should only include metabolites seen in this environmental compartment. There was already an assumption in the assessment that soil metabolites might reach surface waters. Therefore, 635M01 and 635M02 which were seen to increase in the water sediment study were included in the surface water residue definition while 635M04 was not.<br><br>The meeting proposed the residue definition as:<br>Soil and groundwater: tritosulfuron + 635M01 + 635M02 +635M03 +635M04 + [635M17 provisionally).<br>Surface water: tritosulfuron + 635M01 + 635M02<br>Sediment: tritosulfuron + 635M01<br>Air: not discussed<br><br>RMS is to remove reference to the relevance of these metabolites, in the end points under residue definition. | |
| (xi) | From ECCO 135 (Chemistry) meeting:<br>a requirement was set for the applicant to address the ionic species of dissociated tritosulfuron. | ECCO 137 (Fate) experts noted that a data requirement had been set at ECCO 135 (Chemistry) for the applicant to include the ionic species as formulae, as the Pka was 4.7 and this is required for dissociated species. | ECCO 137 (Fate) experts noted that at ECCO 135 (Chemistry) a requirement was set for the applicant to address the ionic species of dissociated tritosulfuron. |

Appendix 2

LIST OF END POINTS: **TRITOSULFURON**

## 2 Environmental Fate and behaviour

**Route of degradation (aerobic) in soil** (Annex IIA, point 7.1.1.1.1)

| | |
|---|---|
| Mineralisation after 100 days | 5 % after 90 d, (21 % after 358 d), triazine label<br>0 % after 91 d (< 3 % after 358 d), phenyl label<br>0 % after 122 d, phenyl label |
| Non-extractable residues after 100 days | 17-25 % after 90 d (both labels)<br>43 % after 358 d (phenyl label<br>28 % after 358 d (triazine label) |
| Relevant metabolites - name and/or code, % of applied (range and maximum) | 635M01 max. 56 % after 60 d (n = 5)<br>635M03 max. 15 % after 120 d (n = 5)<br>635M02 max. 23 % after 118 d (n = 5)<br>635M04 (AMTT) max 6 % after 90 d (n = 1) |

**Route of degradation in soil - Supplemental studies** (Annex IIA, point 7.1.1.1.2)

| | |
|---|---|
| Anaerobic degradation | tritosulfuron: 33 % (phenyl) and 24 % (triazine) remained after 120 d, bound residues 6 %<br>major metabolites:<br>635M01 max. 53 % after 120 d<br>635M19 max. 16 % after 28 d |
| Soil photolysis | after 15 d: 78 - 81 % tritosulfuron remained, 3 - 5 % bound residues, < 1 % $CO_2$, no major metabolites (> 10 %) |

**Rate of degradation in soil** (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

| | |
|---|---|
| Method of calculation | ModelMaker 3.0.3/3.0.4 (Cherwell Scientific Publishing Limited); TOPFIT pharmacokinetic analysis; Timme and Frehse, 1st order kinetics, $DT_{50}$ of metabolites calculated from studies with tritosulfuron |
| Laboratory studies (range or median, with n value, with $r^2$ value) | $DT_{50lab}$ (20 °C, aerobic) in days: |

| soil | as | 635M01 | 635M02 | 635M03 | 635M04 |
|---|---|---|---|---|---|
| Li35b | 31/32 | 110/184 | 96 | 347/737 | 98 |
| Lufa2.2 | 16 | 65 | 37 | 203 | nc |
| US-soil | 19 | 59 | 44 | 32 | nc |
| Bruch | 38 | 23 | 28 | nc | nc |
| Canad. | (124) | 44 | nc | nc | nc |
| Speyer | 20 | 115 | nc | nc | nc |
| mean | 26 | 86 | 51 | 330 | - |
| $r^2$ (low) | 0.970 | 0.886 | 0.900 | 0.893 | 0.962 |
| $r^2$ (high) | 0.997 | 0.979 | 0.951 | 0.977 | - |

| |
|---|
| tritosulfuron: $DT_{90lab}$ (20°C, aerobic): 53 - 125 d (409 d) |
| tritosulfuron: $DT_{50lab}$ (10°C, aerobic, calc.): 42 - 271 d |
| tritosulfuron: $DT_{50lab}$ (20°C, anaerobic): 61 - 82 d |

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

| | |
|---|---|
| | degradation in the saturated zone: not relevant |
| Field studies (state location, range or median with n value) | $DT_{50f}$: 10 locations (3 Germany, 2 Spain, Sweden, California, South Dakota, Indiana, Texas )<br>method of calculation: EU: 1st order, USA: non-linear<br>tritosulfuron: EU: 11 - 21 d, USA: 3 - 15 d<br>635M01: EU: 30 - 336 d, USA: 65 - > 621 d<br>635M02: EU: 36 - 216 d, USA: 76 - > 614 d<br>635M03: EU: nc, USA: 53 - > 417 d<br>635M04 (AMTT): EU: 11 - 133 d, USA: 5 - 69 d |
| | tritosulfuron $DT_{90f}$: EU: 37 - 77 d |
| Soil accumulation and plateau concentration | based on degradation studies, no accumulation is expected |

**Soil adsorption/desorption** (Annex IIA, point 7.1.2)

| | |
|---|---|
| $K_f$ /$K_{oc}$<br>$K_d$ | soils: 5 German, 2 US |

| | Koc | (mean) | $K_F$ | 1/n |
|---|---|---|---|---|
| tritosulfuron | 4 - 11 | (7) | 0.04 – 0.16 | 0.76 - 0.98 |
| 635M01 | 18 – 184 | (89) | 0.32 – 1.47 | 0.90 - 0.96 |
| 635M02 | 16 – 79 | (40) | 0.18 – 0.52 | 0.92 - 0.98 |
| 635M03 | 18 – 51 | (30) | 0.11 – 0.42 | 0.85 - 0.97 |
| 635M04 | 8 – 57 | (21) | 0.1 – 0.29 | 0.90 - 0.98 |

| | |
|---|---|
| pH dependence (yes / no) (if yes type of dependence) | yes, decreasing sorption with increasing pH |

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

**Mobility in soil** (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

| | |
|---|---|
| Column leaching | guideline: BBA IV, 4-2<br>precipitation: 200 mm in 2 days<br>86 % in leachate (all unchanged tritosulfuron) |
| Aged residues leaching | guideline: BBA IV, 4-2<br>precipitation: 200 mm in 2 days, aeging 30 d<br>40 % in leachate (mostly unchanged tritosulfuron) |
| Lysimeter/ field leaching studies | 5 lysimeters, location: Limburgerhof, RP, Germany<br>application: 50 g ($^{14}$C-phenyl) as/ha in spring, 1$^{st}$ year (lys 5, 6, 16, 17), 1$^{st}$ + 2$^{nd}$ year (lys 18)<br>annual rainfall incl. add. irrigation (mm): 802 - 836<br>annual leachate volume (l): 200 - 487<br>annual average concentrations (highest concentration during the study) [µg/l]: |

| | lys 5 | lys 6 | lys 16 | lys 17 | lys 18 |
|---|---|---|---|---|---|
| tritosulfuron | 0.04 | 0.02 | 0.02 | 0.02 | 0.04 |
| 635M01 | 0.54 | 0.39 | 0.1 | 0.36 | 1.04 |
| 635M02 | 0.09 | 0.09 | 0.02 | 0.06 | 0.11 |
| 635M03 | 0.26 | 0.20 | 0.07 | 0.22 | 0.57 |
| 635M04* | <0.05 | <0.05 | <0.1 | <0.05 | <0.05 |
| 635M17 | 0.05 | 0.02 | 0.05 | 0.03 | 0.08 |
| NIR | 0.42 | 0.32 | 0.59 | 0.64 | 0.68 |
| $^{14}$C (as-eq.) | 1.44 | 1.22 | 0.75 | 1.13 | 2.50 |

* analysed by GC/MS, not possible to detect as $^{14}$C, because of the labeling position

**PEC (soil)** (Annex IIIA, point 9.1.3)

| | |
|---|---|
| Method of calculation | First order kinetics (with the worst case field half-life standardised to 15° C): tritosulfuron: 49 d, 635M01: 133 d, 635M02: 171 d, 635M03: 187 d, 635M04: 34 d<br>Maximum amounts of metabolites formed in field studies (% of as): 635M01: 30 %, 635M02: 27 %, 635M03: 16 %, 635M04: 19 %<br>5 cm soil layer, bulk density of 1.5 kg/l |
| Application rate | Single application to maize and cereals<br>tritosulfuron: 0.05 kg as/ha (no interception) |

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

| **PEC$_{(s)}$** (mg/kg) | | Single application Actual | Single application twa | Single application Actual | Single application twa | Single application Actual | Single application twa |
|---|---|---|---|---|---|---|---|
| | | **tritosulfuron** | | **635M01** | | **635M02** | |
| Initial | | 0.067 | 0.067 | 0.020 | 0.020 | 0.018 | 0.018 |
| Short term | 24 h | 0.066 | 0.066 | 0.020 | 0.020 | 0.018 | 0.018 |
| | 2 d | 0.065 | 0.066 | 0.020 | 0.020 | 0.018 | 0.018 |
| | 4 d | 0.063 | 0.065 | 0.020 | 0.020 | 0.018 | 0.018 |
| Long term | 7 d | 0.060 | 0.063 | 0.019 | 0.020 | 0.017 | 0.018 |
| | 28 d | 0.045 | 0.055 | 0.017 | 0.019 | 0.016 | 0.017 |
| | 50 d | 0.033 | 0.048 | 0.015 | 0.018 | 0.015 | 0.016 |
| | 100 d | 0.016 | 0.036 | 0.012 | 0.016 | 0.012 | 0.015 |

| **PEC$_{(s)}$** (mg/kg) | | Single application Actual | Single application twa | Single application Actual | Single application twa |
|---|---|---|---|---|---|
| | | **635M03** | | **635M04 (AMTT)** | |
| Initial | | 0.011 | 0.011 | 0.013 | 0.013 |
| Short term | 24 h | 0.011 | 0.011 | 0.012 | 0.013 |
| | 2 d | 0.011 | 0.011 | 0.012 | 0.012 |
| | 4 d | 0.011 | 0.011 | 0.012 | 0.012 |
| Long term | 7 d | 0.010 | 0.011 | 0.011 | 0.012 |
| | 28 d | 0.010 | 0.010 | 0.007 | 0.010 |
| | 50 d | 0.009 | 0.010 | 0.005 | 0.008 |
| | 100 d | 0.007 | 0.009 | 0.002 | 0.005 |

**Route and rate of degradation in water** (Annex IIA, point 7.2.1)

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) (state pH and temperature) | pH 4 (25 °C):<br>tritosulfuron: 56 d (phenyl), 39 d (triazine)<br>635M01 (11 % after 35 d)<br>635M02 (26 % after 35 d)<br>635M04 (22 % after 31 d) |
| | pH 7 (25 °C):<br>tritosulfuron : > 62 d<br>635M04 : no hydrolysis in sterile buffer at pH 6.5 and 7.5 and in natural water pH 8.1 |
| | pH 9 (25 °C):<br>tritosulfuron: 20 d (phenyl), 17 d (triazine)<br>635M01 (34 % after 31 d)<br>635M19 (28 % after 23 d) |

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

| | | |
|---|---|---|
| Photolytic degradation of active substance and relevant metabolites | | Suntest apparatus, 15 days continuous irradiation<br>tritosulfuron: stable (15 d, 22 °C, pH 5 and 7)<br>635M01: sensitized water : $DT_{50}$ = 3.6 d |
| Readily biodegradable (yes/no) | | no |
| Degradation in water/sediment | - $DT_{50}$ water | 32 - 67 d |
| | - $DT_{90}$ water | 107 - n.c. |
| | - $DT_{50}$ whole system | 36 - 77 d |
| | - $DT_{90}$ whole system | n.c. |
| Mineralization | | ≤ 5 % after 100 d |
| Non-extractable residues | | < 5 % - 10 % after 100 d |
| Distribution in water / sediment systems (active substance) | | sediment: max. 14 % after 14 d, max. 13 % after 28 d |
| Distribution in water / sediment systems (metabolites) | water: 635M01 | max. 28.1 % after 100 d |
| | 635M02 | max. 15 % after 14 d |
| | 635M03 | max. 3.8 % after 100 d |
| | sediment: 635M01 | max. 35 % after 100 d |
| | 635M02 | max. 0.9 % after 100 d |
| | 635M03 | max. 4.8 % after 100 d |

**PEC (surface water)** (Annex IIIA, point 9.2.3)

| | |
|---|---|
| Method of calculation | static water body, depth: 30 cm<br>tritosulfuron: 1st order kinetics (67 d), metabolites: no degradation<br>Maximum amounts of metabolites formed (% as):<br>in water-sediment study (drift-entry): 635M01: 28 %, 635M02: 15 %, 635M04: not formed in w/s-study.<br>Mean of maximum amounts of metabolites formed in field soil (runoff entry): 635M01: 14 %, 635M02: 15 %, 635M04: 12 %<br>The $PEC_{actual}$ are based on the worst case of the $PEC_{initial}$ calculated for spray drift and runoff events |
| Application rate | Single application of 0.050 kg as/ha to maize and cereals |
| Main routes of entry | **Spray Drift:**<br>2.77 % of the applied as (90th percentiles for field crops with 1 m buffer)<br>**Runoff:**<br>0.5 % of the concentration (as) in soil at day 3 after application or 0.5 % of the max. concentrations of metabolites observed reach the water body with a volume of 130000 l.<br>Interception of 25 % of the applic. rate and a dilution factor of 0.5 are considered for calculation. |

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| **PEC$_{(sw)}$** | Single application Actual | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| | **tritosulfuron (drift entry)** | | **635M01 (drift entry)** | |
| Initial | 0.46 | 0.46 | 0.103 | 0.103 |
| Short term 24 h | 0.46 | 0.46 | 0.103 | 0.103 |
| 2 d | 0.45 | 0.46 | 0.103 | 0.103 |
| 4 d | 0.44 | 0.45 | 0.103 | 0.103 |
| Long term 7 d | 0.43 | 0.45 | 0.103 | 0.103 |
| 14 d | 0.40 | 0.43 | 0.103 | 0.103 |
| 21 d | 0.37 | 0.41 | 0.103 | 0.103 |
| 28 d | 0.35 | 0.40 | 0.103 | 0.103 |
| 42 d | 0.30 | 0.37 | 0.103 | 0.103 |

| **PEC$_{(sw)}$** | Single application Time weighted average | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| | **635M02 (runoff)** | **635M02 (drift)** | **635M04 (runoff)** | |
| Initial | 0.055 | 0.034 | 0.039 | 0.039 |
| Short term 24 h | 0.055 | 0.034 | 0.039 | 0.039 |
| 2 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 4 d | 0.055 | 0.034 | 0.039 | 0.039 |
| Long term 7 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 14 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 21 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 28 d | 0.055 | 0.034 | 0.039 | 0.039 |
| 42 d | 0.055 | 0.034 | 0.039 | 0.039 |

**PEC (sediment)**

| | |
|---|---|
| Method of calculation | sediment: 2 cm layer, 1.3 kg/l bulk density (wet sediment), entry route as for surface water (drift and runoff), pattern of decline reflecting that measured in the water sediment study. |
| Application rate | Single application of 0.050 kg as/ha to maize and cereals |

| **PEC$_{(sed)}$** [mg/kg] | tritosulfuron drift (1 m buffer) | 635M01 drift (1 m buffer) |
|---|---|---|
| maximum PEC$_{sed}$ | 0.00066 at day 28 | 0.00042 at day 100 |

**PEC (ground water)** (Annex IIIA, point 9.2.1)

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter ) | lysimeter studies and modelling using FOCUS-PELMO v.1.1.1 (all locations) and MACRO FOCUS v1.2.1 (Chateaudun) |
| Application rate | 0.05 kg as/ ha |

**PEC**$_{(gw)}$

| | |
|---|---|
| Maximum concentration | lysimeter: tritosulfuron: 0.07 µg/l<br>635M01: 1.24 µg/l<br>635M02: 0.18 µg/l<br>635M03: 0.91 µg/l<br>635M04: 0.09 µg/l<br>635M17 0.17 µg/l<br>modelling: not calculated |
| Average annual concentration | lysimeter: tritosulfuron: 0.04 µg/l<br>635M01: 1.04 µg/l<br>635M02: 0.11 µg/l<br>635M03: 0.57 µg/l<br>635M04: < 0.1 µg/l<br>635M17: 0.08 µg/l<br>modelling: see below |

| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v.1.1.1 |
| Application rate | 0.05 kg as/ ha to winter cereals in early spring with 50 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/l) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun | 01/04 | 0.008 | 0.01 | 0.156 | 0.097 | 0.001 |
| Hamburg | 01/04 | 0.066 | 0.040 | 0.218 | 0.166 | 0.008 |
| Jokionen | 01/06 | 0.082 | 0.018 | 0.216 | 0.129 | 0.008 |
| Kremsmünster | 01/04 | 0.079 | 0.059 | 0.207 | 0.153 | 0.014 |
| Okehampton | 01/04 | 0.089 | 0.067 | 0.189 | 0.152 | 0.014 |
| Piacenza | 01/04 | 0.074 | 0.071 | 0.232 | 0.178 | 0.009 |
| Porto | 10/03 | 0.006 | 0.002 | 0.058 | 0.032 | 0.001 |
| Sevilla | 10/03 | 0.000 | 0.000 | 0.007 | 0.002 | 0.000 |
| Thiva | 10/03 | 0.000 | 0.001 | 0.105 | 0.053 | 0.000 |

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| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v1.1.1 |
| Application rate | 0.05 kg as/ ha to spring cereals 3 weeks after emergence with 25 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/l) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun | 31/03 | 0.004 | 0.006 | 0.179 | 0.097 | 0.001 |
| Hamburg | 22/04 | 0.063 | 0.046 | 0.324 | 0.237 | 0.009 |
| Jokionen | 01/06 | 0.143 | 0.018 | 0.296 | 0.166 | 0.009 |
| Kremsmünster | 22/04 | 0.075 | 0.065 | 0.305 | 0.213 | 0.011 |
| Okehampton | 22/04 | 0.099 | 0.064 | 0.309 | 0.224 | 0.017 |
| Porto | 31/03 | 0.002 | 0.001 | 0.060 | 0.025 | 0.000 |

| | |
|---|---|
| Method of calculation and type of study | Modelling using FOCUS-PELMO v1.1.1 |
| Application rate | 0.05 kg as/ ha to maize 3 weeks after emergence with 25 % interception |

| Location | Application time | Predicted 80th percentile concentration (µg/l) | | | | |
|---|---|---|---|---|---|---|
| | | tritosulfuron | 635M01 | 635M02 | 635M03 | 635M04 |
| Châteaudun* | 22/05 | 0.015 | 0.012 | 0.212 | 0.124 | 0.002 |
| Hamburg | 26/05 | 0.084 | 0.048 | 0.347 | 0.240 | 0.013 |
| Kremsmünster | 26/05 | 0.050 | 0.033 | 0.273 | 0.183 | 0.006 |
| Okehampton | 15/06 | 0.083 | 0.050 | 0.298 | 0.223 | 0.011 |
| Piacenza* | 05/06 | 0.062 | 0.091 | 0.254 | 0.218 | 0.010 |
| Porto | 22/05 | 0.001 | 0.000 | 0.036 | 0.010 | 0.000 |
| Sevilla* | 28/03 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Thiva* | 11/05 | 0.000 | 0.000 | 0.060 | 0.023 | 0.000 |

*Scenarios with irrigation

| | |
|---|---|
| Method of calculation and type of study | Modelling using MACRO FOCUS v1.2.1<br>Location: Chateaudun |
| Application rate | 0.05 kg as/ ha to winter cereals in early spring (50 % interception), spring cereals 3 weeks after emergence (25 % interception), to maize 3 weeks after emergence (25 % interception) |

| Crop | Application time (julian days) | Predicted 80th percentile concentration (µg/l) | |
|---|---|---|---|
| | | tritosulfuron | 635M04 (AMTT) |
| Winter cereals | 91 | 0.012 | 0.002 |
| Spring cereals | 90 | 0.017 | 0.003 |
| Maize | 144 | 0.064 | 0.009 |

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**Fate and behaviour in air** (Annex IIA, point 7.2.2, Annex III, point 9.3)

| | |
|---|---|
| Direct photolysis in air | no data, not required |
| Quantum yield of direct phototransformation | < 1.05 x $10^{-4}$ (pH 5)<br>< 2.23 x $10^{-4}$ (pH 7) |
| Photochemical oxidative degradation in air | calculation according to Atkinson (AOP, ver 1.51, Syracuse), $DT_{50}$: 5.2 h (12 h-day) |
| Volatilization | from plant surfaces: 3 % (24 h) |
| | from soil: 2 % (24 h) |

**PEC (air)**

| | |
|---|---|
| Method of calculation | not calculated due to low volatility and rapid photochemical oxidative degradation |

**$PEC_{(a)}$**

| | |
|---|---|
| Maximum concentration | not calculated |

**Definition of the Residue** (Annex IIA, point 7.3)

| | |
|---|---|
| Relevant to the environment | tritosulfuron and metabolites 635M01, 635M02 and 635M03<br>Metabolites 635M01, 635M02 and 635M03 show no biological activity. The ecotoxicological risk assessment 635M01, 635M02 and 635M03 is not yet finished. The toxicological relevance of 635M01 and 635M02 is open. |

**Monitoring data, if available** (Annex IIA, point 7.4)

| | |
|---|---|
| Soil (indicate location and type of study) | none |
| Surface water (indicate location and type of study) | none |
| Ground water (indicate location and type of study) | none |
| Air (indicate location and type of study) | none |

**This version does not reflect the outcome of the meeting. However, an updated version is not available at the moment.**

Appendix 3

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

## 2 Environmental Fate and behaviour

| | | |
|---|---|---|
| Hazard symbol | | Not discussed |
| Risk phrase | | Not discussed |
| Safety phrase | | Not discussed |

**ANNEX 04 TO CONCISE OUTLINE REPORT OF ECCO 139 PEER REVIEW MEETING**

TRITOSULFURON

Rapporteur Member State: GERMANY

Specific comments on the active substances in the section **Ecotoxicology** are listed below. The conclusions of the meeting were as follows:

1a. Comments received and discussed:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| 20-3-03 | INRA | Tritosulfuron_139_com01_FR |
| 6-3-03 | PSD | Tritosulfuron_139_com02_UK |
| 28-04-03 | NL | Tritosulfuron_139_com03_NL |
| 26-5-03 | BE | Tritosulfuron_139_com02_BE |

1b. Comments received but not discussed (because deadline of submission was not met):

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |
| | | |

1c. Documents tabled at the meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |
| | | |

2. **Definition of the residues of ecotoxicological concern:** Water: a.s. Soil: a.s., MO1, MO2, MO3 and MO4 (pending further data.

