CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion regarding the peer review of the pesticide risk assessment of the active substance metamitron

Issued on 29 September 2008

SUMMARY

Metamitron is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

United Kingdom being the designated rapporteur Member State submitted the DAR on metamitron in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 22 August 2007. The peer review was initiated on 24 October 2007 by dispatching the DAR for consultation of the Member States and the sole applicant Makhteshim Agan. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in June – July 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in September 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as herbicide on sugar and fodder beet for the control of annual grasses and broad-leaved weeds as proposed by the notifier. Full details of the GAP can be found in the attached list of endpoints.

[1] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

The representative formulated product for the evaluation was "Goltix SC 700", a suspension concentrate (SC) containing 700 g/l of metamitron.

The specification for the technical material as a whole should be regarded as provisional for the moment.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Adequate methods are available to monitor all compounds given in the respective residue definitions for monitoring for food/feed of plant origin and for environmental matrices.

Mammalian toxicology of metamitron was assessed in a series of investigations. Metamitron is absorbed rapidly and almost completely. It is evenly distributed and has no potential for accumulation. It is rapidly excreted and also quickly and extensively metabolized. Metabolism involves an initial desamination step followed by hydroxylation, oxidation and conjugation reactions. Metamitron is of moderate oral and inhalation, and of very low dermal toxicity. It is neither a skin nor an eye irritant nor a skin sensitizer. Based on the data on acute toxicity a classification as **Xn; R20 "Harmful; Harmful by inhalation"** and **Xn; R22 "Harmful; Harmful if swallowed"** is proposed.

In short term tests with rodents, liver effects (clinical changes and pathology) were predominant. In dogs in addition, also haematological effects were observed. The lowest relevant short-term NOAEL of 3.6 mg/kg bw/d was obtained in a 90-day dog study. Metamitron is not genotoxic. Metamitron was not tumorigenic in chronic studies with rats, mice and dogs. The lowest chronic NOAEL of 3.0 mg/kg bw/d was derived from increased cholesterol levels detected in a 2-year dog study.

In one of two multigeneration studies conducted, reduced corpora lutea and implantations were observed at doses already toxic to the dams. Neither in rats nor in rabbits were specific developmental effects observed. In single dose pharmacological tests metamitron induced behavioural changes in rats. The acceptable daily intake (ADI) was set at 0.03 mg/kg bw/d based on a NOAEL of 3 mg/kg bw/d obtained in a 2-year dog study applying a safety factor of 100. The acceptable operator exposure level (AOEL) was set at 0.036 mg/kg bw/d based on a NOAEL of 3.6 mg/kg bw/d obtained in a 90-day dog study. The Acute Reference Dose (ARfD) was set at 0.1 mg/kg bw based on a maternal NOAEL of 10 mg/kg bw/d obtained in a rat developmental study that was supported by NOAELs obtained in single dose pharmacologic and functional studies in rats. Only when gloves were used when handling the concentrate and when gloves, coverall and sturdy footwear were worn during application of the formulation, operator exposure resulted in a value below the AOEL in the German model (34%). In the UK POEM the AOEL was exceeded in all scenarios. Exposure of an unprotected worker amounted to 73% of the systemic AOEL. Maximum exposure of bystanders accounted for 23% of the AOEL.

The metabolism of metamitron was investigated in sugar beet. Sucrose was the only identified radioactive compound in roots. The experts meeting decided that metabolites found in forage and leaves should not be included in a provisional residue definition for monitoring and risk assessment for root/tuber crops, as their levels were considered not to be significant in the diets of livestock. Therefore the proposed residue definition for monitoring and risk assessment for root/tuber crops is metamitron only. The residue definition is pending the submission of a metabolism study on rotational crops, which was requested by the experts meeting on the basis of the stability of metamitron in soil.

The expert meeting concluded that four residue trials carried out in Northern Europe with acceptable validation data of the analytical methods indicating residues below the LOQ, and in addition trials performed in Southern Europe with residues also below the LOQ, were sufficient to propose a MRL. However, a data gap was formulated for validation data for the method of analysis used in four further residue trials to confirm the validity and completeness of the residue trial data set. Metamitron residues have been shown to be stable under freezing conditions.

As residues found in beet roots and leaves at maturity are below the LOQ, processing studies and metabolism studies in livestock are not required. However, the experts meeting proposed a re-entry period after application of metamitron and EFSA notes that tops should not be fed after thinning or crop failure. These suggestions could be reconsidered after submission of validation data for the method of analysis used in further residue trials.

On the basis of the calculations carried out by the RMS, chronic and acute intake of residues of metamitron after application according to the notified cGAP are not expected to exceed the ADI and ARfD respectively.

In soil under aerobic conditions metamitron exhibits low to moderate persistence forming the major soil metabolite desamino-metamitron[2] (accounting for up to 17.1% of applied radioactivity (AR)), which exhibits moderate persistence. Mineralisation to carbon dioxide of the applied [^{14}C-phenyl]-labelled metamitron accounted for 23.3-57.4% AR after 100-120 days. The formations of unextractable residues were a sink, accounting for 29.5-41.2% AR after 100-120 days. Metamitron exhibits medium to very high mobility in soil. Desamino-metamitron exhibits medium to high mobility in soil. There was no indication that adsorption of either metamitron or desamino-metamitron was pH dependent. There was an unidentified soil metabolite (M3) present in soil that triggers a groundwater exposure assessment. However such an assessment is not available.

Hydrolysis was considered to play a minor role, but photodegradation may be a significant route of degradation of metamitron in aquatic systems particularly close to the surface of natural water bodies where indirect photolysis may be significant due to the presence of photosensitizers.

In natural sediment water systems metamitron exhibited moderate persistence (total system DT_{50} 10.8-11.4 days) degrading to the major metabolite desamino-metamitron (maximum 54% AR in the water phase and 27.5% in the sediment). The terminal metabolite, CO_2, was a minimal sink in the material balance accounting for only 1% AR at the study end. Residues not extracted from sediment

[2] desamino-metamitron: 3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one

accounted for 23-26% AR at study end. The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for metamitron at steps 1-3 for metamitron and up to step 2 for desamino-metamitron. These values are the basis for the risk assessment discussed in this conclusion.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1µg/L was concluded to be low in geoclimatic situations that are represented by the FOCUS groundwater scenarios, except for the FOCUS Piacenza scenario where the limit of 0.1µg/L was exceeded by metamitron (0.002-0.139 µg/L) and desamino-metamitron (0.139-1.440 µg/L).

The first-tier risk assessment for birds resulted in acute and short-term TERs that were above the Annex VI trigger value, except for the acute risk for medium herbivorous birds. The first-tier long-term risk assessment resulted in TERs below the Annex VI trigger value for medium herbivorous and insectivorous birds, respectively, indicating a potential high long-term risk to birds.

The refined risk assessment for herbivorous birds was based on reliable foliar residue decline studies and indicated a low risk from acute exposure. The long-term risk for herbivorous and insectivorous birds was further refined by assessing the risk to skylark, yellowhammer and the yellow wagtail (as "focal species"). The RMS approach included refinements of the dietary consumption (PD) and the proportion of the diet obtained in the treated areas (PT). However, the long-term TERs obtained using the "focal species" approach were below the Annex VI triggers for all three focal species indicating that further refinement of the risk to herbivorous and insectivorous species was required. A less conservative approach was suggested by the applicant to assess the risk to herbivorous birds to estimate a 21 day time weighted average (twa) exposure based on a mean daily exposure level for the time period covering the first (day 1), second (day 6) and third (day12) applications, up to 21days after the first application (= 9 days after last treatment) assuming a DT_{50} of 1.9 days for foliar residues. This approach resulted in a long-term TER for herbivorous birds above the Annex VI trigger value, suggesting a low risk was expected to herbivorous birds.

It was also considered that although a low long-term risk to insectivorous birds had not been demonstrated (long term TER for yellow wagtail = 4.1), a further refinement of the exposure estimate (in a similar way to that undertaken for foliar residues) may enable to conclude on a low risk to insectivorous birds. This could be considered at Member State level for product re-registration following Annex I inclusion.