3. **Data on preparations:** Dossier incomplete.

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

5. **Recommended restrictions/conditions for use:** One application, pre- or post-emergence on wheat and maize at 50 g a.s./ha.

**Areas of concern:** Possible risk to soil organisms from metabolites.

Appendix 1: ECCO 139 reporting table: TRITOSULFURON

Appendix 2: List of end points: TRITOSULFURON

Appendix 3: Suggested classification and labelling: TRITOSULFURON

# Appendix 1: ECCO 139 reporting table Tritosulfuron (Hb)

## 3. Ecotoxicology

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | Section 3<br>Data requirements: 5<br>Open points: 5 |
| (i) | GAP | Pre- and post-emergence herbicide on wheat and maize up to 50 g a.s./ha. One per crop | |
| (ii) | Birds/Mammals | Studies submitted for the a.s. demonstrated low acute, short-term and long-term toxicity to birds and mammals. The RMS was requested to replace the toxicity end points in terms of daily dose.<br>The relevance of AMTT (BH 635/5) for the risk assessment was discussed. It was noted that this is a metabolite of potential environmental concern as well as an impurity (up to 2.5% in the technical specification depending on batch). The toxicology (ECCO 136) meeting had highlighted AMTT as a toxicologically relevant metabolite. AMTT was present in a hen study, it was also in the technical specification used in the avian toxicity studies, therefore birds were expected too have been exposed to it. AMTT turns up only at low levels in the environment (soil: 6% after 90 days; half-life 11 – 133 days) therefore the risk from AMTT was thought to have been addressed in the studies that used the active substance.<br>For mammals data for AMTT (acute, short–term and long-term) were provided in the Toxicology end points. The meeting requested that the applicant should determine if the risk to mammals from AMTT was acceptable.<br>The comments of the Netherlands, Belgium and the UK were taken into account. France highlighted that the TERst should be based on the LC50 and not the NOEC, hence the TER is >3448 and not 893 as quoted. | 3.1 The applicant to define the risk to mammals from AMTT using toxicology end points.<br>Open point 3.1: RMS to convert toxicity values into daily dose values. |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (iii) | Aquatic life | The active substance was of low toxicity to fish and *Daphnia magna* but of high toxicity to algae and *Lemna*. The a.s. was not considered to pose a risk to sediment dwelling organisms as it was not found in high concentrations in sediment and was also of low toxicity to *Daphnia magna*. The most sensitive species was *Lemna*. A safe use was identified without risk mitigation measures (i.e. TER was 54 @ 1m).<br><br>Of the metabolites, M01 (BH 635/4) slowly increases to 28% over 100 days in the water phase and up to 33% in sediment. Toxicity data were available for fish, *Dap*hnia and algae and it was shown to be less toxic than a.s. A proposal was made to test *Lemna* with this metabolite as *Lemna* was shown to be the most sensitive species to the a.s. However, this metabolite appears to have no activity to the other species tested or herbicidal activity and, therefore, the meeting decided that the risk to *Lemna* was acceptable. MO1 does occur in sediment but due to the low chronic the toxicity of a.s. to *Daphnia* and the low acute toxicity of the metabolite to *Daphnia* further studies with sediment dwellers were not considered necessary.<br><br>MO2 and MO3 both appeared in the sediment/water study. Toxicity data on fish, *Daphnia* and algae were provided and, in-line with the comments above, the meeting concluded that no further data were needed. AMTT did not appear in the sediment/water study therefore there were no concerns with this metabolite.<br><br>For ground water, leaching was possible for MO1 at 1.0 ug/l, MO2 at 0.2 ug/l and MO3 at 0.4 ug/l. No a.s. or AMTT was detected. MO1 – 3 were not considered ecotoxicologically relevant and demonstrated no herbicidal activity, therefore, there were no concerns from leaching of these metabolites. The PECgw figures were taken from the ECCO 137 reporting table and associated end point sheet.<br><br>The toxicity of the formulation including BAS 15200 was not higher than the a.s., therefore the risk was covered by the risk assessment for the a.s. No concerns for bioaccumulation were identified as the log Pow less than 3.<br><br>The comments of France, Belgium, the Netherlands and the UK were taken into account. | Open point 3.2: RMS to clarify if nominal or mean measured concentrations were used in the aquatic studies.<br><br>Message from ECCO 137 (Fate):<br>Additional data for MO1 were not considered necessary. |
| (iv) | Honeybees | The toxicity data submitted indicated a low toxicity through both the oral and contact route. The HQ values were below 50, therefore no risk to bees was identified. The crops were not considered attractive to bees at the stage treated, therefore there was not expected to be any systemic risk to bees.<br><br>The comments of the Netherlands were taken into account. | |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (v) | Non target arthropods | Tests were conducted using the proposed formulation + BAS 152000 at up to 70 g a.s./ha. The effects observed were lower than 30% in all cases. RMS was requested to change LR50 to doses used showing % effects in-line with ESCORT I.<br>The comments of Belgium were taken into account. | Open point 3.3: RMS to update end point table with respect to ESCORT I value for *T. pyri*. |
| (vi) | Earthworms | In acute studies no effects were observed at doses up to 1000 mg a.s./kg. No information on chronic effects for earthworms was submitted. However, due to the proposed GAP (1 application) and the DT50 (11 – 21 days) no further long-term testing with the a.s. was requested.<br>Acute toxicity data for the metabolites MO1, MO2 and MO3, indicated no effects at up to 1000 mg metabolite/kg. Additional tests on MO4 indicated slight acute toxicity to earthworms.<br>No information on long-term effects of metabolite MO1, MO2 and MO3 was submitted. Considering the half-life in the field of these metabolites the meeting requested that the long-term risk of these metabolites should be addressed. It was appreciated that these metabolites were not particularly acutely toxic but their persistence in the environment required that further testing be carried out. The meeting noted that MO4 was not persistent in the environment but due to the slight toxicity it had demonstrated and the fact that concerns for this metabolite had been raised in other areas the meeting decided that the chronic risk posed by MO4 should be evaluated.<br>The comments of France, Belgium and the UK were taken into account. | 3.2 The long-term risk to earthworms for MO1, MO2, MO3 and MO4 (AMTT) metabolites to be addressed. The plateau concentration in the environment must be covered.<br>3.3 Regarding the MO4 study, the residues in earthworms should be determined to aid the vertebrate risk assessment (NB This part of the DR is dependent upon the outcome of the results of 3.2). |
| (vii) | Soil macro-organisms | Due to the persistence of MO1, MO2 and MO3, the meeting requested that a litter bag study to address the risk from MO1 – MO4 should be conducted. The doses chosen should cover plateau levels likely to be found in the soil. Analytical measurements should be conducted as well.<br>The comments of Belgium were taken into account. | 3.4 Data are required to address the risk posed to soil macro-organisms. |
| (viii) | Soil microbial processes | Data submitted on the a.s. indicated no concerns. However, only N conversion had been tested for the metabolites not carbon mineralisation. The meeting requested that the applicant either provided a study or addressed why a study had not been submitted.<br>The comments of the UK, Belgium and the Netherlands were taken into account. | 3.5 Data are required to address the address risk posed from metabolites to carbon mineralistion<br>Open point 3.4: RMS to update list of end points. |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (ix) | Non target flora and fauna | For the formulation plus BAS 15200, dose response tests for 6 species were conducted in the laboratory and additional tests were conducted in an extended study. It was agreed that the metabolites were not considered to have herbicidal properties. The meeting discussed the need for risk mitigation measures, as the TER, using the laboratory data at 1m, was less than 5. The extended study tests indicated that risk mitigation measures were probably not required (TER 4.5 @ 1m) due to worst case exposure of the plants. | Open point 3.5: RMS to amend reference to field studies in end point table. |
| (x) | Sewage | No inhibition of microbial activity in sewage observed. | |
| (xi) | Classification | R50/R53 | |
| (xii) | Residue definition | Water: a.s.; soil: a.s. and MO1, MO2, MO3 and MO4 (pending further data) | |

Appendix 2

LIST OF END POINTS: **TRITOSULFURON**

## 3 Ecotoxicology section

**Effects on terrestrial vertebrates** (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

| | |
|---|---|
| Acute toxicity to mammals | $LD_{50}$ = 4700 mg as/kg bw/d (rat) (batch no. N12) |
| Reproduction toxicity to mammals | NOAEL 600 mg as/kg diet (two-generation-test, rat) (batch no. N34) |
| Acute toxicity to birds | $LD_{50}$ > 2000 mg as/kg bw/d (mallard duck, bobwhite quail) (batch no. N24) |
| Dietary toxicity to birds | $LC_{50}$ > 5000 mg as/kg diet (mallard duck, bobwhite quail) (batch no. N24) |
| Reproductive toxicity to birds | NOAEL = 300 mg as/kg diet (one-generation-test, mallard duck) (batch no. N24) |

**Toxicity/exposure ratios for terrestrial vertebrates** (Annex IIIA, points 10.1 and 10.3)

| Application rate (kg as/ha) | Crop | Category (*e.g.* insectivorous bird) | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|---|
| 0.05 kg as/ha | maize/cereals | herbivorous bird | acute | > 1429 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous bird | subacute | 111 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous bird | long-term/ reproduction (one-generation-study) | 53 | 5 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | acute | > 3448 | 10 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | short-term | 431 | 10 |
| 0.05 kg as/ha | maize/cereals | insectivorous bird | long-term / reproduction (one-generation-study) | 207 | 5 |
| 0.05 kg as/ha | maize/cereals | herbivorous mammal | acute | 3357 | 10 |
| 0.05 kg as/ha | maize/cereals | herbivorous mammal | long-term/ reproduction (two-generation-study, rat) | 107 | 5 |

**Toxicity data for aquatic species (most sensitive species of each group)**
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

| Group | Test substance | Time-scale | Endpoint | Toxicity (mg/L)* |
|---|---|---|---|---|
| Laboratory tests | | | | |
| *O. mykiss* | a.s. | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *O. mykiss* | a.s. | chronic, 28 d flow-through | Mortality NOEC | 21.5 |
| | a.s. | acute, 48 h, static | Immobilization $EC_{50}$ | > 100 |
| *D. magna* | a.s. | chronic, 21 d static renewal | Growth NOEC | 56 |
| *A. flos-aquae* | a.s | chronic 96 h static | Biomass $EC_{50}$ | 0.58 |
| *P. subcapitata* | a.s. | chronic, 72 h static | Biomass $EC_{50}$ | 0.23 |
| *L. gibba* | a.s. | chronic, 7 d static renewal | Fronds $EC_{50}$ | 0.0255 |
| *P. putida* | a.s. | acute | Growth $EC_{50}$ | > 10000 |
| *O. mykiss* | 635M02 (BH 635-2 Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic | Biomass $EC_{50}$ | > 100 |
| *O. mykiss* | 635M03 (BH 635-3, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 48 (m) |
| *D. magna* | " | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | > 100 |
| *O. mykiss* | 635M01 (BH 635-4, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | > 54 (m) |
| *D. magna* | " | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | > 100 |
| *B. rerio* | 635M04 (BH 635-5, AMTT, Metab.) | acute, 96 h static | Mortality $LC_{50}$ | 170 |
| *D. magna* | ” | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic | Biomass $EC_{50}$ | > 100 |

| | | | | |
|---|---|---|---|---|
| *O. mykiss* | BAS 635 00 H | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *P. subcapitata* | " | chronic, 72 h static | Biomass $EC_{50}$ | 0.42 |
| *O. mykiss* | 70 g BAS 635 00 H + 1.5 L BAS 15200S | acute, 96 h static | Mortality $LC_{50}$ | > 100 |
| *D. magna* | " | acute, 48 h static | Immobilization $EC_{50}$ | > 100 |
| *L. gibba* | " | chronic, 7 d static | Fronds $EC_{50}$ | 0.0355 |
| Microcosm or mesocosm tests | | | | |
| | | | | |

*: **with exception of the concentrations signed with (m), all concentrations were given as nominal**

**Toxicity/exposure ratios for the most sensitive aquatic organisms** (Annex IIIA, point 10.2)

| Application Rate (kg as/ha) | Crop | Organism | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|
| 0.05 | field crop | *L. gibba* | chronic | 1 | 54 | 10 |

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) | not relevant; logPow < 3 |
| Annex VI Trigger for the bioconcentration factor | |
| Clearance time ($CT_{50}$) ($CT_{90}$) | |
| Level of residues (%) in organisms after the 14 day depuration phase | |

**Effects on honeybees** (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

| | |
|---|---|
| Acute oral toxicity | $LD_{50}$ = 200 µg/bee (active substance)<br>$LD_{50}$ = 121.62 µg/bee (formulation: BAS 63500 H + BAS 15200 S) |
| Acute contact toxicity | $LD_{50}$ = 200 µg/bee (active substance)<br>$LD_{50}$ = > 100 µg/bee (formulation: BAS 63500 H + BAS 15200 S) |

**Hazard quotients for honey bees** (Annex IIIA, point 10.4)

| Application rate (kg as/ha) | Crop | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|---|
| Laboratory tests (active substance) | | | | |
| 0.05 | maize, cereals | oral | 0.25 | 50 |
| 0.05 | maize, cereals | contact | 0.25 | 50 |
| Laboratory tests (formulation: BAS 635 00 H + BAS 15200 S) | | | | |
| 0.05 | maize, cereals | oral | 0.41 | 50 |
| 0.05 | maize, cereals | contact | 0.5 | 50 |

| Field or semi-field tests |
|---|
| Not required |

**Effects on other arthropod species** (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

| Species | Stage | Test Substance | Dose (kg as/ha) | Endpoint | Effect (%) | Annex VI Trigger |
|---|---|---|---|---|---|---|
| Laboratory tests | | | | | | |
| *T. pyri* | protonymphs | BAS 635 00 H + BAS 152 00 S | 0.05<br>0.002-0.05 | mortality<br>fertility | 74<br>($LR_{50}$: 28.6 g a.s./ha) | 30 |
| *T. pyri* (natural substrate) | protonymphs | ” | 0.05 | mortality<br>fertility | 0<br>3.6 | 30 |
| *A. rhopalos.* | imagines | ” | 0.150 | mortality<br>parasitation capacity | 10<br>30 | 30 |
| *C. carnea* | larvae | ” | 0.05 | mortality<br>fertility | 0<br>0 (+ 11) | 30 |
| *P. cupreus* | imagines | ” | 0.05 | mortality<br>food uptake | 0<br>0 | 30 |
| *A. bilineata* | imagines | ” | 0.05 | parasitation capacity | 14 | 30 |
| *Pardosa sp.* | adult | ” | 0.05 | mortality<br>food uptake | 0<br>0 (+ 23) | 30 |

| Field or semi-field tests |
|---|
| Not required |

**Effects on earthworms** (Annex IIA, point 8.4, Annex IIIA, point 10.6)

| | |
|---|---|
| Acute toxicity | $LC_{50}$ > 1000 mg as/kg (technical tritosulfuron)<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M02 BH 635-2))<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M03 (BH 635-3))<br>$LC_{50}$ > 1000 mg/kg (metabolite 635M01 (BH 635-4))<br>$LC_{50}$ = 671 mg/kg (metabolite 635M04 (BH 635-5))<br>$LC_{50}$ > 34.2 mg as/kg (formulation BAS 635 00 H + BAS 152 00 S) |
| Reproductive toxicity | - |

**Toxicity/exposure ratios for earthworms** (Annex IIIA, point 10.6)

| Application rate (kg as/ha) | Crop | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|
| 0.05 | maize, cereals | Acute | > 510 | 10 |
| 0.05 | maize, cereals | chronic | | 5 |

**Effects on soil micro-organisms** (Annex IIA, point 8.5, Annex IIIA, point 10.7)

| | |
|---|---|
| Nitrogen mineralisation | No effects > 25 % up to 0.35 kg BAS 635 00 H + 6.25 L BAS 152 00 S |
| Carbon mineralisation | No effects > 25 % up to 0.35 kg BAS 635 00 H + 6.25 L BAS 152 00 S |

**Effects on terrestrial non-target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)**

| | |
|---|---|
| Greenhouse test | *Brassica napus* (most sensitive species):<br>$ED_{50}$ 4.3 g BAS 635 00 H + 76.4 ml BAS 152 00 S |
| Extended study, plants moved in the field | *Brassica napus* (most sensitive species):<br>$ED_{50}$ 8.7 g BAS 635 00 H + 126 ml BAS 152 00 S |

**Toxicity/exposure ratios for terrestrial non-target plants (Annex IIIA, point 10.8)**

| Distance from treated area (m) | Drift (%) | Amount of drift (g product/ha) | TER ( $ED_{50}$ 4.3 g/ha) | TER ( $ED_{50}$ 8.7 g/ha) |
|---|---|---|---|---|
| 1 | 2.77 | 1.94 | 2.2 | 4.5 |
| 5 | 0.57 | 0.399 | 10.8 | 21.8 |

Appendix 3

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

## 3 Ecotoxicology section

| | | |
|---|---|---|
| Hazard symbol | **N** | Dangerous for the environment |
| Risk phrase | **R 50** | Very toxic to aquatic organisms |
| | **R 53** | May cause long-term adverse effects in the aquatic environment |

**ANNEX 4 TO CONCISE OUTLINE REPORT OF ECCO 136 PEER REVIEW MEETING**

# Tritosulfuron

Rapporteur Member State: GERMANY

Specific comments on the active substances in the section **Mammalian toxicology** are listed below. The conclusions of the meeting were as follows:

1a. Comments received and discussed:

| Date | Supplier | File Name |
|---|---|---|
| 7 February 2003 | France | COM 01 FR |
| 10 February 2003 | UK | COM 02 UK |
| 17 February 2003 | Belgium | COM 03 BE |
| 3 March 2003 | Netherlands | COM 04 NL |

1b. Comments received but not discussed (because deadline of submission was not met):

| Date | Supplier | File Name |
|---|---|---|
| - | - | |

1c. Documents tabled at the meeting:

| Date | Supplier | File Name |
|---|---|---|
| - | - | - |

2. **Residues relevant to worker safety:** A number of outstanding issues need to be resolved concerning the metabolites of tritosulfuron before an assessment can be made. The RMS to provide a revised list of endpoints.

3. **Data on preparations:** The data package submitted for 'Penncap M' was considered to be complete.

4. **Classification and labelling:** The experts provisionally proposed classification for Tritosulfuron (≤0.02% AMTT): Xi, R43 and the metabolite AMTT : T, R40, R 48/22, R61 (R64).

5. **Recommended restrictions/conditions for use:** Until outstanding issues are addressed no uses are considered acceptable. RMS to provide an Addendum when all outstanding information is available.

**Areas of concern:** The main area of concern was the possible formation of AMTT and/or it's metabolite's in treated crops, the environment and in solution in the spray tank.

Appendix 1: ECCO 136 reporting table: TRITOSULFURON

Appendix 2: List of end points: TRITOSULFURON

Appendix 3: Suggested classification and labelling: TRITOSULFURON

# Appendix 1: ECCO 136 reporting table Tritosulfuron

## 4. Mammalian toxicology

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (i) | General | Comments from UK, FR, BE and NL were discussed. One of the main issues raised was presence of AMTT in the technical material and the possible exogenous formation of this metabolite. The meeting noted that the Notifier had conducted a great number of animal studies, particularly long term and reproduction studies, with tritosulfuron.<br>These studies were conducted with various batches of technical material, containing AMTT at levels ranging from 0.006 – 2.45% w/w. It appeared, based on the these studies, that most of the toxicological findings were likely to be a consequence of the presence of AMTT, rather than the parent a.s.<br>The RMS informed the meeting that Notifier had proposed to limit AMTT in the technical material to 0.02% w/w. The meeting decided to set endpoints for tritosulfuron and AMTT separately.<br>For tritosulfuron the studies with the lowest levels of AMTT were used (i.e. most relevant to the proposed technical specification) for setting endpoints. It was noted that this approach was problematical, because some endpoints would need to be based on studies with relatively high AMTT content giving an apparently low NOAEL.<br>Members stressed the need to indicate that the endpoints set applied to tritosulfuron containing 0.02% w/w AMTT.<br>A general issue regarding the suitability of maize as a representative crop for plant metabolism was raised, as this was the case with tritosulfuron. | |
| (ii) | Rate and extent of excretion | The meeting was noted that based on the quoted plasma half-lives in the study reports, the levels of radioactivity in plasma over time at the low dose followed a biphasic pattern, whereas it was monophasic at the top dose. | Open Point 4.1: The Notifier to comment on the differences in absorption, distribution and excretion leading to the biphasic and monophasic patterns at the low and high |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | dose levels, respectively. |
| (iii) | Metabolism in animals | It was noted that AMTT was quoted as a metabolite in the rat, however the levels of AMTT in the dosing solutions was unknown. | |
| (iv) | Toxicologically significant compounds | The meeting considered that toxicologically the most significant compounds, were the parent compound and metabolites, especially AMTT (2-amino-4-trifluoromethyl-6-methoxy-1,3,5-triazine) and 635 M02, and possibly AHTT (major metabolite of AMTT). This would need to be clarified at the residues/Fate and Behaviour Meetings. It was also noted that the methods of analysis would need to be capable of determining the levels of AMTT down to appropriately low levels, both in plants and the environment. | Open Point 4.2: ECCO residues/Fate and Behaviour Meetings to consider the formation of these metabolites in plant and the environment.<br>Open Point 4.3: For the residues/Fate and Behaviour Meetings to consider, how robust are the methods for determining AMTT in plants and the environment.<br>Open Point 4.4: The Notifier to comment on the relevance of exposure to AMTT, and 635MO2 to man (paying special attention to potential for reproductive toxicity). |
| (v) | Acute | The meeting noted that the MMAD of the particles in the test chamber generated during the acute inhalational toxicity study was 9.2 μm (i.e. most of the particles outside the respirable range). However the acute inhalational toxicity study with the formulated product the particle size generated was much smaller and in this study death had been seen. It was felt the Notifier should comment on the reasons why it was not possible to generate a smaller particle size distribution with the a.s. given that it could be done with the formulation. | Open Point 4.5: The Notifier to explain why it was not possible to generate a smaller particle size distribution with the a.s. given that it could be done with the formulation. |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (vi) | Short-term toxicity: lowest relevant oral NOAEL | The critical NOAEL was that from the 12 month dog study of 6 mg/kg bw/day with tritosulfuron batch N24. It was noted that the Notifier had not repeated this study with a batch of tritosulfuron containing less AMTT. Therefore this became the critical NOAEL, possibly due to the comparatively high levels of AMTT, rather than the toxicity of tritosulfuron to dogs. | |
| (vii) | Genotoxicity | Comments from the UK were noted. The meeting concluded that there was evidence of clastogenic potential under *in vitro* conditions. Although the mouse micronucleus assay was negative, there was evidence that mice were more tolerant to tritosulfuron/AMTT than rats. Concerns were also raised regarding the mammary tumours seen in the rat not the mouse, suggesting there maybe species differences.<br>The meeting discussed the possible use of another *in vivo* assay in rats to clarify the genotoxic potential of tritosulfuron/AMTT. The use of a comet assay on mammary cells was suggested to gain an insight into the possible mechanism of tumour formation. The meeting concluded that in the first instance a *in vitro* cytogenetics assay with AMTT was required. | Data requirement 4.1: An a *in vitro* cytogenetics assay with AMTT is required.<br>Open Point 4.6: RMS to consider additional genotoxicity study with tritosulfuron |
| (viii) | Long term toxicity and carcinogenicity lowest relevant NOAEL | The meeting noted that in the long term rat studies, increased water consumption was a frequently observed finding. Concern was expressed that a NOAEL had not been defined for this effect given that it was seen at the lowest doses tested (50 and 100 ppm). The Notifier would need to comment on the toxicological significance of this finding. It was noted that in two of the chronic studies the top dose groups were sacrificed early without any explanation and no tissues were examined from these groups.<br>The meeting noted that no NOAEL had been defined in the mouse 18 month study as reductions in bodyweight gain were seen at the lowest dose tested (250 ppm). However this was considered acceptable as the ADI had been based on the 12 month dog study which gave a 600 fold safety factor over the mouse LOAEL.<br>The meeting agreed the critical long term toxicity and carcinogenicity NOAEL for tritosulfuron (<0.02% AMTT) was that from the 2 year rat study with batch N59, of 100 ppm (50 mg/kg bw/day) | Open Point 4.7: The Notifier to comment on the toxicological significance of the increased water consumption seen down to the lowest dose levels in the chronic rat studies.<br>Open Point 4.8: The Notifier to give the rationale for the premature termination of the top dose groups in the chronic rat studies (BASF doc 2001/1006060 and 2001/1006064) |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (ix) | Reproductive toxicity: lowest relevant reproductive NOAEL | The meeting noted that cleft palate had been observed in 2 F1a and in 1 F1b pups in the 2 generation study. It was considered unusual to see gross malformations in such a study due to the cannibalism of such pups, and it was possible that the actual numbers of affected pups was greater than the 3 seen. It was also noted that cleft palate had been reported in the range finding study in the rats<br>The meeting considered that AMTT had not been adequately assessed for developmental toxicity therefore no ADI, ARfD or AOEL could be set for AMTT | |
| (x) | Supplementary studies with metabolites | The meeting noted that based on the environmental fate data there was a potential metabolite 635MO2 to occur in groundwater at >0.1 μg/litre. Based on the acute study and a summary of the recently submitted 28 days study with this metabolite it was significantly more toxic than the parent and had a different profile of toxicity to AMTT. It was also noted the 635MO2 was positive in an *in vitro* cytogentics assay (+S9). | Open Point 4.9: RMS to provide details of the 28 day study on M02 in the new addendum |
| (xi) | ADI | The meeting discussed comments received from a number of MSs and concluded that the most appropriate study on which to base an ADI (tritosulfuron) was the 12 month dog study. An ADI of 0.06 mg/kg bw/d was agreed, based on the NOAEL of 6 mg/kg bw/d and using a safety factor of 100. The database for AMTT was not considered sufficient to set an ADI. | |
| (xii) | AOEL | The meeting discussed comments received from a number of MSs and concluded that the most appropriate study on which to base an AOEL (tritosulfuron) was the 90 day dog study. An AOEL of 0.15 mg/kg bw/d was agreed, based on the NOAEL of 15 mg/kg bw/d and using a safety factor of 100. The database for AMTT was not considered sufficient to set an AOEL. | |
| (xiii) | ARfD | Taking into account the toxicity profile of tritosulfuron it was considered that there was no need to set an ARfD. | |
| (xiv) | Dermal absorption | Comments from a number of MSs were discussed. Based on the *in vivo* rat study and *in vitro* data in rat and human skin 1 and 2 % absorption factors were set for the concentrate and in use dilutions respectively. | |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (xv) | Operator exposure | The meeting expressed concern over the possible formation of AMTT in solution in the spray tank. It was considered that this aspect would need to be fully addressed by the Notifier. Operator exposure would need to be reassessed following clarification of the outstanding issues. | Data requirement 4.2: The Notifier must address the possibility of the formation of AMTT and it's metabolites in tank mix (including the effect of adding the specified adjuvant). |
| (xvi) | Worker exposure | Worker exposure would need to be reassessed following clarification of the outstanding issues. | |
| (xvii) | Bystander exposure | Bystander exposure would need to be reassessed following clarification of the outstanding issues. | |

Appendix 2

LIST OF END POINTS: **TRITOSULFURON**

## 4 Mammalian toxicology section

**NOTEs: FIGURES IN PARENTHESIS INDICATE BATCH NUMBER OF TRITOSULFURON USED IN STUDY (N24 contained 2.4% AMTT other batches contained AMTT ranging from 0.006 – 2.45% w/w)**
**ENDPOINTS APPLY TO TRITOSULFURON CONTAINING 0.02% AMTT**

*Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)*

| | |
|---|---|
| Rate and extent of absorption | Rapid ($T_{max}$0.5h) nd complete (≥90 % based on urinary and bile (10-27%) excretion over 48 h)-rats |
| Distribution | Widely distributed |
| Potential for accumulation | No potential for accumulation |
| Rate and extent of excretion | Rapid (approx. 80 % via urine and 12 % via feces over 48 h) |
| Metabolism in animals | Limited (hydroxylation at the 4-position of the phenyl ring followed by conjugation; cleavage of the triazine ring and degradation to sulfonamide and sulfonate) |
| Toxicologically significant compounds (animals, plants and environment) | Parent compound and metabolites (especially AMTT (2-amino-4-trifluoromethyl-6-methoxy-1,3,5-triazine ***and 635 M02***) and possibly AHTT (major metabolite of AMTT). *To be clarified at the residues/Fate and Behaviour Meetings)* |

*Acute toxicity (Annex IIA, point 5.2)*

| | |
|---|---|
| Rat $LD_{50}$ oral (N12) | 4700 mg/kg bw |
| Rat $LD_{50}$ dermal (N12) | > 2000 mg/kg bw |
| Rat $LC_{50}$ inhalation (N12) | > 5.4 mg/l air (dust aerosol, 4 h, MMAD 9.2 μm) |
| Skin irritation (N12) | Not irritating |
| Eye irritation (N12) | Not irritating |
| Skin sensitisation (test method used and result) N12) | Sensitising (M&K test)<br>**R43** |

*Short term toxicity (Annex IIA, point 5.3)*

| | |
|---|---|
| Target / critical effect | Liver, kidney/centrilobular hypertrophy, nephropathy (rat and dog). Urinary bladder and kidney (mouse) |
| Lowest relevant oral overall NOAEL/NOEL* | 12-month, dog (N24): 200 ppm (6 mg/kg bw/d)<br>[calculated level of AMTT: 0.15 mg/kg bw/day] |
| Lowest relevant dermal NOAEL/NOEL* | 28-day (20 exposure), rat (N24): 1000 mg/kg bw based on systemic effects |
| Lowest relevant inhalation NOAEL / NOEL | No data-not necessary |

*Genotoxicity* (Annex IIA, point 5.4)*

| | |
|---|---|
| (N24) | No evidence of genotoxic potential *in vivo* based on a mouse micronucleus assay; clastogenic effect |

| | |
|---|---|
| | under in vitro conditions . |

*Long term toxicity and carcinogenicity (Annex IIA, point 5.5)*

| | |
|---|---|
| Target / critical effect | Kidney (interstitial nephritis), Liver (pericholangitis) |
| Lowest relevant NOAEL / NOEL* | 2-yr, rat (N24): 100 ppm (5 mg/kg bw/d)<br>[calculated level of AMTT: 0.123 mg/kg bw/Day]<br>2-year rat (N59): 1000 ppm<br>18-month mouse: LOAEL 250 ppm (36 mg/kg bw/day) |
| Carcinogenicity* | Mammary gland tumours in female rats at 1000ppm (N24). NOAEL (tumours 250 ppm, 16 mg/kg bw/day)<br>**R 40** |

*Reproductive toxicity (Annex IIA, point 5.6)*

| | |
|---|---|
| Reproduction target / critical effect* | Pup mortality in absence of parental toxicity |
| Lowest relevant reproductive NOAEL / NOEL* | 2-gen. rat: 25 ppm (N24) (2.4 mg/kg bw/d)<br>[calculated level of AMTT: 0.06 mg/kg bw/d]<br>**R61**<br>2-gen. rat: 600 ppm (N34) (40 mg/kg bw/d)<br>[calculated level of AMTT: 0.01 mg/kg bw/d] |
| Developmental target / critical effect | 2-gen. rat: cleft palate in 2 F1a and in 1 F1b pups, agenesia of kidney in F2 pups at 3500/2100 ppm (N24)<br>Developmental rat (N12): Hydrourethers, renal pelves dilatation<br>Developmental rabbbit (N14): accessory 13t$^{h}$ rib(s) (rabbits). |
| Lowest relevant developmental NOAEL / NOEL | 120 mg/kg bw/d (rat) |

*Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7)*

| | |
|---|---|
| Acute oral and 90-day neurotoxicity* | No signs of neurotoxicity in the presence of general toxicity (rat)<br>NOAELs Acute (N24): 2000 mg/kg, 90 day (N24) 3500 ppm<br>**(NOAEL General toxicity, 90-d, rat: 100 ppm (7 mg/kg bw/d))** |
| Developmental neurotoxicity | No developmental neurotoxicity (N59) |
| Lowest relevant NOAEL for neurotoxicity* | 90-d, rat: 3500 ppm (243 mg/kg bw/d) |

*Other toxicological studies (Annex IIA, point 5.8)*

| | |
|---|---|
| Supplementary studies with metabolites: | 635M01: $LD_{50}$ oral rat: > 5000 mg/kg bw; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative<br><br>635M02: $LD_{50}$ oral rat: 1000 mg/kg bw; Ames test, CHO-HPRT test: negative, in vitro chromosome aberration test: ***positive*** (with activation)<br><br>635M03: $LD_{50}$ oral rat: > 5000 mg/kg bw; subchronic study in rats: no effects; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative<br><br>635M017: $LD_{50}$ oral rat: > 2000 mg/kg bw; Ames test, CHO-HPRT test, in vivo mouse micronucleus test: negative<br>Supplementary studies with AMTT (635M04): Toxicokinetic, rats: rapid excretion, major metabolite AHTT (635M11); $LD_{50}$ oral rat: > 200 < 2000 mg/kg bw (ulcer in glandular stomach); no changes in estrus cycle and hormone analysis parameters; Ames test, CHO-HPRT test, mouse micronucleus test: negative; developmental toxicity < 20 mg/kg bw/d; low bonding capacity of tritosulfuron and AMTT to the estrogen receptor in the presence of endogenous estrogens |

*Medical data (Annex IIA, point 5.9)*

| |
|---|
| Limited data (new compound); no human health problems reported |

*Summary (Annex IIA, point 5.10) Proposal*

| | Value | Study | Safety factor |
|---|---|---|---|
| ADI (temporary) | 0.06 mg/kg bw | 12-mo dog | 100 |
| AOEL systemic (temporary) | 0.15 mg/kg bw/d | 90-day dog | 100 |
| ARfD | Not allocated- | Not necessary | |

**These reference values relate to tritosulfuron containing <0.02% AMTT.**

*Dermal absorption (Annex IIIA, point 7.3)*

| |
|---|
| 1% (concentrate), 2% (in-use dilution) based on *in vitro* (rat/human) and *in vivo* (rat) studies conducted using the commercial formulation |

Acceptable exposure scenarios (including method of calculation)

| | |
|---|---|
| Operator<br>Workers<br>Bystanders | The possible formation of AMTT and/or it's metabolite's in the spray tank must be considered. Exposures to be recalculated, as required. |

Appendix 3

SUGGESTED CLASSIFICATION AND LABELLING: TRITOSULFURON

Classification and proposed labelling (Annex IIA, point 10)

| | |
|---|---|
| with regard to toxicological data | Tritosulfuron (≥0.02% AMTT): Xi, R43<br>AMTT : T, R40, R 48/22, R61 (R64) |

* batch no. N24 is containing 2.45 % AMTT
** AMTT

**ANNEX 04 TO CONCISE OUTLINE REPORT OF ECCO 138 PEER REVIEW MEETING**

TRITOSULFURON

Rapporteur Member State: GERMANY

Specific comments on the active substances in the section **Residues** are listed below. The conclusions of the meeting were as follows:

1a. Comments received and discussed:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| 7 April 2003 | United Kingdom | Tritosulfuron 138 com01 UK |
| 23 April 2003 | The Netherlands | Tritosulfuron 138 com02 NL |
| | | |

1b. Comments received but not discussed (because deadline of submission was not met):

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |
| | | |

1c. Documents tabled at the meeting:

| **Date** | **Supplier** | **File Name** |
|---|---|---|
| None | | |
| | | |

2. **Definition of the residues relevant to MRLs:** parent compound plus metabolites AMTT and 635M02 (provisional pending confirmation of toxicological significance of 635M02).

3. **Data on preparations:** The data set for the plant protection product was considered more or less complete

4. **Classification and labelling:** Not discussed.

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

**Areas of concern:**
General concern expressed over the amount, nature and unknown source(s) of toxic metabolites in plant metabolism. Further information required.

Appendix 1: ECCO 138 reporting table: TRITOSULFURON

Appendix 2: List of end points: TRITOSULFURON

Appendix 3: Suggested classification and labelling: TRITOSULFURON

# Appendix 1: ECCO 138 reporting table Tritosulfuron (Hb)

## 5. Residues

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| | | | Section 5<br>Data requirements: 1<br>Open points: 2 |
| (i) | General | For use in maize and winter and spring cereals (all Europe). Timings proposed are BBCH 12-18 maize; 21-39 winter cereals (autumn or spring); 13-39 spring cereals. Dose 50g as/ha. | |
| (ii) | Plant metabolism | Studies in maize were submitted as representative of the proposed uses. Maize residue trials (radiolabeled) at exaggerated doses (180g as/ha; 3.6N) showed residues of 2mg/kg at 30 days after application, reducing to traces only at harvest (<0.01mg/kg). The parent was fairly stable and also formed stable metabolites in the plant.<br>There was concern over metabolites AMTT and 635M02 which are not found in maize but are found in other crops. It was also suggested that AMTT, which is of toxicological significance, may be present as an impurity of the active substance.<br>It was suggested that the higher level of AMTT in wheat, compared with maize, may be due to dilution of the metabolite/impurity in maize, which has a much higher dry matter content.<br>AMTT, however, was also present in rotational crops (see iii) and it was possible that it may also be formed on mixing in the spray tank, especially under alkaline conditions.<br>There was concern that the GAP intended use of the product with an adjuvant. There was however, no information on the effects of the adjuvant on uptake of the product by the plant. | 5.1 There is concern that a number of toxic metabolites (eg. AMTT and 635M02) are found for which there is insufficient information on their source (eg. impurities, formed during tank mixing, formed in plant metabolism).<br>Further information is required, including details of the effects of the proposed adjuvant on the amount and nature of the residue.<br>(IIA, 6.1 and 6.7) **A** |
| (iii) | Rotational crops | It was agreed that the residue definition (see iv) should also apply to rotational crops. There was concern over the quantitative estimation of rotational crop residues. There was generally enough evidence to say that AMTT and 635M02 can be present. Also concern over accumulation in soil, following successive applications of product. | |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (iv) | Crop residue definition (for monitoring and risk assessment) | It was agreed that metabolites AMTT and 635M02 should be included along with the parent in the residue definition, for risk assessment only. This is on the basis of toxicological significance and presence at harvest. | |
| (v) | Animal metabolism | Concern was expressed that the residue definition was based on the parent compound only. There was a need for metabolite data. From the available animal metabolism data a residue definition of 'parent + AMTT' should be established for investigation of future uses. | |
| (vi) | Animal residue definition (for monitoring and risk assessment) | The residue definition should be amended to 'parent plus AMTT'. | |
| (vii) | Residues in succeeding crops | It was agreed that, from the information available, residues in following crops do not appear to be of concern for consumers (see iii). | |
| (viii) | Residues from livestock feeding studies | It was the opinion of the meeting that the residue trials submitted were representative of the proposed GAP. | |
| (ix) | Consumer risk assessment | The current risk assessment has not considered the toxic metabolites and is therefore not appropriate to the revised residue definition. It is necessary to establish ADIs for the other toxic metabolites before the risk assessment can be performed.<br>It was agreed that the possible inclusion of 635M02 would depend on its toxicity. A statement on the toxicological significance of M02 was required. | Open point 5.1:<br>RMS to provide a new risk assessment, to include metabolite AMTT (and 635MO2 if toxicologically relevant).<br>Message to ECCO 140 (overview meeting):<br>A statement on the toxicity of metabolite 635M02 is required. |

| No. | Subject | Discussion ECCO-Peer Review Meeting | Recommendations ECCO-Peer Review Meeting (Annex point) |
|---|---|---|---|
| (x) | Processing data | Processing data show significant hydrolysis of tritosulfuron to AMTT (see discussion at ii).<br>The nature of the residue following processing has not been studied. This may be required following the revised risk assessment (ix) and assuming 100% conversion of parent to AMTT. | Open point 5.2:<br>Given the significance of processing in consumption of cereal products, the RMS should establish a NEDI value (possibly including 635M02, pending confirmation of toxicological relevance) |

Appendix 2

LIST OF END POINTS: **TRITOSULFURON**

## 5 Residues section

Appendix III.4: Chapter 4 (residues)

**Metabolism in plants** (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Plant groups covered | maize |
| Rotational crops | ~~radish,~~ lettuce, wheat, carrots, beans |
| Plant residue definition for monitoring | tritosulfuron, AMTT, 635M02 expressed as tritosulfuron (depending on results of new wheat metabolism study) |
| Plant residue definition for risk assessment | tritosulfuron, AMTT, 635M02 expressed as tritosulfuron (depending on results of new wheat metabolism study)~~tritosulfuron~~ |
| Conversion factor (monitoring to risk assessment) | none |

**Metabolism in livestock** (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

| | |
|---|---|
| Animals covered | goat, hen |
| Animal residue definition for monitoring | tritosulfuron, AMTT expressed as tritosulfuron |
| Animal residue definition for risk assessment | tritosulfuron, AMTT expressed as tritosulfuron |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | Yes |
| Fat soluble residue: (yes/no) | no |

**Residues in succeeding crops** (Annex IIA, point 6.6, Annex IIIA, point 8.5)

| | |
|---|---|
| | 30, 120, 365 days plant back interval after application of 60 g as/ha to soil.<br>The total radioactive residues were low for carrot root (≤ 0.011 mg/kg / parent: ≤ 0.001 mg/kg), green beans (≤ 0.005 mg/kg), lettuce head (≤ 0.022 mg/kg/ parent: ≤ 0.006 mg/kg) and wheat grain (≤ 0.019 mg/kg / parent: < 0.001 mg/kg)) after all 3 plant back intervals.<br>In carrot foliage and bean plants only few samples showed residues of tritosulfuron slightly above 0.01 mg/kg.<br>The metabolite AMTT (635M04) was detected in almost all samples of the triazine label but mostly at low absolute concentrations (< 0.01 mg/kg). Only after plant back intervals of 30 days in early samplings of bean plant and wheat forage and in wheat straw amounts in the range of 0.011 – 0.029 mg/kg were found. |

**Stability of residues** (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

| |
|---|
| Food of plant origin (maize grain, maize forage, wheat grain, wheat straw, radish root): tritosulfuron was stable over a period of 3 years. |

**Residues from livestock feeding studies** (Annex IIA, point 6.4, Annex IIIA, point 8.3)

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: yes/no | Poultry: yes/no | Pig: yes/no |
|---|---|---|---|
| Muscle<br>Liver<br>Kidney<br>Fat<br>Milk<br>Eggs | No ruminant feeding study conducted | No hen feeding study conducted | No pig feeding study conducted. Metabolism in rat and ruminant similar |

**Summary of critical residues data** (Annex IIA, point 6.3, Annex IIIA, point 8.2)

| Crop | Northern or Mediterranean Region | Trials results relevant to the critical GAP (a) | Recommendation/comments | MRL | STMR (b) |
|---|---|---|---|---|---|
| Summer barley | N | 7 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 5 x < 0.01 mg/kg | | | |
| Winter barley | N | 11 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 8 x < 0.01 mg/kg | | | |
| Summer wheat | N | 3 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Winter wheat | N | 15 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 10 x < 0.01 mg/kg | | | |
| Durum wheat | S | 6 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Winter rye | N | 1 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| Maize | N | 15 x < 0.01 mg/kg | grain | 0.01 mg/kg | 0 |
| | S | 21 x < 0.01 mg/kg | | | |

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x < 0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

**Consumer risk assessment** (Annex IIA, point 6.9, Annex IIIA, point 8.8)

| | |
|---|---|
| ADI | ~~0.5~~0.06 mg/kg bw/d for tritosulfuron with max 0.02 % AMTT |
| TMDI (European Diet) (% ADI) | ~~0.07~~0.61 % (German diet) / ~~0.04~~0.35 % (WHO diet) |
| NEDI (% ADI) | not calculated |
| Factors included in NEDI | - |
| ARfD | Not assigned |
| Acute exposure (% ARfD) | Not applicable |

**Risk assessments for AMTT and 635M02 cannot be carried out yet because of lacking data bases.**

**Processing factors** (Annex IIA, point 6.5, Annex IIIA, point 8.4)

| Crop/processed crop | Number of studies | Transfer factor | % Transference * |
|---|---|---|---|
| Not conducted | | | |

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

**Proposed MRLs** (Annex IIA, point 6.7, Annex IIIA, point 8.6)

| | |
|---|---|
| barley, oats, maize, rye, triticale, wheat | 0.01 mg/kg |
| | |

Appendix 3

SUGGESTED CLASSIFICATION AND LABELLING: **TRITOSULFURON**

## 5 Residues section

Not discussed

**DOCUMENTS ON TRITOSULFURON DRAFT ASSESSMENT REPORT**

**Section: Physical Chemical Properties (ECCO 135)**

**1. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**2. Comments**

| Date | Supplier | File name |
|---|---|---|
| 14 January 2003 | United Kingdom | tritosulfuron 135 com01 UK |
| 3 February 2003 | Belgium | tritosulfuron 135 com02 BE |
| | | |
| | | |
| | | |
| | | |
| | | |

**3. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |
| | | |

**4. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**5. Addenda (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**6. Other Documents (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**PESTICIDES SAFETY DIRECTORATE**
Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX, UK
Switchboard: 01904 640500 GTN: 5138 5813
Direct Dial: 01904 455813 Fax: 01904 455722
International: (+44) 1904 455813 International Fax: (+44) 1904 455722
e-mail emma.hedges@psd.defra.gsi.gov.uk

Mr Herbert Koepp
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienststelle Braunschweig
Messeweg 11 –12
38104
Braunschweig

Our ref: ASY 221

Date: 14 January 2003

Dear Mr Koepp,

**EC REVIEW MONOGRAPH FOR TRITOSULFURON**
**RAPPORTEUR:- GERMANY**

**ECCO 135 - MEETING TO DISCUSS PHYS. CHEM. PROPERTIES**

On behalf of the Pesticides Safety Directorate of the Department for Environment, Food and Rural Affairs, please find attached our comments on the monograph for MCPB. We are submitting these comments for your information as rapporteur and for discussion at ECCO 135 in February 2003.

Yours sincerely

Emma Hedges

Emma Hedges
Approvals Committee Branch

cc: ECCO Team (PSD)

The Pesticides Safety Directorate agrees with the technical evaluation and risk assessment given in the monograph, except in the following areas:

**Confidential information:**

The a.s. technical specification has been assessed on 4 batches rather than five. The data also indicate that one of these batches fails to meet the specification proposed (for maximum AMTT level – batch N34) and therefore further 5 batch analysis data should be considered and evaluated before the specification can be considered proposed and supported. The UK are aware that the company have available new 5 batch analysis data from commercial production and would suggest these data be used to produce and confirm the technical specification.

Water and chloride were only determined in 2 and 3 of the 4 batches respectively and although closure is >98% in the 4 batches, the UK considers it more appropriate to use the new 5 batch analysis data available to propose and confirm the technical specification.

Some nitrosamine analysis (method M 91/120) was included in the UK data package, but it only considered a single batch. Under an application for UK provisional approval, the company has been asked to confirm these analyses for all batches and to confirm the levels of nitrosamines in the batches used to conduct the toxicity tests.

**Physical/chemical properties**

Section B 2.2.7.1
The accelerated data indicated that AMTT levels increased 3 fold during accelerated storage, though the tritosulfuron content did not decrease by more than 5%.

Section B 2.2.7.3
The ambient data indicated a 3% decline in the as substance content and given the data for accelerated studies, it was suggested this may again be AMTT forming during storage. The company has been asked to comment on this under an application for UK provisional approval. Given the toxicological concerns with this impurity and metabolite, the company has been asked to confirm AMTT levels in the product following 2 years ambient storage.

The suspensibility figures after storage were just outside the upper acceptable limit of 105% (106% - 108%). However, a sprayability study (Hassink, 1999) that was provided for the application for UK provisional approval demonstrated that the product can be applied through conventional spray equipment without any problem. This was considered acceptable.

The product is always to be used with an adjuvant, but the physical tests such as suspensibility were performed without any adjuvant being present. However, the sprayability data submitted were generated with the adjuvant as proposed label concentrations and confirmed acceptable spraying characteristics.

Section B 2.2.8.6.3
Data were submitted using the DAPF method FK 81, FK 36/1, which was considered acceptable as a new development of MT 176 for a WG rather than a GR formulation.

**Methods of analysis**

Water and chloride were determined by Karl Fischer titration and ion chromatography respectively. Validation data were not submitted nor requested given the widespread and established use of these methods. They have been included for completeness and because the levels of these impurities were > 0.1% w/w.

The confidential information included analysis of a single batch of technical material for nitrosamines. The company have been asked to supply full details of the method used together with appropriate validation data (see also 'Confidential information' above) as part of an application for UK provisional approval.

**Tritosulfuron** : Comments from Belgium on the Draft Assessment Report (RMS : Germany)
Sections : Identity, Physical and chemical properties, Methods of analysis (ECCO 135)
Date : 3 February 2003
Contact : Dr. ir. Annick De Meester (Tel. : (+32) (0)2 210 51 05 / e-mail : Annick.De.Meester@cmlag.fgov.be)

| **DAR point (Annex point)** | **Comment** |
|---|---|
| ***Identity*** | |
| Volume 4, C.1.2.4 (IIA 1.10 and 1.11) | Although it is not explicitly mentioned, we presume the 4-batch analytical profile refers to pilot scale production. Batch analysis data for 5 full scale production batches will thus have to be submitted once commercial production methods have stabilised, in order to confirm (or revise) the proposed technical specification. |
| ***Physical and chemical properties*** | |
| Volume 1, endpoints | – relative density : could the RMS check if the result 1.678 is correct (B.2 states 1.687)<br>– vapour pressure : according to B.2 the result should read < 1.0 x$10^{-5}$ Pa<br>– solubility in organic solvents : we propose to add that a.s. is insoluble in n-heptane<br>– quantum yield : it is unclear to us why the results are stated as "<" |
| Volume 3, B.2.2 (IIIA 2) | Apparently the physical tests (e.g. suspensibility, persistent foaming,…) were conducted without the obligatory adjuvant being present. Did the notifier provide data addressing the effect of the adjuvant on these parameters? |
| Volume 3, B.2.2.8.6.3 (IIIA 2.8.6) | As provisional CIPAC method MT 178.2 has become available for WG in the meantime, we believe a study on attrition resistance using this method should be submitted. |
| ***Methods of analysis*** | |
| Volume 1, Endpoints | With respect to the residue methods, we propose to add which analyte(s) is (are) being determined by each method. |
| Volume 4, C.1.2.5 (IIA 4.1.2) | Could the RMS clarify which methods were used for the determination of chloride and water in technical material? |
| Volume 3, B.5.5.2 | Table B.5.5-1 : according to the data in Table B.5.3-4, the LOQ for M02 in drinking and surface water should read 0.5 µg/L instead of 0.05 µg/L. |

**DOCUMENTS ON TRITOSULFURON DRAFT ASSESSMENT REPORT**

**Section: Mammalian Toxicology (ECCO 136)**

**1. Evaluation Table**

| Date | Supplier | File name |
|---|---|---|
| 16 May 2003 | Germany | Tritosulfuron Eval Table 136 Rev0 |

**2. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| 16 May 2003 | Germany | tritosulfuron 136 2endpoints |

**3. Comments**

| Date | Supplier | File name |
|---|---|---|
| 7 February 2003 | France | tritosulfuron 136 com01 FR |
| 10 February 2003 | United Kingdom | tritosulfuron 136 com02 UK |
| 25 February 2003 | Belgium | tritosulfuron 136 com03 BE |
| 4 March 2003 | The Netherlands | tritosulfuron 136 com04 NL |
| | | |
| | | |
| | | |

**4. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |
| | | |

**5. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**6. Addenda (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**7. Other Documents (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

MINISTERE de l'EDUCATION NATIONALE et de la RECHERCHE et de la TECHNOLOGIE
MINISTERE de l'AGRICULTURE et de la PÊCHE

**DGAL**

**S. S. M.**
**STRUCTURE SCIENTIFIQUE MIXTE**

**Date: 07/02/03**

**Competent Authority :**
**Sylvie Malezieux**
Ministère de l'Agriculture et de la Pêche
Direction Générale de l'Alimentation
251, rue de Vaugirard
75732 - PARIS Cedex 15
Tel: 33 1 49 55 81 85 FAX 33 1 49 55 49 59
e.mail : sylvie.malezieux@agriculture.gouv.fr

**From**
**Annick Venant**
INRA – GMPV – Route de Saint-Cyr – F 78026
Versailles Cedex
Tel: 33 1 30 83 32 91 FAX 33 1 30 83 31 49
e.mail : venant@versailles.inra.fr

**To** **Ecco team (BBA)**
**e.mail :** ecco@bba.de

**cc** **Rapporteur member state : Deutschland**
**e.mail :** nsh@mst.dk

**Objet : comments from France on draft monograph on TRITOSULFURON**

**Dear Colleagues,**

**Please find attached our comments on the Toxicology section of the draft Assessment Report for the new active substance TRITOSULFURON.**

**Yours sincerely,**

**Annick Venant**
**P/L'Ingénieur d'Agronomie**
**Sylvie Malézieux**

**EU Review program on active substances in Plant Protection Products**

**Comments of France on TRITOSULFURON draft monograph**

**Section: Toxicology**

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The section concerned and the related summary are clearly presented. In general, we agree with the conclusions on individual studies. Nevertheless, based on this section there is a great concern about the possible presence of the impurity/metabolite AMTT which has many adverse toxicology properties.
Therefore we would like to add the following specific comments:

| **Document** | **Comment** |
|---|---|
| Volume 1, level 1, point 1.3.9:<br>Specification of purity of the active substance (see also Volume 3, point B.1.1.9)<br>See also Volume 1, level 2, point 2.3:<br>Impact on human and animal health (tables 2.3-1 and 2.3-2) | In the view of the purity of the tested batches (AMTT excluded), the purity of the technical product should be increased to 98%. |
| Volume 1, level 1, point 1.3.9:<br>Specification of purity of the active substance (see also Volume 3, point B.1.1.9)<br>See also Volume 1, level 2, point 2.3:<br>Impact on human and animal health Preamble | The notifier claims that only batches containing less than 0.02% AMTT would be placed on the market. In the view of the synthesis method, this seems to be difficult to attain in all cases. We should know how they will guarantee these specifications and what they will do with batches that would not fit them. |
| Volume 1, level 2, point 2.4.1.2 and point 2.7.1 Figures 2.7-1 to 2.7-4:<br>Residues in animals and metabolic pathways (see also Volume 3, point B.6.1.2; point B.7.2.1.2; point B.7.2.2.2) | AMTT is a metabolite (635M04) in mammals and birds. Therefore it is not possible to correctly evaluate the potential risk linked to metabolism of tritosulfuron in man. |
| Volume 1, level 2, point 2.3.1.2 and Volume 3; point B.1.1.2 ; point B.6.12:<br>Dermal absorption | The dermal absorption study was terminated after 72 hours. It is not mentioned if the radioactivity remaining in the skin was taken into account in the calculations. If not, the % absorbed should be increased accordingly. |
| Volume 1, level 2, point 2.7.3:<br>Fate and behaviour in the environment (soil, water, air), (see also Volume 3, point B.8.1.1.1; point B.8.1.1.2; point B.1.2.2; point B.8.4.1; point B.8.4.3.2) | AMTT is also found in transformation studies in water and soil. Risk assessment for man is necessary for these potential indirect exposures. |
| | It is proposed that tritosulfuron is not included in annex I of the 91/414 Directive in the view of:<br>- The toxicological properties of AMTT (should be classified T, R40, R43, R48/22, R61) which is carcinogenic, toxic to reproduction, with no NOEL in the subacute and subchronic toxicity studies and severe clinical signs are noted at 200 mg/kg in the acute toxicity study in the rat<br>In addition, the content of AMTT in the formulated product was not communicated while similar |

| | |
|---|---|
| | clinical signs to that of AMTT were noted in the acute toxicity study with this formulated product while they were not noted in the acute toxicity study with tritosulfuron without AMTT.<br>- The fact that it is a metabolite in mammals, birds, plants and it is found in water and in soil. |

If this proposal is not accepted, the following comments are added:

| | |
|---|---|
| Volume 1, level 2, point 2.3.2.1:<br>ADI for tritosulfuron, (see also Volume 3, point B.1.1.11.1) | The studies in dog do not allow to exclude that the toxicity observed is not also due to tritosulfuron. Therefore, the one-year dog study should be retained for the calculation of the **ADI for tritosulfuron**:<br>**0.06 mg/kg/j** (NOEL 1-year dog: 6 mg/kg/j ; Safety Factor : 100). |
| Volume 1, level 2, point 2.3.3.1:<br>Systemic AOEL for tritosulfuron, (see also Volume 3, point B.1.1.12.1) | For the same reason as above, the 90-day study in dog should be retained for the **systemic AOEL for tritosulfuron :**<br>**0.15 mg/kg/j** (NOEL 90-day dog: 15 mg/kg/j ; SF: 100 ; oral absorption: 100 %). |
| Volume 1, level 2, point 2.3.2.2:<br>ADI for AMTT, (see also Volume 3, point B.1.1.11.2) | For the calculation of the ADI for AMTT, considering the toxicity of this substance, a Safety Factor of 500 should be applied. The NOEL of the 2-generation study is the lowest: 0.06 mg/kg/day AMTT. The **ADI for AMTT** should be:<br>**0.0001 mg/kg/day** |
| Volume 1, level 2, point 2.3.3.2:<br>Systemic AOEL for AMTT, (see also Volume 3, point B.1.1.12.2) | For the calculation of the systemic AOEL for AMTT, considering the toxicity of this substance, a Safety Factor of 200 should be applied. The NOEL of the 1-year dog study should be retained: 0.123 mg/kg/day AMTT. The **systemic AOEL for AMTT** should be: **0.0006 mg/kg/day** |
| Volume 1, level 2, point 2.3.4.2:<br>ARfD for AMTT, (see also Volume 3, point B.1.1.1.2) | In the view of the effects noted on the pups in the 2-generation study, it is proposed to retain an **ARfD for AMTT** identical to the ADI:<br>**0.0001 mg/kg/day** |
| Volume 1, level 2, point 2.3.5:<br>Drinking water limit, (see also Volume 3, point B.6.10.14) | Based on the ADI, the limit in drinking water should be:<br>**0.3 µg/L** at maximum |

**PESTICIDES SAFETY DIRECTORATE**
Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX, UK
Switchboard: 01904 640500 GTN: 5138 5813
Direct Dial: 01904 455813 Fax: 01904 455722
International: (+44) 1904 455813 International Fax: (+44) 1904 455722
e-mail emma.hedges@psd.defra.gsi.gov.uk

Mr Herbert Koepp
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienststelle Braunschweig
Messeweg 11 –12
38104
Braunschweig

Our ref: ASY 221

Date: 10 February 2003

Dear Mr Koepp,

**EC REVIEW MONOGRAPH FOR TRITOSULFURON**
**RAPPORTEUR:- GERMANY**

**ECCO 136 - MEETING TO DISCUSS MAMMALIAN TOXICOLOGY**

On behalf of the Pesticides Safety Directorate of the Department for Environment, Food and Rural Affairs, please find attached our comments on the monograph for Tritosulfuron. We are submitting these comments for your information as rapporteur and for discussion at ECCO 136 in March 2003.

Yours sincerely

Emma Hedges

Emma Hedges
Approvals Committee Branch

cc: ECCO Team (PSD)

The Pesticides Safety Directorate agrees with the technical evaluation and risk assessment given in the monograph, except in the following areas:

Background

Long-term studies and a 2-generation study were conducted with batch N24. In these studies, high pup mortality was observed in the rat multigeneration study and an increased incidence of mammary gland tumors was found in the long-term rat studies. The available data appears to indicate that the AMTT content was responsible for these serious adverse effects.

A NOAEL of 0.4 mg/kg bw/day AMTT can be determined for the increased incidence of mammary gland tumors seen at the LOEL of 1.67 mg/kg bw/day in the carcinogenicity studies. No mechanism has been provided for the AMTT-induced mammary gland tumours

A NOAEL of 0.06 mg/kg bw/day AMTT can be determined for the increased incidence of dead pups at the LOEL of 1.5 mg/kg bw/day in the rat multigeneration study. No mechanism has been provided for the AMTT-induced effects on breast tissue during pregnancy/lactation resulting in pup deaths (i.e. no or severely reduced milk production).

Although reference doses can theoretically be set for tritosulfuron (≤0.02% AMTT) and AMTT, there are a number of unresolved issues with respect to tritosulfuron stability during storage, in aqueous dosing solutions, formulations and tank mixes (i.e. predicting human exposure to AMTT). In addition, further information on the metabolite 635M02 might be required depending on human exposure. These concerns need to be resolved before the UK can support Annex I listing.

B.6. Toxicology and metabolism

B.6.1.2.2 Investigation of the formation of AMTT after oral administration of 14C-BAS 635 H in rats (Leibold & Hoffmann, 2001; BASF doc ID 1013503 & the report of the analytical phase Hafemann, 2000).

**AMTT content in the dosing solutions**

It is not clear why the AMTT levels in the dosing solutions varied from 0.5% to 3.24%.

The purity statement/product specification states that the **initial (14C-triazine)-tritosulfuron contained <0.1% AMTT** (Batch No 437-1406/analysed 10-12 November 1999). The dosing solution used in the phase of the study that involved urine and faeces collections contained 0.5-0.53% AMTT **(i.e. at least a 5-fold increase in AMTT).** Whereas the dosing solution used in the phase of the study that involved bile collection contained 1.85-3.24% AMTT (**i.e. an 18 to 33-fold increase).** It should also be noted that the results for the 3-hour control investigations into the levels of AMTT in the dosing solution (biliary excretion study) were not included in the report.

BASF maintain that the increase in AMTT was produced by radiolysis during the storage time. The company has submitted the following statement:

*Original batches from 14C-tritosulfuron synthesis were dissolved in organic solvent like toluene. The dosing solution, for which 0.5% AMTT content was determined, was prepared from crystalline 14C-tritosulfuron immediately after toluene had been evaporated. The later dosing solutions (1.85 and 3.24% AMTT) were also prepared from the same crystalline 14C-tritosulfuron which however had been stored in a refrigerator at 4 degrees Celsius in the meantime. During storage time of the crystalline material AMTT has been generated most likely due to radiolysis, because it is known that radiolysis occurs to a sizeable extent in neat material, but not in solutions.*

Given the toxicity profile of AMTT, **data are required** to demonstrate that radiolysis occurs and is responsible for the increased levels of AMTT in the dosing solutions (e.g. comparisons of hot and cold material in relevant conditions).

B.6.2 Acute toxicity including irritancy and skin sensitisation

Table B.6.2-1. Skin sensitisation maximisation test: the comment section states that 5/20 animals exhibited edema whereas the text of the study evaluation refers to erythema

B.6.3 Short-term toxicity

B.6.3.1.1 Rat

Based on the significant increase in mean total bilirubin at 3000 ppm and above, the NOAEL of 3000 ppm determined for females is equivocal.

B.6.3.3.1 Rat

The NOAEL of 1000 ppm determined for males is equivocal. Liver weight was increased at this dose level. Although centrilobular hypertrophy correlates with the increases in relative liver weight, these effects are considered to be indicative of the liver toxicity seen in this study at higher dose levels (e.g. clinical chemistry changes and necrosis).

B.6.4.1.3 *In vitro* cytogenetic test

The RMS has concluded this study is negative whereas the UK considers that there are some indications of positive responses. The tabulated results for this study are presented below:

Positive results in the chromosome aberration assays (with S-9 mix and duplicate cultures)

| Conc (μg/ml) | [a]Exp/Sam time (hours) | Metaphases | Including gaps | Excluding gaps | Exchanges |
|---|---|---|---|---|---|
| **2nd experiment** | | | | | |
| Acetone (vehicle) | 4/18 | 200 | 12 (6.0%) | 3 (1.5%) | 2 (1.0%) |
| 500 | 4/18 | 200 | 7 (3.5%) | 7 (3.5%) | 4 (2.0%) |
| 1000 | 4/18 | 200 | 7 (3.5%) | 6 (3.0%) | 4 (2.0%) |
| 2000 | 4/18 | 200 | 23 (11.5%) | 21 (10.5)** | 9 (4.5%)# |
| CPP | 4/18 | 100 | 15 (15.0%) | 15 (15.0%) | 13 (13.0) |
| **3rd experiment** | | | | | |
| Acetone (vehicle) | 4/18 | 200 | 13 (6.5%) | 6 (3.0%) | 1 (0.5%) |
| 1000 | 4/18 | 200 | 21 (10.5) | 15 (7.5%) | 6 (3.0%) |
| 2000 | 4/18 | 200 | 12 (6.0%) | 11 (5.5%) | 9 (4.5%)* |
| [b]CPP | 4/18 | 100 | 21 (21.0) | 21 (21.0) | 19 (19.0) |

Key: a) Exp/Sam = exposure/sampling time in hours. b) CPP = Cyclophosphamide. c) # Although this value was not flagged up as statistically significant, it was stated to be above the upper value of the historical control data (3%). d) * P<0.05, ** P<0.01.

All of the significant increases were stated to be slightly above the historical control data for the laboratory. However, the historical control data provided were for untreated controls and ethanol and DMSO vehicles (not acetone). The report considered these increases to be secondary effects due to extreme culture conditions rather than the test substance itself. Although the report concluded that the test substance did not cause any biologically relevant or dose-dependent increases in the number of chromosomal aberrations, the positive results (exchanges) and the pattern of findings in two independent experiments performed under identical conditions suggest that tritosulfuron might have clastogenic potential.

B.6.4.2.3.1 *In vivo* cytogenetic test

A possible issue is the use of the mouse micronucleus test to evaluate the *in vivo* genotoxicity of tritosulfuron and AMTT (tritosulfuron is a possible *in vitro* clastogen and AMTT was not tested in vitro). Mice appear to be more tolerant than rats to tritosulfuron/AMTT administration (mammary gland tumours were observed in rats and there may be species differences).

B.6.5.1 Chronic toxicity rat

The UK considers the NOAEL of 1000 ppm determined for this study to be equivocal. Relevant effects are presented below:

Overt signs of toxicity and microscopic findings

| Dose (ppm) | 0 | 100 | 1000 | 3500 | 7000 |
|---|---|---|---|---|---|
| **Males (n = 20)** | | | | | |
| Anogenital region smeared with urine | 0 | 0 | 0 | 5 | 10 |
| Kidneys: Cortical cysts | 1 | - | - | - | 3 |

| | | | | | |
|---|---|---|---|---|---|
| Interstitial nephritis | 1 [a][grade 3] | 2 [grade 3] | 4 [grade 3] | 4 [b][grade 2-4] | 7 [c][grade 2-4] |
| **Females (n = 20)** | | | | | |
| Anogenital region smeared with urine and/or inflammation in the anogenital region | 0/20 | 0/20 | 2 | 5 | 12 |
| Kidneys: Cortical cysts<br>Interstitial nephritis | 1<br>1 [a][grade 3] | -<br>2 [grade 3] | -<br>4 [grade 3] | -<br>4 [b][grade 2-4] | 3<br>7 [c][grade 2-4] |
| Liver Pericholangitis | - | - | 1 [grade 1] | 1 [grade 1] | 5 [d][grade 1-3] |

Key: a) Severity: 1 = minimal, 2 = slight, 3 = moderate, 4 = marked/severe & 5 = massive/extreme. b) 1 grade 2, 2 grade 3 & 1grade 4. c) 1 grade 2, 5 grade 3 & 1grade 4. d) 2 grade 1, 2 grade 2 & 1 grade 3.

Based on the increased incidence of chronic interstitial nephritis in the kidneys at 1000 ppm and above in males, the anogenital effects and the pericholangitis in the liver at 1000 ppm and above in females, the NOAEL for this study 100 ppm (5.2 and 6.5 mg/kg bw/day for males and females, respectively).

B.6.6 Reproductive toxicity

Given that cleft palate is a rare event in rats and rabbits, its occurrence in the F1a and F1b pups in the rat multigeneration study and its occurrence in the rabbit range-finding study may be indicative of tritosulfuron-induced teratogenic activity.

B.6.6.1.2 Second multigeneration study.

Cleft palate (a rare event in rats) was evident in F1a pups (2 pups/1 litter) and F1b pups (1 pup) and agensia of the kidneys was also seen in F2 pups (2 pups/1 litter) at the top dose level.

B.6.6.2.2 Rabbit developmental study

In this study (0.05%AMTT in the test material), cleft palate (a rare event in rabbits) was observed in pups in the range-finding study at 600 mg/kg bw/day and open eye was evident at 120 mg/kg bw/day in the main study.

B.6.8.1.1 635M02

Two additional 28-day feeding studies have been submitted to the UK for evaluation: BASF Doc ID 2003/1004048 (evaluated) & 2003/1004048 (not yet evaluated). The evaluated study indicates the main target organs were the kidneys, liver, spleen, ovaries and uterus (and possibly the male thyroid). There are indications of hormone disruption being a possible factor in the ovarian and uterine effects (and possible effects on the male thyroid). A NOAEL was not set for this study, based on RBC effects, increased kidney weight in males, increased $\alpha$2u-globulin in males (a sex

and species specific effect), increased haemosiderin deposition in females and hyperplasia of the stroma in the ovaries at 200 ppm (equivalent to 18.6 and 20 mg/kg bw/day in males and females, respectively). The second study reports a NOAEL of 150 ppm (equivalent to 13.9 and 14.7 mg/kg bw/day in males and females, respectively

Metabolite 635M02 was more acutely toxic than the parent compound. An acute dose of 635M02 induced serious adverse effects in the main target organs established in the repeat-dose toxicity studies with tritosulfuron. This metabolite may also have some clastogenic potential *in vitro*. A comparison of the 28-day rat feeding studies with the 28-day rat feeding study conducted with tritosulfuron (batch N14) indicate that 635M02 is approximately 20 time more toxic than tritosulfuron based on these subacute studies. The 635M02-induced effects on ovarian and uterine tissue indicated that further reproductive/hormonal data might be required for this metabolite depending on the predicted human exposure.

B.6.8.1.1.3 Third mutagenicity study with 635M02 (metabolite)

The RMS has concluded this study is negative whereas the UK considers that there are some indications of positive responses. The results and historical control data are presented in the tables below:

Summary of metaphases with chromosome aberrations

| **Dose (µg/ml)** | **No of Metaphases** | **Including gaps** | | **Excluding gaps** | | **Exchanges** | |
|---|---|---|---|---|---|---|---|
| | | No | % | No | % | No | % |
| 1st experiment (4 hours exposure, 18 hours harvest time, with S-9 mix) | | | | | | | |
| DMSO | 200 | 6 | 3.0 | 2 | 1.0 | 1.0 | 0.5 |
| 575 | 200 | 4 | 2.0 | 1 | 0.5 | 1.0 | 0.5 |
| 1150 | 200 | 18 | 9.0* | 7 | 3.5 | 2 | 1.0 |
| 2300 | 200 | 21 | 10.5** | 10 | 5.0 | 5 | 2.5 |
| CPP 0.5 | 100 | 21** | 21.0** | 21** | 21.0** | 18 | 18** |
| 2nd experiment (18 hours exposure, 18 hours harvest time, without S-9 mix) | | | | | | | |
| DMSO | 200 | 4 | 2.0 | 1 | 0.5 | 1.0 | 0.5 |
| 287.5 | 200 | 14 | 7.0* | 5 | 2.5 | 4.0 | 2.0 |
| 575 | 200 | 7 | 3.5 | 1 | 0.5 | 1.0 | 0.5 |
| 1150 | 200 | 7 | 3.5 | 1 | 0.5 | 0 | 0.0 |
| EMS 350 | 100 | 19 | 19.0** | 17 | 17.0** | 16 | 16** |

Key: a) * P<0.05, ** P<0.01

At 1150 and 2300 µg/ml (with S-9 mix), there were some significant dose-related increases in the number of aberrations. These significant results include gaps (gaps are not considered an indication of clastogenicity), however, when gaps are excluded a dose-related increase is still evident at 1150 and 2300 µg/ml (with S-9 mix). The number of exchanges also appears to be increased at 2300 µg/ml (with S-9 mix).

Historical negative control data

| Untreated controls (with S-9 mix) | | | | | | |
|---|---|---|---|---|---|---|
| Treatment/harvest | 4/18 hours | | | 4/28 hours | | |
| No of experiments | 46 | | | 18 | | |
| Aberrations | Incl gaps | Excl gaps | Exch | Incl gaps | Excl gaps | Exch |
| Mean (%) | 4.4 | 1.7 | 0.7 | 4.5 | 1.6 | 0.5 |
| Minimum (%) | 1.5 | 0.0 | 0.0 | 2.0 | 0.5 | 0.0 |
| Maximum (%) | 10.5 | 5.0 | 2.5 | 9.0 | 3.0 | 1.0 |

Based on the results of this study and the historical control data, the report stated that the test substance did not cause any biologically relevant increase in the number of structurally aberrant metaphases at both sampling times (with or without S-9 mix) in two independent experiments. In addition, no increase in the frequency of cells containing numerical aberrations was demonstrated. The report concluded that 635M02 was not clastogenic in isolated V79 cells under the conditions of this study. However, the increase in aberrations (excluding gaps) at 1150 and 2300 µg/ml (with S-9 mix) is dose-related and the increase at 2300 µg/ml (with S-9 mix ) is at the maximum value for the historical control data. Hence, 635M02 may have some clastogenic potential with S-9 mix.

B.6.8.2 Supplementary studies-AMTT (635M04)

The summary at the beginning of this section states that AMTT does not accumulate in rats. This statement appears to be based on the biokinetic study at B.6.8.21. This study only used a single dose; repeat dosing was not carried. The results of the long-term studies and multigeneration studies conducted with tritosulfuron containing 2.46% AMTT suggest that the severity of the AMTT-induced effects increase with the duration of the study.

It has also been noted that an *in vitro* clastogenicity test has not been performed with AMTT (see point B.6.4.2.3.1).

B.6.10.11.1 ADI for tritosulfuron (AMTT max 0.02%)

The RMS has proposed an ADI of 0.5 mg/kg bw/day based on the NOAEL of approximately 50 mg/kg bw/day determined for a rat generation study (batch N34 tested) and an assessment factor of 100. The UK regards this approach to the setting of the ADI to be inappropriate. The dog studies were conducted with tritosulfuron (2.46% AMTT content), it is not possible to determine the tritosulfuron-induced (0.02% AMTT content) effects on the dogs. Therefore, based on the NOAEL of 6.0 mg/kg bw/day determined for both sexes in the 12-month dog study.and applying a standard assessment

factor of 100, **an ADI of 0.06 mg/kg bw/day is proposed for tritosulfuron (≤ 0.02% AMTT).**

B.6.10.11.2 ADI for AMTT

The UK regards the use of the 100-assessment factor to be inappropriate. **An assessment factor of at least 200 is more appropriate.**

B.6.10.12.1 Systemic AOEL for tritosulfuron (AMTT max 0.02%)

The RMS has proposed a systemic AOEL of 0.75 mg/kg bw/day based on the NOAEL of 75 mg/kg bw/day determined for the 90-day rat feeding study (batch N 14) and an assessment factor of 100. The UK regards this approach to the setting of the systemic AOEL to be inappropriate.

Based on the NOAEL of 15 mg/kg bw/day tritosufuron (equivalent 0.003 mg/kg bw/day AMTT) determined for females in the 90-day dog study and applying a standard assessment factor of 100, **a systemic AOEL of 0.15 mg/kg bw/day can be proposed for tritosulfuron (equivalent to 0.00003 mg/kg bw/day AMTT).** This level of exposure would be acceptable based on the ADI, AOEL and ARfD proposals for AMTT.

B.6.10.12.2 Systemic AOEL for AMTT

The RMS has stated that a systemic AOEL is not necessary because the Annex I inclusion is only supported for tritosulfuron with an AMTT content ≤0.02%. However, the UK considers it is appropriate to set a systemic AOEL for AMTT for risk assessment purposes.

The most critical effect endpoint of concern with AMTT administration was the pup-deaths in the early post-natal period. This effect appears to be caused by AMTT administration during the pre/post natal period (i.e. a short-term effect). Therefore, based on the NOAEL of 0.06 mg/kg bw/day determined for pups in the rat multigeneration study (conducted with tritosulfuron containing 2.46% AMTT) and applying an assessment factor of 200, **a systemic AOEL of 0.0003 mg/kg bw/day can be proposed for AMTT.**

B.6.10.13.2 ARfD for AMTT

The UK regards the use of the 100-assessment factor to be inappropriate. **An assessment factor of at least 200 is more appropriate.**

B.6.10.14 Drinking water level

The RMS has stated that a MAC value is not necessary according to Directive 91/414/EC. However, given the potency of the AMTT and the present reservations on the stability of tritosulfuron in aqueous solutions, the UK considers it appropriate to set MACs for tritosulfuron and AMTT for risk assessment purposes.

No human data are available and there are no chronic exposure animal studies in which tritosulfuron or AMTT have been administered in drinking water. Because of the potential AMTT levels in ground water, the effects seen a very low dose levels (pup deaths), it is considered necessary to derived a MAC for AMTT as well as tritosulfuron (0.02% AMTT).

a) Tritosulfuron (0.02% AMTT)

Using the WHO 1994 model to calculate the MAC for drinking water it is appropriate to divide the ADI by an additional assessment factor of 10 and thus derive an intake of 0.006 mg/kg bw/day.

Assuming the average value for consumption by a typical 60 kg person is 2 litres/day, a daily intake of 0.006 mg/kg bw/day would be achieved by drinking water containing 0.18 mg/litre. Thus, **a MAC of 180 μg/l of water can be derived for tritosulfuron containing 0.02% AMTT (estimated to be equivalent to approximately 0.04 μg/l AMTT).**

b) AMTT

Using the WHO 1994 model to calculate the MAC for drinking water it is appropriate to divide the ADI by an additional assessment factor of 10 and thus derive an intake of 0.00003 mg/kg bw/day.

Assuming the average value for consumption by a typical 60 kg person is 2 litres/day, a daily intake of 0.00003 mg/kg bw/day would be achieved by drinking water containing 0.0009 mg/litre. Thus, **a MAC of 0.9 μg/l of water can be derived for AMTT.**

B.6.12 Dermal penetration

Taking the *in vivo* and *in vivo* dermal penetration data together, they support the use of a dermal penetration figure of 1% for the concentrate and 2% for the in-use dilution in the operator exposure calculations.

SCIENTIFIC INSTITUTE OF PUBLIC HEALTH
-Louis Pasteur-

phone : +32 2 642 5351
telefax : +32 2 642 5224
contact person : Ph. Castelain
e-mail : ph.castelain@iph.fgov.be

Division Toxicology

your letter dated
your references :

our references PhC-ecco136-tritosulfuron
date 17.02.2003

annex(es)

e-mail
RMS: h.koepp@bba.de
ecco@bba.de
p.s.d.ecco@psd.defra.gsi.gov.uk

**Ecco 136 – mammalian toxicology**
**CONCERNS Belgian comments on draft : TRITOSULFURON**

P97
B.6.1.2.2. Metabolism of tritosulfuron with defined quantities of AMTT
If the same batch of tritosulfuron (437-1406) was used to prepare the dosing solutions for the Urine/Faeces and Bile experiment, the study director should have explained why in the first experiment the initial AMTT-content was 0.5%, while it was 1.9-3.2% in the second. Is the latter to be understood as a cleavage of the a.s. under certain experimental conditions ? Since there was no clarity about the initial impurity content, the endogeneous formation of AMTT from the parent compound can not be excluded.

P140
B.6.4.1.3 In vitro cytogenetic test
In the study, an increase of chromosome aberrations (excl. gaps) [exp 2] and of exchanges [exp 2, 3] has been observed in V79 cells, at the top dose and in the presence of S9. The culture conditions at the top dose lead to a mild drop of both M.I. and cell count (exp 2: M.I.=58.2%, cell cnt=83.6%; exp3: M.I.=107.6%, cell count=70%). Some cytotoxicity was obvious (appearance of rounded cells, detachment from substrate) but not extreme. Therefore, it is suggested to mention the in-vitro clastogenic effect of tritosulfuron as positive in the presence of S9.

P147
B.6.5.1. Chronic rat toxicity
Based upon the incidence of anogenital soiling at 1000ppm in the females, the NOAEL could have been established at 100 ppm in this sex. However, the finding is unremarkable in the 2yr carcinogenicity study at 1000 ppm. Thus, we agree with an overall NOAEL of 1000 ppm for this clinical sign.

P162-163
B.6.5.2 Rat carcinogenicity study
In the fifth and sixth study (0, 50, 100 ppm) with tritosulfuron (+2.45% AMTT) carcinogenicity NOAEL was established = 100 ppm. On the other hand, increased water consumption was



Federal Ministry of Social Affairs,
Public Health
and Environment

Address : Juliette Wytsman 16
B-1050 BRUSSELS
Phone. : +32 2 642 5111
Telefax : + 32 2 642 5001
http://www.iph.fgov.be

systematically above control in both studies at 50 ppm study 5: 37-42%) and 100ppm (study 5: 19-33%). Therefore, toxicity NOEL<50 ppm. Despite the absence of dose-dependency, and in the light of the effects at higher doses, the finding should be considered substance-related.

P170
B.6.6.1 Two generation study in rat (first study)
-Minor point: the test article intake of reference was based upon the premating period; hence, 600 ppm corresponds to 65.3 mg/kg bw/d instead of 40 mg/kg bw/d.

P241
B.6.10 Summary, proposed ADI, AOEL, ArfD
The proposal of the RMS is questionable. Whether ADI and AOEL have been derived from the 2yr rat study and the 90d rat study on tritosulfuron (0.02% AMTT). However, no dog studies are present with 0.02% AMTT, but only with 2.45% AMTT. These studies give lower NOAEL values. It is unclear whether the dog is more sensitive than the rat. On the one hand, a comparison between the NOAEL's from the 90d neurotoxicity study (2.45% AMTT) and the 90d dog study (2.45%) seems to suggest that rat would be more sensitive (NOAEL=7 mg/kg/d) than the dog (NOAEL=15 mg/kg/d). On the other hand, it is not excluded that the effects observed in the dog may also be caused by tritosulfuron itself.
Therefore, from the precautionary principle, it would be adviseable to calculate the ADI from the 1yr dog study, i.e. 6mg/kg bw/d / 100 = **0.06 mg/kg bw/d**.
Likewise, the AOEL would be calculated from the 90d dog oral study, i.e. 15 mg/kg bw/d / 100 = **0.15 mg/kg bw/d**.

On the other hand, it is doubtful whether an ADI and an AOEL for AMTT could be attributed based on the existing studies with tritosulfuron containing 2.45% AMTT:
-in the 18 month mouse study no NOAEL was determined (<250 ppm, 36-44 mg/kg bw/d)
-the relevance of the observed effects at the lowest dose in the 2yr rat study was also questioned (NOEL or NOAEL?)
-the compound is carcinogenic, inducing mammary tumours; a mechanism of action was not proposed
-no valid developmental study was undertaken with tritosulfuron (+2.45% AMTT).

If existing studies are deemed sufficient to establish an ADI, a supplementary assessment factor would be appropriate. From the 2G-NOAEL, it calculates (2.4*0.0245)= 0.0588/200=0.0003 mg/kg bw/d.
Likewise, the ArfD would be defined on the same value=0.0003 mg/kg bw/d.

Yours sincerely,

Ph. Castelain

Board for the authorisation of pesticides, Stadsbrink 5, NL-6707 AA, Wageningen, P.O. Box 217, phone +31 317 471810, Fax +31 317 471899

To: ECCO-Team PSD
Cc: ECCO-Team BVL
From: CTB
Date: 3 March 2003

Subject: Comments of **the Netherlands** on EU-monograph **tritosulfuron**

## Mammalian toxicology, metabolism and classification and labelling

### Volume 1, Level 2, 3 and 4

Adjustments should be made according to the comments on the summaries in Volume 3, Annex B.

### 2.4 Impact on human health

### Appendix 3, End point list

**Absorption, distribution, excretion and metabolism in mammals** (Annex IIA, point 5.1)

| | |
|---|---|
| Rate and extent of absorption | Rapid and complete (≥ 90 % based on ~~urinary and bile excretion over 48 h~~ based on comparison urinary excretion after oral and i.v. administration[1]) |
| Distribution | Widely distributed |
| Potential for accumulation | Low potential for accumulation |
| Rate and extent of excretion | Rapid (approx. 80 % via urine and 12 % via feces over 48 h) |
| Metabolism in animals | Limited (hydroxylation at the 4-position of the phenyl ring followed by conjugation; cleavage of the triazine ring and degradation to sulfonamide and sulfonate) |
| Toxicologically significant compounds (animals, plants and environment) | Parent compound and metabolites (especially AMTT (2-amino-4-trifluoromethyl-6-methoxy-1,3,5-triazine). |

**Acute toxicity** (Annex IIA, point 5.2)

| | | |
|---|---|---|
| Rat $LD_{50}$ oral (N12) | | 4700 mg/kg bw |
| Rat $LD_{50}$ oral** | | > 200 < 2000 mg/kg bw |
| Rat $LD_{50}$ dermal | (N12) | > 2000 mg/kg bw |
| Rat $LC_{50}$ inhalation | (N12) | > 5.4 mg/l air (dust aerosol, 4 h, ) |
| Skin irritation | (N12) | Not irritating |
| Eye irritation | (N12) | Not irritating |
| Skin sensitisation (test method used and result) | | Sensitising (M&K test) **R43** |

[1] Bile cannulation studies are not very suitable for the determination of bioavailability, as biliary excretion may occur on first pass. In this case, the parent compound and/or metabolites excreted will not have entered systemic circulation.

| | |
|---|---|
| (N12) | |

## **Short term toxicity** (Annex IIA, point 5.3)

| | |
|---|---|
| Target / critical effect | Liver, kidney/centrilobular hypertrophy, nephropathy |
| Lowest relevant oral NOAEL/NOEL (N14) | 90-day, rat: 1000 ppm (75 mg/kg bw/d) |
| Lowest relevant oral overall NOAEL/NOEL* (N24) | 90-day & 12-month, dog: 500 ppm (15 mg/kg bw/d )<br>AMTT: 0.37 mg/kg bw/d |
| Lowest relevant dermal NOAEL/NOEL* (N24) | 28-day, rat: 1000 mg/kg bw |
| Lowest relevant inhalation NOAEL / NOEL | No data-not necessary |

## **Genotoxicity*** (Annex IIA, point 5.4)

| | |
|---|---|
| (N24) | No evidence of genotoxic potential |

## **Long term toxicity and carcinogenicity** (Annex IIA, point 5.5)

| | |
|---|---|
| Target / critical effect | Kidney, liver/interstitial nephritis, pericholangitis |
| Lowest relevant NOAEL / NOEL (N34-59) | 2-year, rat: 1000 ppm (48 mg/kg bw/d) |
| Lowest relevant NOAEL / NOEL* (N24) | 2-year, rat: 100 ppm (5 mg/kg bw/d)<br>AMTT: 0.123 mg/kg bw/d |
| Carcinogenicity (N34-59) | No evidence of a carcinogenic potential |
| Carcinogenicity* (N24) | Mammary gland tumours in rats |

## **Reproductive toxicity** (Annex IIA, point 5.6)

| | |
|---|---|
| Reproduction target / critical effect (N34) | Lower bw gain, increased incidence of dilated renal pelves |
| Reproduction target / critical effect* (N24) | Pup mortality in absence of maternal toxicity |
| Lowest relevant reproductive NOAEL / NOEL (N34) | 2-gen. rat: 600 ppm (40 mg/kg bw/d) |
| Lowest relevant reproductive NOAEL / NOEL* (N24) | 2-gen. rat: 25 ppm (2.4 mg/kg bw/d, premating period)<br>AMTT: 0.06 mg/kg bw/d |
| Developmental target / critical effect (N12/N14) | Slightly increased incidences of hydrourethers in combination with renal pelves dilatation (rat) and of accessory 13t$^{h}$ rib(s) (rabbits), in the presence of maternal effects.<br>Tritosulfuron is not teratogenic. |
| Lowest relevant developmental NOAEL / NOEL (N12/14) | 120 mg/kg bw/d (rat)<br>150 mg/kg bw/d (rabbit) |

## **Neurotoxicity / Delayed neurotoxicity** (Annex IIA, point 5.7)

| | |
|---|---|
| Acute oral and 90-day neurotoxicity* | No signs of neurotoxicity |
| Developmental neurotoxicity (N24) | No developmental neurotoxicity |
| Lowest relevant NOAEL for neurotoxicity* (N59) | 90-day rat: 3500 ppm (243 mg/kg bw/d) |

## **Other toxicological studies** (Annex IIA, point 5.8)

Supplementary studies with metabolites:
635M02: LD50 oral rat: 1000 mg/kg bw (0.5 % Tylose CB 30.000 in aqua bidest); > 2000 mg/kg bw (olive oil); Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative
BH 635-3: LD50 oral rat: > 5000 mg/kg bw; subchronic study in rats: no effects; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative
635M01: LD50 oral rat: > 5000 mg/kg bw; Ames test, CHO-HPRT test, in vitro chromosome aberration test: negative
Reg.-No. 373 906: LD50 oral rat: > 2000 mg/kg bw; Ames test, CHO-HPRT test, in vivo mouse micronucleus test: negative
Supplementary studies with the impurity AMTT (635M04):
Biokinetik and metabolism study in rats: rapid excretion, major metabolite AHTT (635M11); LD50 oral rat: > 200 < 2000 mg/kg bw; subchronic study with estrus cycle determination and hormone analysis in female rats: no changes in estrus cycle and hormone analysis parameters; Ames test, CHO-HPRT test, mouse micronucleus test: negative; pre-/postnatal screening toxicity study in rats: maternal and developmental toxicity at 20 and 50 mg/kg bw/d; Study of a possible bond of AMTT and tritosulfuron to the estrogen receptor in the cytosol from the endometrial RUCA-I adenocarcinoma cell line: extremely low bonding capacity of tritosulfuron and AMTT to the estrogen receptor in the presence of endogenous estrogens

## **Medical data** (Annex IIA, point 5.9)

Limited data (new compound); no human health problems reported

**Summary** (Annex IIA, point 5.10)

| | Value | Study | Safety factor |
|---|---|---|---|
| ADI | 0.5 mg/kg bw | 2-gen. rat & 24-month rat | 100 |
| ADI** | 0.0006 mg/kg bw | 2-gen. rat | 100 |
| AOEL systemic | 0.75 mg/kg bw/d | 90-day rat | 100 |
| AOEL systemic** | Not allocated- | Not necessary | |
| ARfD | Not allocated- | Not necessary | |
| ARfD** | 0.0006 mg/kg bw | 2-gen. rat | 100 |

**Dermal absorption** (Annex IIIA, point 7.3)

| |
|---|
| 1% (in vivo rat, in vitro rat/human) (however, see comment on B.6.12) |

**Acceptable exposure scenarios** (including method of calculation)

| | |
|---|---|
| Operator | Intended uses acceptable (operator exposure < systemic AOEL; German model and UK-POEM without PPE) |
| Workers | Intended uses acceptable |
| Bystanders | Intended uses acceptable |

* batch no. N24 is containing 2.45 % AMTT
** AMTT

**Volume 3, Annex B**

## B.4 Proposals for the classification and labelling

Since the $LC_{50}$ is between 2.1 and 5.9 mg/l, labelling for acute inhalation should be considered
(see comment on B.6.11).

## B.6 Toxicology and metabolism

Only issues which to the opinion of the reviewer would change the overall picture of toxicity, exposure and risk in a significant way are commented upon.

### B.6.1 Absorption, distribution, excretion and metabolism

No comments.

### B.6.2 Acute toxicology including irritancy and skin sensitization

*Acute toxicology*
No comments.

*Irritation*
No comments.

*Sensitisation*
No comments.

### B.6.3 Short-term toxicity

No comments.

### B.6.4 Genotoxicity

No comments.

### B.6.5 Long-term toxicity and carcinogenicity

No comments.

### B.6.6 Reproductive toxicity

No comments.

### B.6.7 Neurotoxicity

No comments.

### B.6.8 Further toxicological studies

**B.6.8.1 to B.6.8.2.6:** No comments.

### B.6.8.2.7 Pre-/postnatal screening toxicity study in Wistar rats

It should be noted that AMTT was only tested at doses (severely) toxic for the exposed dams.

### B.6.8.2.8 Study of a possible bond of AMTT and Tritosulfuron to the estrogen receptor

No comments.

### B.6.9 Medical data

No comments.

### B.6.10 Summary of mammalian toxicology and conclusion

### B.6.10.1 to 10 Summary of mammalian toxicology

Adjustments should be made according to the comments on the summaries in sections B.6.1 to B.6.8 and section B.6.12.

### B.6.10.11 Acceptable daily intake (ADI)

No comments.

### B.6.10.12 Acceptable operator exposure level (AOEL)

No comments.

### B.6.10.13 Acute Reference Dose (ARfD)

No comments.

### B.6.10.14 Drinking water limit

No comments.

### B.6.11 Acute toxicity including irritancy and skin sensitisation of preparations

$LD_{50}$ and $LC_{50}$ values should be based on the values obtained for the most sensitive sex in these acute tests, the females. Therefore the acute oral $LD_{50}$ should be ca. 2000 mg/kg bw and the acute inhalation $LC_{50}$ >2.1 and <5.9 mg/l. Since the $LC_{50}$ is between 2.1 and 5.9 mg/l, labelling for acute inhalation should be considered.

### B.6.11.1 Oral

The $LD_{50}$ value should be calculated separately for both sexes.

### B.6.11.2 Percutaneous

No comments.

### B.6.11.3 Inhalation

The $LC_{50}$ value should be calculated separately for both sexes.

**B.6.11.4 to B.6.11.7:** No comments.

### B.6.12 Dermal absorption

The reviewer feels that for dermal absorption a value of 4% of the applied dose during an 8-hour exposure period should be used. However, since, in this case, it will not alter the conclusion of the risk assessment (due to very low exposures) this is not further considered here.

### B.6.13 Toxicological data of non-active substances

No comments.

### B.6.14 Exposure data

Adjustments should be made according to the comments on section B.6.10.3.

No comments with respect to the exposure scenarios and calculations.

**DOCUMENTS ON TRITOSULFURON DRAFT ASSESSMENT REPORT**

**Section: Fate & Behaviour (ECCO 137)**

**1. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**2. Comments**

| Date | Supplier | File name |
|---|---|---|
| 6 March 2003 | Denmark | tritosulfuron 137 com01 DK |
| 14 March 2003 | UK | tritosulfuron 137 com02 UK |
| 31 March 2003 | France | tritosulfuron 137 com03 FR |
| 3 April 2003 | Greece | tritosulfuron 137 com04 GR |
| | | |
| | | |
| | | |

**3. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |
| | | |

**4. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**5. Addenda (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**6. Other Documents (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**Danish Environmental Protection Agency**
Danish Ministry of the Environment

ECCO-Team PSD

cc. RMS Germany

Pesticides
In your reply, please refer to File No.
File no. M: 7042-0345
Ref.: cdh/11
6 March 2003

**Re: ECCO 137**

Danish comments on the draft assessment report on **tritosulfuron** prepared by Germany concerning **fate and behaviour**.

This DAR is very well written and presented and we agree to most of the conclusions. We agree to the conclusion regarding groundwater contamination with the metabolites 635M01, 635M02 and 635M03. All of the metabolites have been found in both lysimeter studies and in the majority of the FOCUS scenarios simulated in concentrations above 0.1 µg/l.
We can therefore not support an inclusion of tritosulfuron in annex 1, regardless of the metabolites toxicological properties.

Yours sincerely,

Christian Deibjerg Hansen

Contact point e-mail: stm@mst.dk



Danish Environmental Protection Agency · Strandgade 29 · DK-1401 Copenhagen K
Phone +45 32 66 01 00 · Fax +45 32 66 04 79 · Telex 31 209 miljoe dk · CVR 10 05 86 35 · mst@mst.dk · ww.mst.dk/homepage

**PESTICIDES SAFETY DIRECTORATE**
Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX, UK
Switchboard: 01904 640500 GTN: 5138 5813
Direct Dial: 01904 455813 Fax: 01904 455722
International: (+44) 1904 455813 International Fax: (+44) 1904 455722
e-mail emma.hedges@psd.defra.gsi.gov.uk

Mr Herbert Koepp
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienststelle Braunschweig
Messeweg 11 –12
38104
Braunschweig

Our ref: ASY 221

Date: 14 March 2003

Dear Mr Koepp,

**EC REVIEW MONOGRAPH FOR TRITOSULFURON**
**RAPPORTEUR:- GERMANY**

**ECCO 137 - MEETING TO DISCUSS FATE AND BEHAVIOUR**

On behalf of the Pesticides Safety Directorate of the Department for Environment, Food and Rural Affairs, please find attached our comments on the monograph for tritosulfuron. We are submitting these comments for your information as rapporteur and for discussion at ECCO 137 in April 2003.

Yours sincerely

Emma Hedges

Emma Hedges
Approvals Committee Branch

cc: ECCO Team (PSD)

The Pesticides Safety Directorate agrees with the technical evaluation and risk assessment given in the monograph, except in the following areas:

i) The PECsoil calculation is based on the worst case field DT50 values which has been normalised to 20 degrees C and then further adjusted to 15 degrees C. Recalling the application submitted to the UK for provisional approval of this active substance, the notifier argued that 15 degrees was appropriate on average for Europe. Typical approaches so far in Europe to the calculation of PECsoil are to use the longest DT50 value, and usually to favour field derived data where it is appropriate. Whilst the notifier's approach seems to follow this, the assumption of normalising to 15 degrees C appears to be too general. Certainly applications could be made at times and in places where soil temperatures are significantly lower. For this reason, we suggest that for consideration for Annex I inclusion, a more typical approach to PECsoil calculation is adopted and the values recalculated. It may be of interest to the meeting to note that the 'normalise to 15 degrees C' approach was adopted by the notifier for the UK application for provisional approval. After discussion, and to reflect what could be typically encountered conditions during early spring application to winter cereals in the UK, the temperature was changed to 5 degrees C.

ii) There are indications from field dissipation studies that some of the metabolites (M01, M02 and M04) could be prone to accumulation given the longest DT90 values. The notifier should be requested to address this point.

iii) The Rapporteur has concluded that the active substance and main soil metabolites all exhibit stronger adsorption under acid conditions - a suitable data requirement has been set, with which we agree. This obviously has implications for leaching potential on neutral and alkaline soils. It is noted that the lysimeter studies were conducted in relatively acid soils that would tend to reduce the leaching potential of parent and metabolites. We also note the conclusion that FOCUS modelling tended to confirm the results of the lysimeter study. However, it is considered that this modelling is inappropriate due to the use of mean adsorption Koc values. It is suggested that as a first stage in examining the implications of this pH dependence that the notifier submit further FOCUS modelling using appropriate pH values for the individual scenarios modelled. We also suggest that the metabolites are subsequently assessed against the criteria presented in the most recent version of the guidance document on assessment of the relevance of metabolites in groundwater (rev. 10).

iv) We note that the aquatic PEC values have assumed an entry route of surface run off as well as spray drift. Whilst this is likely to be a worse case compared to the consideration of spray drift only, for the sake of consistency, we suggest that the standard assumptions used for calculation of spray drift PEC values are used. However, if the FOCUSsw approach is adopted by the time of the meeting, the experts may wish to discuss the general point whether substances under consideration ought to have PEC values calculated by this new approach. We also note that PECsediment values have been calculated using an assumed depth of 2cm. For the sake of consistency with other

evaluations, this should be recalculated with the assumed standard depth of 5cm.

MINISTERE de l'EDUCATION NATIONALE et de la RECHERCHE et de la TECHNOLOGIE
MINISTERE de l'AGRICULTURE et de la PÊCHE

**DGAL**

**S. S. M.**
**STRUCTURE SCIENTIFIQUE MIXTE**

**Date: 07/02/03**


**Competent Authority :**
**Sylvie Malezieux**
Ministère de l'Agriculture et de la Pêche
Direction Générale de l'Alimentation
251, rue de Vaugirard
75732 - PARIS Cedex 15
Tel: 33 1 49 55 81 85 FAX 33 1 49 55 49 59
e.mail : sylvie.malezieux@agriculture.gouv.fr

**From**
**Annick Venant**
INRA – GMPV – Route de Saint-Cyr – F 78026
Versailles Cedex
Tel: 33 1 30 83 32 91 FAX 33 1 30 83 31 49
e.mail : venant@versailles.inra.fr


**To** **Ecco team (BBA)**
**e.mail :** ecco@bba.de

**cc** **Rapporteur member state : Germany**
**e.mail :** h.koepp@bba.de

**Objet : comments from France on draft monograph on TRITOSULFURON**

**Dear Colleagues,**

**Please find attached our comments on the Environmental fate and behaviour section of the draft's Assessment Report for the new active substance TRITOSULFURON.**

**Yours sincerely,**

**Annick Venant**
**P/L'Ingénieur d'Agronomie**
**Sylvie Malézieux**

**EU Review program on active substances in Plant Protection Products**

**Comments of France on TRITOSULFURON draft monograph**

**Section : Environmental fate and behaviour**

| Document | Comment |
|---|---|
| Volume 1, Level 2<br>2.5<br>Fate and behaviour in the environment<br>p. 37 | Table<br>Metabolites PECsw<br>According to the monograph p.444, there could be some errors in the PECsw reported. |
| Volume 1, Level 2<br>2.5.4<br>Fate and behaviour in air<br>p. 40 | According to the monograph (B.8.7 Fate and behaviour in air p.449 and to the End Points p.72, the Henry's law constant seems to be < $10^{-4}$ instead of $10^{-7}$ $Pa.m^3.mol^{-1}$. |
| Volume 1, Level 2<br>Endpoints<br>p. 86 | PEC soil<br>Method of calculation<br>'Maximum amounts of metabolites formed in field studies (% of as)'.<br>It could be useful to mention that these percentages correspond to molar fractions. |
| Volume 3,<br>B.8.1.1.1<br>Aerobic degradation<br>p. 376 | Aerobic degradation (Kellner, 1997, 1998 a)<br>Table B.8.1-3<br>In the non-extractable residues, the metabolite 635M01 was around 9 % AR in the fulvic acid fraction. If this amount is taken into account, the metabolite 635M01 could represent more than 56 % AR (maximum of all tests). |
| Volume 3,<br>B.8.1.1.3<br>Anaerobic degradation<br>p. 386-387 | Anaerobic degradation<br>For triazine label, the sum of non-identified products reached 10.1 % TAR (day 92).<br>Is it possible to know if this amount corresponds to more than one compound ?<br>It would have been interested to know if the formation of the metabolite 635M04 (AMTT) can occur under anaerobic conditions. |
| Volume 3,<br>B.8.1.2.1<br>Rate of degradation<br>Laboratory studies<br>p. 392 | Table B.8.1-14 is very useful to compare the different methods of calculation of tritosulfuron DT50.<br>- However, it would have been useful to point out which values are finally chosen to characterize the active substance.<br>- When two labels are tested with the same soil (soil Li35b), we prefer considering finally only one DT50 (mean of the DT50 obtained with the two labels), instead of one DT50 for each label, in order to give the same weight to each soil when a global mean value is then calculated.<br>- The higher DT50 value (Canadian soil, 124 or 141 days depending on the method of calculation) seems to have been more or less excluded (it is in brackets in the End Points p.84). However the soil biomass was not negligible. Why is this DT50 value excluded ?<br>We think that it should be taken into account for the mean DT50 calculation. |

| | |
|---|---|
| | We would propose a laboratory mean DT50 value of 41 days instead of 26 days for tritosulfuron (End Points p.84) |
| Volume 3,<br>B.8.1.2.2<br>Field studies<br>p. 399 | (Kellner and Keller, 1998 ; Kellner and Richter, 1998)<br>635M04 concentrations are always low in studies ALO/11/97 (Spain) and HUS/11/97 (Sweden), varying from lower than detection limit to 0.001 or 0.002 mg/kg.<br>In these conditions, the derived field DT50 133 and 11 days are probably not reliable. |
| Volume 3,<br>B.8.1.2.2<br>Field studies<br>p. 400 | (Jackson et al. , 2001)<br>- It should be useful to mention in a table the main measured data for residues of tritosulfuron and metabolites in soil in the four US field studies (as done for European field studies), due to the importance of these studies for the PEC soil and groundwater calculations.<br><br>- Considering the low recoveries (35 %) for the Indiana site, are the corresponding DT50 values for tritosulfuron, 635M01, 635M02, 635M03 and 635M04 acceptable ?<br><br>- If the field study in Indiana was considered to be acceptable, the metabolite 635M04 would be major (maximum concentration 10 % of parent concentration). |
| Volume 3,<br>B.8.1.2.2<br>Field studies<br>p. 401 | (Dressel and Beigel, 2001)<br>Table B.8.1-27<br>We think that the comparability of the USA trials with European conditions is not acceptable in all cases, because there are significant differences in annual rainfall : Heraklion (Greece) 501 mm seems very different from California 188 mm, Karlsruhe (Germany) 770 mm seems different from Indiana 536 mm, Paris (France) 388 mm seems different from California 260 mm. Most of the European sites considered for the comparison have a relatively high yearly average temperature. |
| Volume 3,<br>B.8.1.2.2<br>Field studies<br>p. 402 | (Dressel and Beigel, 2001)<br>Table B.8.1-28<br>We would like to know field DT50 values calculated with first order kinetics and before standardisation (20°C, pF 2) for tritosulfuron and metabolites in the four US field studies, in order to characterize the persistence of each compound and to calculate PEC soil. |
| Volume 3,<br>B.8.1.2 | Rate of degradation<br>We agree with the UK comment on the possible accumulation of metabolites. |
| Volume 3,<br>B.8.2<br>Adsorption, desorption and mobility in soil<br>p. 405-408-410 | Sorption behaviour of tritosulfuron and metabolites<br>The effect of soil pH on adsorption is unclear for tritosulfuron, 635M01, 635M02, 635M03 and 635M04 (for each compound the correlation coefficient is not very high). There could be relationships with the organic matter too.<br>In particular, the effect of pH on tritosulfuron adsorption is not significant, all Koc values being very low (2-11).<br>For the metabolites, the effect of pH on adsorption seems more evident for pH lower than 6. |
| Volume 3,<br>B.8.2.1.3 | For both groups of lysimeters, it could be pointed out that the soil pH is relatively low (from 5.7 in topsoil to 6.2-6.8 at 1 m). |

| | |
|---|---|
| Lysimeter studies<br>p. 417 and 421 | |

| | |
|---|---|
| Volume 3,<br>B.8.2.1.3<br>Lysimeter studies<br>p. 421 | (Staudenmaier, 2001)<br>'Maximum concentrations in individual leachate samples were 0.17 µg/L' (beginning of the fourth paragraph).<br>635M17 should probably be added. |
| Volume 3,<br>B.8.2.1.3<br>Lysimeter studies<br>p. 422 | Table B.8.2-30<br>- According to the text p.421 and the End Points p.86, the yearly mean concentration of 635M02 in the third year and lysimeter 17 seems to be 0.03 µg/L instead of 0.34 µg/L. Could you specify the right value ?<br><br>- Is the non-identified radioactivity expressed in µg/L (like in Table B.8.2-19) or in % ? |
| Volume 3,<br>B.8.3<br>Predicted environmental concentrations in soil<br>p. 425 | PECsoil<br>We support the UK comment :<br>'The assumption of normalising to 15 degrees C appears to be too general. Certainly applications could be made at times and in places where soil temperatures are significantly lower. For this reason, we suggest that for consideration for Annex I inclusion, a more typical approach to PECsoil calculation is adopted and the values recalculated'. |
| Volume 3,<br>B.8.6.1<br>Predicted environmental concentrations in surface water<br>p. 444-445 | PECsw<br>The PECsw runoff calculation proposed here is rather unusual.<br>For tritosulfuron and 635M01, 635M02, it could have been concluded that PECsw drift and PECsw runoff had the same order of magnitude.<br>We support the UK comment, suggesting either to use the PECsw calculated with the standard assumptions for spray drift or to follow the FOCUS surface water approach, if it is adopted.<br>A PECsw runoff calculation is important for 635M04, because this metabolite is not expected to contaminate surface water by drift.<br>It could also have been pointed out that an entry route by drainage is possible, because all these compounds are mobile. |
| Volume 3,<br>B.8.6.3<br>Predicted environmental concentrations in groundwater<br>p. 447 | PECgw simulation<br>We wonder if the characterization of 635M04 with a standardized field DT50 value (20°C, pF 2) of 9.7 days is appropriate for the risk assessment of groundwater contamination. This value seems low, compared with the only laboratory DT50 of 98 days (20°C).<br>An additional simulation with a less favourable DT50 for 635M04 could be considered. |
| Volume 3,<br>B.8.9<br>Definition of the residue<br>p. 450 | The metabolite 635M04 should be added in the definition of the residue, because it is toxicologically relevant and can reach 10 % at field. |

NAGREF
NATIONAL AGRICULTURAL RESEARCH FOUNDATION

*Address:* *19 Egialias & Chalepa str.*
*151 25, Maroussi, Athens, Greece*
*Phone:* *+30-210-81.75.495*
*Fax:* *+30-210-68.45.870*
*e- mail:* *pesticide@nagref.gr*
*Info:* *P. Lolos*

Maroussi, 3 / 04 / 2003

Ref. Number: 4380

**TO:** ECCO Team PSD
Pesticides Safety Directorate
Room 208, Mallard House, Kings Pool
3 Peasholme Green
YORK Y01 7PX
UNITED KINGDOM
Tel: +44 (1904) 45 57 12
Fax: +44 (1904) 45 57 22
e-mail: ecco@psd.defra.gsi.gov.uk

**CC:** ECCO-Team (BBA)
Biologische Bundesanstalt für
Land- und Forstwirtschaft
Abteilung für Pflanzenschutzmittel
und Anwendungstechnik
Messeweg 11/12
D-38104 Braunschweig
Tel: +49 / 5 31 / 2 99-34 71 or - 34 73
+49 / 5 31 / 2 99-34 51
Fax: +49 / 5 31 / 2 99-30 20 or - 30 03
e-mail: ecco@bba.de

**CC:** Ministry of Agriculture
Directorate of Plant Protection
Department of Pesricides
Ippokratous 3-5
10164 Athens
Tel: +30-210-36.42.975
Fax: +30-210-36.17.103

**SUBJECT: Comments on the draft assessment report for the active substance "Tritosulfuron"**

Please find hereby our comments concerning the section "Fate and behaviour in the environment" of the draft assessment report. For any question or clarification please do not hesitate to contact us.

**1. Annex B, Table B.8.1-13, page 387**:

635M19 is an anaerobic major metabolite (>10%). In addition, 635M19 is rather stable (11.5% at day-7 & 13.4 at day-120) under anaerobic conditions. This metabolite was not detected under aerobic conditions. Therefore, 635M19 is relevant only under anaerobic conditions. The environmental importance of that metabolite in soil should be addressed, especially when the aerobic conditions in soil re-establish.

**2. Annex B, Table. B.8.1-12, page 393**:

The $DT_{50}$ for 635M02 in LI35B soil type is estimated to be 96 days (Topfit model). However, from the relevant amounts (% of applied radioactivity) of that metabolite (Table B.8.1-2, page 375), it seems that this metabolite is rather stable (11.1 % at day-113 and 10.5 % at day-358). So the calculated $DT_{50}$ for 635M02 in LI35B soil type might not be relevant.

**3. Annex B, findings, page 421**:

The 635M17 was found in the leachate at concentrations above 0.1 μg/l. The formula of that metabolite is not provided in the monograph. This metabolite was not detected in soil metabolism studies and is considered a plant metabolite. However, it is considered as necessary the biological and (eco-) toxicological profile of 635M17 be investigated further.

**4. Annex B, Table B.8.3-2, page 425**:

PECs values for the metabolite 635M04 have been calculated. However, this metabolite is minor (<10 %) and for that reason 635M04 was not included in the definition of the residue. Therefore, PECs values are not considered as necessary.

**5. Annex B, Table B.8.6-2, page 444**:

Overspray is considered rather as a "bad" use than as another option of spray drift.

**Annex B, Point B.8.6.2, page 445**:

The $PEC_{SED}$ where calculated assuming 2 cm depth and bulk density 1.3 Kg/l. However, the standard depth for the sediment is 5 cm, while the bulk density is 1.5 Kg/l. Consequently, $PEC_{SED}$ values should be recalculated using the standard values.

**Annex B, Point B.8.6.3, page 446**:

It is stated, "*As recommended by FOCUS, the average values of the sorption parameters were used for the simulations.*" However adsorption is influenced by soil pH (page 405 & 408). In the guidance document SANCO/321/2000 rev.2 (FOCUS groundwater scenarios in the EU review of active substances) is proposed, "*If sorption is soil pH dependent (e.g. ionic compounds) then a single value should be used (in relation to the pH of the soils in the scenario)*". Therefore $PEC_{GW}$ values should be re-calculated taking into account the effects of soil pH to the adsorption.

**P. Lolos**

P. Lolos

Agronomist

(Evaluation of the Environmental Fate & Behaviour of the Actives Substances and their Plant Protection Products)

**DOCUMENTS ON TRITOSULFURON DRAFT ASSESSMENT REPORT**

**Section: Residues (ECCO 138)**

**1. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**2. Comments**

| Date | Supplier | File name |
|---|---|---|
| 7 April 2003 | United Kingdom | tritosulfuron 138 com01 UK |
| 23 April 2003 | The Netherlands | tritosulfuron 138 com02 NL |
| | | |
| | | |
| | | |
| | | |
| | | |

**3. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |
| | | |

**4. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**5. Addenda (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**6. Other Documents (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**PESTICIDES SAFETY DIRECTORATE**
Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX, UK
Switchboard: 01904 640500 GTN: 5138 5813
Direct Dial: 01904 455813 Fax: 01904 455722
International: (+44) 1904 455813 International Fax: (+44) 1904 455722
e-mail emma.hedges@psd.defra.gsi.gov.uk

Mr Herbert Koepp
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienststelle Braunschweig
Messeweg 11 –12 Our ref: ASY 221
38104
Braunschweig Date: 7 April 2003

Dear Mr Koepp,

**EC REVIEW MONOGRAPH FOR TRITOSULFURON**
**RAPPORTEUR:- GERMANY**

**ECCO 138 - MEETING TO DISCUSS RESIDUES**

On behalf of the Pesticides Safety Directorate of the Department for Environment, Food and Rural Affairs, please find attached our comments on the monograph for tritosulfuron. We are submitting these comments for your information as rapporteur and for discussion at ECCO 138 in May 2003.

Yours sincerely

Emma Hedges

Emma Hedges
Approvals Committee Branch

cc: ECCO Team (PSD)

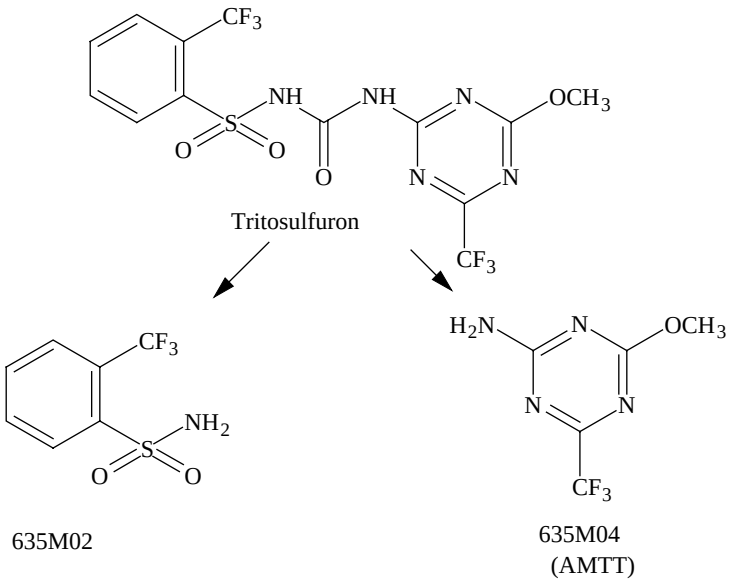
The Pesticides Safety Directorate has the following comments to make on the draft assessment report for tritosulfuron. These comments have not been associated with specific studies or study areas, because in isolation many of the studies appear robust. PSD is currently evaluating an application for UK provisional approval and has found that concerns have arisen through inconsistencies between different areas of the dossier.

The maize metabolism study does not provide any information on the metabolism of tritosulfuron to AMTT or 635M02, nor does it give any information on the metabolism of either of the impurities/metabolites.

AMTT reference standard was made in corn cell culture suspension. The notifier advised PSD that although no AMTT was found in the maize metabolism study, it was formed in corn cell suspension by virtue that the cells were undifferentiated.

Processing data submitted using [$^{14}$C]-triazine tritosulfuron indicate that AMTT is the only metabolite formed (similarly, the [$^{14}$C]-phenyl labelled processing study also indicated a single metabolite formed - 635M02). Data indicate that AMTT may also be formed in the spray tank solution and therefore it is suggested that AMTT (as well as 635M02) may have been formed by simple hydrolysis of tritosulfuron in the cell culture medium.

Further, if AMTT can be formed in the spray tank solution (by hydrolysis), then 635M02 may also be formed (the reference material for 635M02 was also isolated from corn cell culture – hydrolysis again?). Metabolite 635M02 was also found in the succeeding crop metabolism study but was not found in the maize metabolism study. 635M02 was not sought in any of the residue trials, but is a major metabolite in soil as is AMTT. The diagram below shows the relationship of metabolites 635M02 and AMTT to each other and to parent tritosulfuron.



Given the above observations it is plausible to consider that AMTT and possibly 635M02 may have been applied to the maize plants as an impurity in the technical material (formed on manufacture) or as a hydrolysis product formed in the spray tank prior to application. There are no data to indicate how much, if any, AMTT or 635M02 was applied to the maize plants; whether any of this AMTT or 635M02 was taken up by the maize plant or whether the metabolism of maize is such that any AMTT or 635M02 formed is metabolised very quickly.

The residues trials studies with maize indicate that AMTT was only found in the maize plants on the day of application which may add weight to the assumption that maize does not form AMTT during the metabolism of tritosulfuron.

Residues of AMTT were found in the wheat and barley straw as well as the wheat and barley forage, but residues of AMTT were only found on day of application in the maize samples. If we assume that AMTT was applied to the crops, then these data suggest that either, the maize metabolises the AMTT very quickly such that none is found at harvest, or, that the maize does not form AMTT and residues on the day of application are from the hydrolysis of tritosulfuron in the spray tank. However, it does not indicate the metabolism of tritosulfuron by wheat (and other traditional cereals).

Given the toxicological concern over AMTT and the observed differences between the wheat and maize residue trials. For the UK application, PSD considered that the metabolism studies on maize were not sufficient to represent the more standard cereals such as wheat. Therefore during the course of the evaluation, PSD recommended that a wheat metabolism study would be required before use on wheat could be considered. The company have accepted this reasoning and agreed to undertake a wheat metabolism study (started late 2002).

From consideration of the succeeding crop metabolism data, residues of AMTT were found in wheat grain at 0.001 mg/kg, whilst it was not recorded in cereal grains in any of the 23 residues trials conducted in 1999/2000. AMTT was also found in other plant matrices in the succeeding crop metabolism studies but was not seen in any of the primary metabolism studies. Whilst it was found in day 0 samples of maize plants from the residues trials, the day 0 samples from the maize metabolism study were not investigated any further than a determination of the TRR. The primary maize metabolism study suggests AMTT may not be formed in some plants when treated with tritosulfuron, the presence of AMTT in other plant tissues suggests that the succeeding crops may be taking up AMTT from the soil where it is a major soil metabolite. Given that AMTT was found in wheat grain, it again raises the question whether the cereal has metabolised tritosulfuron to AMTT and this has been translocated to the grain or whether the wheat doesn't metabolise AMTT and that residues found in the grain were taken up from the soil. Neither the maize metabolism study nor the succeeding crop metabolism study provides information on how wheat metabolises tritosulfuron and or AMTT.

The levels of AMTT in the succeeding crops cannot be confirmed as worst case at this time because a) we do not know how much AMTT was formed in the spray tank and thus ultimately applied to the soil in the succeeding crop metabolism study, b) whether the wheat, bean or carrot plants form AMTT from metabolism of tritosulfuron, whether they are able to metabolise AMTT to other compounds or whether the AMTT in the plants is attributed to uptake only. Finally, the likely maximum levels of AMTT (or other significant metabolites) in soil have not been established. Therefore it is not possible to decide whether the succeeding crop metabolism study is worst case or whether the potential exposure has been underestimated.

Impurity/metabolite 635M02 was also found in the wheat straw from the succeeding crop metabolism study at 0.015 mg/kg, 0.020 mg/kg and 0.035 mg/kg at the 30, 120 and 365 days planting interval respectively. However, it was not found in the maize metabolism study. 635M02 was not sought in the residue trials data but given it forms at similar levels to AMTT in the processing study, it is considered likely that it would be found possibly at levels similar to AMTT.

Overall, the plant metabolism data are not sufficient to address whether plants metabolise tritosulfuron to AMTT and or 635M02 or to what extent they are capable of metabolising AMTT and or 635M02. However, the data do suggest that the metabolism of tritosulfuron and AMTT and or 635M02 by maize (primary plant metabolism) is quite different to the manner and extent that wheat metabolises tritosulfuron and AMTT and or 635M02 (succeeding crop metabolism). Many additional metabolites were seen in the succeeding metabolism study that were not found in the maize studies. Given this, it is considered that the metabolism study on maize is not sufficient to address the metabolism of tritosulfuron and AMTT and or 635M02 in wheat, barley or other cereals.

The differences in AMTT and 635M02 seen in the primary maize metabolism and succeeding crop metabolism data indicate that residues of AMTT (plus 635M02) in succeeding crops may be significant to warrant consumer exposure considerations (human and livestock). Therefore, for the UK application, PSD has recommended that cold succeeding crop residues trials studies are required with crops which are grown in rotation with maize, wheat, barley and other cereals. Whilst the primary data are not considered sufficient to support use on wheat and barley cereals, the data do support use on maize, however, the succeeding residues data are also required before provisional approval for maize may be recommended in the UK.

Under the UK application for PA, concerns have also been raised about metabolite 635M11. This is known as AHTT and is the metabolite of AMTT. There is no evidence that this compound was found in either the primary metabolism data or the succeeding crop metabolism studies. Further information on the toxicological profile of this compound has been requested from the applicant. They will need to confirm whether this compound was sought in any of the metabolism studies. If the profile is similar to that of AMTT, then further residues data analysing for AHTT may be required.

**Summary.**

There are a number of uncertainties surrounding this molecule and it's metabolism:

- AMTT and 635M02 are both impurities of tritosulfuron technical material
- AMTT and 635M02 were the only metabolites formed from the simulated processing study (reflux in pH 5.0 buffer)
- Both AMTT and 635M02 are major soil metabolites
- Reference standards for AMTT and 635M02 were both isolated from corn cell suspension cultures and it is unclear whether these were made by the cells or by hydrolysis in the cell culture medium.
- Residues of AMTT and 635M02 were both found in wheat matrices in the succeeding crop metabolism study but neither were found in any of the maize tissues at any of the time points in the maize metabolism study.
- Residues of AMTT were sought and found in the residue trials on wheat and barley, but were only found in the maize plants on the day of application. It is considered likely that that metabolite 635M02 could also be found at similar levels. However, this was not sought.
- It is clear that metabolism of tritosulfuron (and similarly AMTT and 635M02) is not the same in maize and in wheat. Therefore, to support use on wheat, barley and other cereals a metabolism study specific to these crops is required. The company agree with the UK view and have agreed to conduct a wheat metabolism study (started late 2002)
- The succeeding crop metabolism study indicated AMTT and 635M02 are likely to be found in a range of plant matrices at significant levels such that cold succeeding crop residue trials are required. The formation/likely levels of AMTT/635M02 in soils have not been confirmed in the UK evaluation.
- No data are available on levels of AMTT (or 635M02) applied to the crops in either the primary metabolism or the succeeding crop metabolism study or the residue trials on wheat, barley and maize.
- Residues of 635M02 in the wheat straw were still increasing with increasing planting interval. Data are required to confirm the maximum level for this compound.
- AMTT has been suggested as a potential component of the residue definition (in addition to parent). AHTT has also been mentioned for possible inclusion as has 635M02. The applicant has also proposed 635M09 in tissue of animal origin.

For the application for UK PA, PSD has requested new wheat metabolism data before the application for use on wheat and barley can be progressed. PSD has also proposed succeeding crop residue trials data are required because AMTT and 635M02 were found in many succeeding crop tissues and levels of 635M02 were still increasing. The maximum level of AMTT and 635M05 in soils has not been established.

Board for the authorisation of pesticides, Stadsbrink 5, NL-6707 AA, Wageningen, P.O. Box 217, phone +31 317 471810, Fax +31 317 471899

To: ECCO-Team PSD
Cc: ECCO-Team BVL
From: CTB
Date: 3 April 2003

Subject: Comments of **the Netherlands** on EU-monograph **tritosulfuron**

## Residues

### General

In the intended use is stated that tritosulfuron **must** be used as a mixture with an adjuvant (surfactants as e.g. Citowett New). It is noted that most of the studies, especially studies on plant metabolism and storage stability were conducted with tritosulfuron only. The influence of an adjuvant was not investigated. Surfactants are used to aid the penetration of the active compound and as such this can have influence on kinetics and metabolism of the active compound in plants. The impact of the application of the adjuvant must be elucidated before final conclusions can be drawn.
Furthermore, due to the toxicological properties of the metabolite AMTT it must be clearly specified and controlled that the content of AMTT as impurity of the plant protection product does not exceed 0.02%. Exceeding this level implies a potential toxicological risk to consumers.

### Volume 1, Level 2, 3 and 4

Comments to the sections of Volume 3, Annex B also apply to the corresponding sections of Volume 1. No further comments.

### Appendix 3: End point list

**Metabolism in plants:**

| | |
|---|---|
| plant groups covered: | maize |
| rotational crops: | ~~radish,~~ lettuce, wheat, carrots, beans |
| plant residue definition for monitoring: | tritosulfuron |
| plant residue definition for risk assessment: | tritosulfuron |
| conversion factor (monitoring to risk assessment): | none |

**Metabolism in livestock:**

| | |
|---|---|
| animals covered: | goat, hen |
| animal residue definition for monitoring: | tritosulfuron |
| animal residue definition for risk assessment: | tritosulfuron |
| conversion factor (monitoring to risk assessment): | not applicable |

| | |
|---|---|
| metabolism rat versus ruminants the same: (yes/no) | yes |
| fat soluble residue: (yes/no) | **no** |

**Methods of analysis:**

| | |
|---|---|
| plant products:<br>principal method and general LOQ for monitoring: | HPLC-UV 0.01 mg/kg (wheat, maize)<br>~~LC-MS/MS 0.001 mg/kg (wheat, maize)~~<br>(see remark B.5.2.) |
| animal products:<br>principal method and general LOQ for monitoring: | HPLC-UV 0.01 mg/kg (milk, egg, muscle, fat, kidney, liver) |

**Residues in succeeding crops:**

30, 120, 365 days plant back interval after application of 60 g as/ha to soil.

The total radioactive residues were low for carrot root (≤ 0.011 mg/kg / parent: ≤ 0.001 mg/kg), green beans (≤ 0.005 mg/kg), lettuce head (≤ 0.022 mg/kg/ parent: ≤ 0.006 mg/kg) and wheat grain (≤ 0.019 mg/kg / parent: < 0.001 mg/kg)) after all 3 plant back intervals.

In bean plants, carrot foliage only few samples showed residues of tritosulfuron slightly above 0.01 mg/kg.

The metabolite AMTT (635M04) was detected in almost all samples of the triazine label but mostly at low absolute concentrations (< 0.01 mg/kg). Only after plant back intervals of 30 days in early samplings of bean plant and wheat forage and in wheat straw amounts in the range of 0.011 – 0.029 mg/kg were found.
(see remark B.9)

**Storage stability of residues:**

food of plant origin (maize grain, maize forage, wheat grain, wheat straw, radish root): tritosulfuron was stable over a period of 3 years.

**Residues from livestock feeding studies:**

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: no | Poultry: no | Pig: no |
|---|---|---|---|
| Muscle<br>Liver<br>Kidney | no ruminant feeding study conducted | no hen feeding study conducted | no pig feeding study conducted; metabolism in rat and ruminant similar |

| | |
|---|---|
| Fat<br>Milk<br>Eggs | |

**Consumer risk assessment:**
**Based on FAO/WHO EURdiet:**

| | |
|---|---|
| ADI | 0.5 mg/kg bw/d for tritosulfuron with max 0.02 % AMTT |
| TMDI (European Diet) (% ADI) | 0.07 % (German diet) / ~~0.04~~ 0.007 % (WHO diet)<br>(see remark B.7.13) |
| NEDI (% ADI) | not calculated |
| Factors included in NEDI | - |
| ARfD | not assigned |
| Acute exposure (% ARfD) | not applicable |

**Processing factors:**

| crop/processed crop | Number of studies | transfer factor | % transference* |
|---|---|---|---|
| not conducted | | | |

***** calculated based on the distribution between the different portions, parts or products as determined through balanced

**Proposed MRLs:**

| | |
|---|---|
| barley, oats, maize, rye, triticale, wheat | 0.01 mg/kg |

**Volume 3, Annex B**

## B.5 Methods of analysis

### B.5.2 Analytical methods for the determination of residues in food and feed

The mentioned LC-MS/MS method is not fully validated and can therefore not be used for monitoring, but only as confirmatory method.
For the analytical method for determination of residues in plant (products) the eventual use of additional buffer solution in order to increase the low recovery rate of the extraction step is stated (see B.5.2.1, page 60). It can not be proven whether or not this is verified, validated and included in the final protocol.

## B.7 Residue data

### B.7.1 Metabolism, distribution and expression of residues in plants

No comment, but attention should be paid to General remarks.

### B.7.2 Metabolism, distribution and expression of residues in livestock

No comment.

### B.7.3 Definition of the residue

**Definition of the residue for plant products**
No comment, but attention should be paid to remark B.7.9.

**Definition of the residue for animal products**
No comment.

### B.7.4 Use pattern

The obliged use of an additive (see Volume 1, 1.5.3.) is not mentioned (also not under the cited point B.3.3). It is noted that the function of the additive and its influence on uptake and plant metabolism, residues etc. is not further elucidated. This must be clarified before a final conclusion can be drawn (see also General remarks).

### B.7.5 Identification of critical GAP's

There is a discrepancy about the latest possible growth state for maize in the intended use: in Volume 1, 1.5.3 and also under B.3.3 growth state BBCH 18 is mentioned, not BBCH 17, as stated under B.7.5 and B.7.10.

### B.7.6 Residues resulting from supervised trials

**Methods of analysis applied in the supervised residue trials**
The LOQs reported in B.7.6.1.3. (analytical method used for samples from field trials) are different from those reported for straw in chapter B.5.2. This can be justified if additional validation data in the trials are acceptable, but since it is referred to chapter B.5 this is doubtful. Elucidation is needed because of possible consequences for the TDMI of livestock.

**Supervised residue trials**
No comment.

**Stability of residues prior to analysis**
No comment.

### B.7.7 Effects of industrial processing and/or household preparation
No comment.

### B.7.8 Livestock feeding studies
See remarks under B.7.6 and B.7.9.

### B.7.9 Residues in succeeding crops or rotational crops
It is noted that the levels of the toxicological relevant metabolite AMTT were present in all succeeding and rotational crops. Although levels were low and predominately present in forage and straw it is not clear whether this is due to differences in plant metabolism or if they are soil metabolites formed prior planting. This has to be taken into account in case the intended use will be extended (especially for residues in feed).

### B.7.10 Proposed pre-harvest intervals for envisaged uses, or withholding periods, in the case of post harvest uses
No comment.

### B.7.11 Community MRLs and MRLs in EU Member States
No comment

### B.7.12 Proposed MRLs and justification for the acceptability of those residues
No comment.

### B.7.15 Estimates of potential and actual dietary exposure through diet and other means
Calculations performed in this section may have to be re-evaluated following the evaluation of the comments made to Section B.7.12 (MRL proposals) and to this section (comments below).

Furthermore, the safety margin estimated in the consumers risk assessment (comparison of the TMDI, EDI and/or NESTI with respectively the ADI and the ARfD) may be subject to adjustments depending on the finally established ADI/ARfD.

**Intakes by domestic animals**
No comment, but attention should be paid to remark B.7.6, B.7.9 and General remarks.

**Intakes by humans**
It is noted that intake calculations were performed with an ADI and ArfD for tritosulfuron only. This is only correct if the level of AMTT is below 0.02%, as stated in the Monograph.
See also remark B.7.9 (succeeding and rotational crops).
The TDMI calculation for adults according to the German model is based on the consumption of processed wine grapes, tea, hops, and coffee beans. This is not in accordance with the intended use.

**B.7.14 Summary and evaluation of residue behaviour**
No further comments.

**ESTIMATE OF THE POTENTIAL AND ACTUAL DIETARY EXPOSURE OF HUMANS, BASED ON THE DUTCH TMDI MODEL (RIKILT-DLO model, The Netherlands):**

A NTMDI calculation was performed using a Dutch dietary consumption figure (Dutch TMDI model, RIKILT-DLO, The Netherlands). The calculation was based on the MRL proposals made by the Rapporteur Member State in Section B.7.12.

The Dutch NTMDI calculation may have to be reevaluated following the evaluation of the comments made to Section B.7.12 (MRL proposals). In addition, the safety margin estimated in the consumers risk assessment (comparison of the TMDI, EDI and NESTI with respectively the ADI and the ARfD) may be subject to adjustments depending on the finally established ADI/ARfD.

**Consumer risk assessment:**
**Based on Dutch TMDI model:**
(RIKILT-DLO model, The Netherlands)

| | |
|---|---|
| ADI: | 0.5 mg/kg bw/d tritosulfuron with max. 0.02% AMTT |
| NTMDI (% ADI): | Adults: 0.0016 mg/pers/d (0.005% ADI)<br>Children (1-6y): 0.0009 mg/pers/d (0.01% ADI) |
| NEDI (%ADI): | not needed |
| factors included in NEDI: | - |
| Acute reference dose (ArfD) | not assigned |
| Acute exposure (NESTI) (% ArfD) | not applicable |

Based on the NTMDI as calculated using the Dutch TMDI model, it can be concluded that a sufficient safety margin exists for consumers at the applied Dutch dietary consumption figure. When taking into account an additional theoretical intake via drinking water of 0.2 µg per person (based on a maximum level in drinking water of 0.1 µg/l and an arbitrary consumption assumption of 2 l), a sufficient safety margin still exists. Exposure to tritosulfuron through drinking water should further account for no more than 10% of the ADI. If it is assumed that the average daily consumption of water amounts to 2 litre per person of 63 kg, 10% of the ADI would not be exceeded with drinking water residue levels at or below 1.57 mg/l.

**DOCUMENTS ON TRITOSULFURON DRAFT ASSESSMENT REPORT**

**Section: Ecotoxicology (ECCO 139)**

**1. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**2. Comments**

| Date | Supplier | File name |
|---|---|---|
| 23 April 2003 | France | tritosulfuron 139 com01 FR |
| 7 May 2003 | United Kingdom | tritosulfuron 139 com02 UK |
| 28 April 2003 | The Netherlands | tritosulfuron 139 com03 NL |
| 26 May 2003 | Belgium | tritosulfuron 139 com04 BE |
| | | |
| | | |
| | | |

**3. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |
| | | |

**4. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**5. Addenda (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**6. Other Documents (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| | | |

MINISTERE de l'EDUCATION NATIONALE et de la RECHERCHE et de la TECHNOLOGIE
MINISTERE de l'AGRICULTURE et de la PÊCHE

**DGAL**

**S. S. M.**
**Structure Scientifique Mixte**

**Date: 20/03/03**

**Competent Authority :**
**Sylvie Malezieux**
Ministère de l'Agriculture et de la Pêche
Direction Générale de l'Alimentation
251, rue de Vaugirard
75732 - PARIS Cedex 15
Tel: 33 1 49 55 81 85 FAX 33 1 49 55 49 59
e.mail : sylvie.malezieux@agriculture.gouv.fr

**From**
**Annick Venant**
INRA – GMPV – Route de Saint-Cyr – F 78026 Versailles Cedex
Tel: 33 1 30 83 32 91 FAX 33 1 30 83 31 49
e.mail : venant@versailles.inra.fr

**To** **Ecco team (BBA)**
**e.mail :** ecco@bba.de

**cc** **Rapporteur member state : Germany**
**e.mail :** h.koepp@bba.de

**Objet : comments from France on draft monograph on TRITOSULFURON**

**Dear Colleagues,**

**Please find attached our comments on the " Ecotoxicology " section of the draft Assessment Report for the new active substance TRITOSULFURON.**

Yours sincerely,

**Annick Venant**
**P/L'Ingénieur d'Agronomie**
**Sylvie Malézieux**

## Active substance: tritosulfuron

### Ecotoxicology: Comments of France on draft Monograph prepared by Germany

### Ecotoxicology : ECCO 139

| | Comments |
|---|---|
| **Point 2.8.3.6 Effects on terrestrial vertebrates** | The TERst for birds should be based on CL50, not NOEC, leading to TERst value of > 893 and > 3 448, for herbivorous and insectivorous birds, respectively.<br>This does not modify the overall conclusion of the RMS. |
| **Point 2.6.2 Effects on aquatic species** | It is agreed that the *metabolite M01* is a major metabolite in sediment and *L gibba* the most sensitive species. However, M01 is of low toxicity to aquatic organisms, especially to algae. There is a strong evidence of low herbicidal activity, thus of low risk to aquatic plants. Testing on *L gibba* is not necessary.<br><br>The *metabolite M04* is toxic and can reach surface water by run-off or drainage. The Notifier should perform long-term studies on fish (ELS) and daphnids, and assess the risk. |
| **Point 2.6.4 Effects on earthworms and other soil macro-organisms** | It is agreed that long-term data are necessary for metabolites M01, M02 and M03, due to persistance. However, M04 is slightly toxic to earthworms and is not rapidly degraded. It is believed that long-term data are also necessary for this metabolite. |

**PESTICIDES SAFETY DIRECTORATE**
Mallard House, Kings Pool, 3 Peasholme Green, York YO1 7PX, UK
Switchboard: 01904 640500 GTN: 5138 5813
Direct Dial: 01904 455813 Fax: 01904 455722
International: (+44) 1904 455813 International Fax: (+44) 1904 455722
e-mail emma.hedges@psd.defra.gsi.gov.uk

Mr Herbert Koepp
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit
Dienststelle Braunschweig
Messeweg 11 –12 Our ref: ASY 221
38104
Braunschweig Date: 6 May 2003

Dear Mr Koepp,

**EC REVIEW MONOGRAPH FOR TRITOSULFURON**
**RAPPORTEUR:- GERMANY**

**ECCO 139 - MEETING TO DISCUSS ECOTOXICOLOGY**

On behalf of the Pesticides Safety Directorate of the Department for Environment, Food and Rural Affairs, please find attached our comments on the monograph for tritosulfuron. We are submitting these comments for your information as rapporteur and for discussion at ECCO 139 in June 2003.

Yours sincerely

Emma Hedges

Emma Hedges
Approvals Committee Branch

cc: ECCO Team (PSD)

The Pesticides Safety Directorate agrees with the technical evaluation and risk assessment given in the monograph, except in the following areas:

B.9.1.3. Risk assessment for birds

It is stated that a herbivorous bird will consume 40% of its bodyweight/day. How is this figure derived? It is generally accepted that a small bird may forage for insects in a cereal crop. A small bird eats 30% of its bodyweight as dry food/day and this is converted to wet weight by multiplying by a factor of 2.4. Thus a small bird will consume 72% of its bodyweight/day.

Making this assumption, a small bird will take in 1.044 mg a.s./kg bw/day, leading to an acute TER of 1916.

B.9.5.1. Risk assessment for mammals

Mammals may consume contaminated vegetation. It is not stated in the risk assessment what size of mammal is assumed but as the consumption is 25% of bodyweight it appears it is a large mammal. However, as a worst case a small mammal should be considered. A small mammal would have a higher intake, 72% of bodyweight as wet weight of food. This should still lead to an acceptable TER.

A discussion of the risk posed by active substance that contains higher levels of the impurity AMTT is presented. The endpoint from a study using a batch with impurity of 2.45% AMTT, which is mentioned, should be provided and clearly referenced in support of this.

B.9.2. Effects on aquatic organisms

The mortality endpoint for fish is ‘LC50’ rather than ‘EC50’.

The report of the study on *Pseudomonas putida* is more relevant to consideration of effects on sewage treatment processes and should appear in that section.

The risk assessment should include the TERs for the most sensitive of all groups of aquatic organisms in order to make it completely transparent.

There is discussion of the potential risk from the metabolites but no information on their concentrations or persistence is given or referenced. This would be helpful.

The absence of a test on *Lemna*, the most sensitive species, with the metabolite 635M01 is stated to be a data gap. In tests with the parent compound the toxicity to *Lemna* was lower than that to algae by a factor of approximately 10. The toxicity of the metabolite to algae is considerably lower than that of the parent compound. In the first instance it might be possible to draw conclusions on the risk posed by the metabolite based on consideration of relative toxicities and comparison of molecular structures and predicted activities of the active substance and the metabolite.

B.9.8.2. Risk to earthworms

It is stated that the metabolites degrade slowly and that the long term risk they pose must be assessed. Further information is needed to support this assertion and the fate data should be referenced.

B.9.10. Risk assessment to micro-organisms

Studies on the effect of the metabolites on N conversion have been evaluated and are mentioned in the risk assessment. No studies on respiration were submitted but it is not clear if their absence is critical.

Volume 1 Endpoints

In the table for non-target arthropods the percentage of effects on T pyri in the first tier test should be quoted, as this is the value to which the trigger of 30% given in the following column applies. For an LR50 the relevant trigger is a hazard ratio of 2.

Board for the authorisation of pesticides, Stadsbrink 5, NL-6707 AA, Wageningen, P.O. Box 217, phone +31 317 471810, Fax +31 317 471899

To: ECCO-Team BBA en RMS DE
From: CTB
Date: 24 april 2003

Subject: Comments of the Netherlands on monograph tritosulfuron ecotoxicology

## *Volume 1, Level 2*

*2.6.1 Effects on terrestrial vertebrates, p. 40*
Risk assessment should be based on LC50 and NOEC as a daily dose as this is the end point to be used in the risk assessment according to the Guidance document on birds and mammals.

*2.6.3 Effects on bees and other arthropod species, p.41*
Risks to bees considering the systemic properties of tritosulfuron need to be adressed.

## *Volume 1, level 3*
See comments on level 4.

## *Volume 1, level 4*

**Ecotoxicology**
Risk assessment of metabolites AP2 and AP9 which were found in the photochemical degradation study (B.8.4.2) in >10% of TAR is lacking.

Based on effects >30% higher tier studies are needed for T. pyri (43% on mortality, corrected for control level?).
Laboratory study with Pardosa sp. is required.
Repetition of the extended laboratory test with Aphidius is required.

Given the fact that for earthworms TERlt <5 a field study is required.

## *List of end points*

*Effects on terrestrial vertebrates*
LC50 and NOEC for birds should also be reported as daily dose.

*Toxicity exposure ratios for terrestrial vertebrates*
Risk assessment for birds and mammals should be based on LC50 and NOEC as daily dose.

*Toxicity data for aquatic species*
Results for A. flos-aqua from report no: WAT2001-450 were considered not valid and should be deleted.
Results for L. gibba from report WAT2001-463 were considered not valid and should be deleted.

## *Volume 3*

**General**
Summaries are very short compared to the fate and behaviour section. It is not possible to judge the studies based on the information given. Presenting some basic data in tables as was done in the fate and behaviour section gives a much better insight in the study.

**B.9.1 Effects on birds**

Board for the authorisation of pesticides, Stadsbrink 5, NL-6707 AA, Wageningen, P.O. Box 217, phone +31 317 471810, Fax +31 317 471899

*B.9.1.1 Dieatary toxicity, p. 460*
LC50 should also be calculated and reported as daily dose according to the guidance in SANCO/4145/2000 (Guidance document on risk assessment for birds and mammals).

*B.9.1.1 Effects on reproduction, p. 461*
NOEC should also be calculated and reported as daily dose according to the guidance in SANCO/4145/2000.

*B.9.1.5 Risk assessment for birds, p.463*
Risk assessment should be based on LC50 and NOEC values as a daily dose (mg/kg bw/d) as motivated in the guidance in SANCO/4145/2000.

**B.9.2 Effects on aquatic organisms**

*General*
It should be noted that highest tested levels for tritosulfuron of 100 mg/L are above water solubility (38.6 mg/L at pH 7). I cannot conclude from the summaries that homogeneity of the test solutions has been proven.

*Toxicity data, p. 467-468*
Conc. levels(nom.) : 0 ; 50 ; 100 ; 100 ; 100 mg/L
What does three times the conc. level 100 mg/L mean?

*Summary of aquatic toxicity data, p. 479*
Results for A. flos-aqua from report no: WAT2001-450 were considered not valid and should be deleted.
Results for L. gibba from report WAT2001-463 were considered not valid and should be deleted.

**B.9.5 Effects on other terrestrial vertebrates**

*B.9.1.5 Risk assessment for mammals, p.481*
Risk assessment should be based on LC50 and NOEC values as a daily dose (mg/kg bw/d) as motivated in the guidance in SANCO/4145/2000.

**B.9.6 Effects on bees**

*B.9.6.7 Risk assessment for bees, p. 483*
Risks to bees considering the systemic properties of tritosulfuron need to be adressed.

**B.9.10 Effects on soil micro-organisms**

*B.9.8.1 Nitrogen conversion, p. 494-497*
It is not clear from the summaries if the tests are valid with regard to the difference between both controls (<15%). Does the effect in tables B.9.10-1 to 5 refer to absolute levels compared to the control or nitrogen turnover rate compared to the control. In the OECD 216 guideline the latter is the preferred parameter since it is more relevant for the effects on the process.

*B.9.8.2 Carbon conversion, p. 497*
It is not clear from the summaries if the tests are valid with regard to the difference between both controls (<15%). Does the effect in table B.9.10-6 refer to absolute levels compared to the control or carbon conversion rate compared to the control. In the OECD 217 guideline the latter is the preferred parameter since it is more relevant for the effects on the process.

From: Hofkens Sofie [Sofie.Hofkens@health.fgov.be]
Sent: 26 May 2003 14:40
To: 'h.koepp@bba.de'; ECCO (PSD) (E.C.C.O. Account); 'ecco@bba.de'
Cc: Fontier Herman; Hucorne Pierre
Subject: tritosulfuron

Dear all,

Hereby the Belgian comments on the DAR on tritosulfuron concerning ecotoxicology:

1. Birds

Doses should also be expressed in mg a.s./kg bw/day.

2. Aquatic organisms

- From the resume in the DAR (p473), it seems that the long term Daphnia test only lasted for 21h. We suppose that the test lasted for 21 days. The NOEC resulting from this test equals 56 mg/L on p473. On p479 this effects becomes an EC50. In the list of endpoints this is again a NOEC which is probably correct.
- All relevant metabolites should be tested for their toxicity for Lemna gibba.

3. Mammals

Doses should also be expressed in mg a.s./kg bw/day.

4. Other arthropods

If the reduction of the beneficial capacity is calculated for A. rhopalosiphi, this gives 37% which exceeds the trigger of 30%. An extended lab study seems appropriate.

5. Earthworms

Given the DT50-values of the metabolites, long term risk assessment is considered necessary.

6. Other soil non-target macro organisms

Given the DT50-values of the metabolites, long term risk assessment is considered necessary.

7. Other soil non-target micro-organisms

A more solid argumentation for not testing carbon conversion with the metabolites is considered necessary.

Kind regards,

Sofie Hofkens

ir. S. Hofkens

Federale Overheidsdienst Volksgezondheid, Veiligheid van de  Voedselketen en Leefmilieu
DG Dier, Plant en Voeding
Arkadengebouw 5de verdieping
1010     BRUSSEL
Tel 02/210 50 87
Fax 02/210 51 15
www.fytoweb.fgov.be

Service Public Fédéral Santé publique, Sécurité de la Chaîne alimentaire et Environnement
DG Animaux, Végétaux et Alimentation
Quartier Arcades  - 5ème étage
1010     BRUXELLES
tél 02/210.50.87
fax 02/210.51.15
www.phytoweb.fgov.be

**DOCUMENTS ON TRITOSULFURON ASSESSMENT REPORT**

**Section: Overview Meeting (PSD 140)**

**1. List of end points (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| August 2003 | RMS/Germany | tritosulfuron_140_2endpoints_Aug03 |

**2. Comments**

| Date | Supplier | File name |
|---|---|---|
| August 2003 | Germany | tritosulfuron_140_com01_DE |

**3. Comments received but not discussed (because deadline of submission was not met)**

| Date | Supplier | File name |
|---|---|---|
| | | |

**4. Documents tabled at the meeting**

| Date | Supplier | Content | File name |
|---|---|---|---|
| | | | |

**5. Addenda and Evaluation Table (not included in Full Report)**

| Date | Supplier | File name |
|---|---|---|
| August 2003 | RMS/Germany | tritosulfuron_140_3eval_table_0-2_Aug03 |

**BUNDESAMT FÜR VERBRAUCHERSCHUTZ
UND LEBENSMITTELSICHERHEIT**

Geschäftszeichen (bei Antwort bitte angeben)
AP WNL 005157-00/00 BS/Sc

☎ 0531/299 – 34 69
E-Mail: b.schreiber@bba.de

Datum: 14. August 2003

# German comments regarding the inclusion of the active substance tritosulfuron in Annex I of the Directive 91/414/EEC

## ECCO 136 – Comments on the end points (7070/ECCO/PSD/03, 14 March 2003) and evaluation table (10397/2002 rev. 0, 14 March 2003) (German response to the comments of the chair of ECCO 136)

End-point sheet (section on metabolites: Annex IIA, 5.8)

Germany agrees with the chair for ECCO 136 to leave out the comments on the 28-day studies with 635M02 until MS have had the chance to consider the addendum with the details of these studies.

Germany will report on the results concerning the 28-day study with 635M02 in an addendum and the results will be included in the revised end point sheet.

Evaluation table (open point 4.11 (originally 4.9) – on 28-day studies with metabolites)

At present Germany has only received the 28-day study with the metabolite 635M02.

The 28-day study with the metabolite 635M01 is still awaited. The RMS (DE) even does not know whether this study has already been initiated by the notifier.

In the German opinion the requirement for the 28-day study should be included in the open point. The results will be reported in the addendum (as soon as the study is submitted).

Evaluation table (new data requirement 4.2)

The chair of ECCO 136 declares that the LD50 of 635M01 is not low and it is not genotoxic. A requirement of additional new data would have to come from the residues or E-Fate meetings. Such requirements should be discussed at the Overview Meeting and the reasons should be clearly explained.

Germany is of the opinion that the requirement for a 28-day study with the metabolite 635M01 is triggered by the draft working document, Guidance document on the assessment of the toxicological relevance of metabolites in groundwater of active substance regulated under Council Directive 91/414/EEC (SANCO/221/2000, presently rev. 7, 7 March 2002). The submitted studies for the evaluation of the toxicological relevance of the metabolite

635M01 were considered not sufficient to exclude that the 635M01 has toxicological significance.

General remarks

According to the request of the chair for ECCO 136 the RMS will clarify the proposals in respect of the metabolite 635M01 and will describe the results of the 28-day studies with the metabolites 635M01 and 635M02 in an addendum to the DAR and will revise the wording in the end point sheet and in the evaluation table.