The acute and long-term risk to mammals was considered to be low. No risk assessment for secondary poisoning was triggered for metamitron since the log $P_{ow} < 3$. A potential high risk to birds and mammals from intake of contaminated water from in-field puddle water was identified. In case of Annex I inclusion, risk mitigation measures or further refinements of the risk assessment should be considered at Member State level.

Metamitron is very toxic to aquatic invertebrates, algae and to higher aquatic plants. The TERs based on FOCUS PEC_{sw} step 3 were above the Annex VI trigger value for all the representative scenarios, except for the R_3 run-off scenario. From the microcosm study a NOAEC of 1120 µg a.s./L was proposed by the applicant. The RMS suggests to apply an assessment factor of 3 for the microcosm NOAEC = 1.12 mg a.s./L. The estimated TER values based on the FOCUS Step 3 PECsw were above the Annex VI trigger values for all the representative scenarios. Based on this it could be concluded that the acute and chronic risk to aquatic organisms from exposure to metamitron and the metabolite desamino-metamitron was low.

The lowest ER_{50} values for the non-target plants were observed for rape (ER_{50} = 54.9 g a.s./ha, pre-emergence exposure) and for lettuce (ER_{50} = 171.6 g a.s./ha, post-emergence exposure). The refined TER values for pre and post-emergence were respectively 0.99 and 4.4 from spray drift at 1 m and 4.9 and 21.5 from spray drift at 5 m. A potential high risk was identified from metamitron exposure to the off-crop non-target plants, therefore risk mitigation measures, similar to a 5 m non-spray buffer zone, were required to identify a low risk.

The risk to bees, non-target arthropods, earthworms, soil macro and micro-organisms and biological methods of sewage treatment was assessed as low.

Key words: metamitron, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Metamitron is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, United Kingdom submitted the report of its initial evaluation of the dossier on metamitron, hereafter referred to as the draft assessment report, received by EFSA on 22 August 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1095/2007 on 26 November 2007 to the Member States and on 24 October 2007 to the main applicant Makhteshim Agan as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in June – July 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in September 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 11c(1) of the amended Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (rev. 1-1 of 14 March 2008)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (rev. 2-1 of 23 September 2008).

Given the importance of the draft assessment report including its addendum (compiled version of September 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Metamitron is the ISO common name for 4-amino-4,5-dihydro-3-methyl-6-phenyl-1,2,4-triazin-5-one (or 4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one) (IUPAC).

Metamitron belongs to the class of triazinone herbicides. It is a selective systemic herbicide, acts through the inhibition of photosynthesis by disturbing the electron transport in susceptible plants. It is predominantly absorbed by the roots, but also by the leaves, and then translocated acropetally and distributed. Metamitron is used pre-emergence and post-emergence in sugar and fodder beet for the control of annual grasses and broad-leaved weeds.

The representative formulated product for the evaluation was "Goltix SC 700", a suspension concentrate (SC) containing 700 g/l of metamitron, registered under different trade names in Europe.

The representative uses evaluated comprise pre- and post-emergence applications with conventional tractor-mounted spraying devices to control annual grasses and broad-leaved weeds in sugar and fodder beets, in Northern Europe, up to growth stage of BBCH 18, up to maximum 3 treatments per year, with application rates of maximum 700 g a.s./ha for the first application, and maximum 1400 g a.s./ha for the succeeding applications, with interval between applications of 6-14 days.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of metamitron is 980 g/kg, which is meeting the requirement of the FAO specification 381/TC/S/F (1992) in the FAO document AGP:CP/313, (Rome, 1994) of minimum 960 g/kg.

It should be mentioned that confidential batch data from three different sources of metamitron have been evaluated by the RMS.
Makhteshim Agan acquired a Bayer source and a Feinchemie Schwebda (FSG) source of metamitron. The 'former Agan' source is no longer used for production.
The experts at PRAPeR Meeting 51(June 2008) agreed with the assessment of the RMS that the technical materials of the FSG source cannot be considered equivalent to the Agan (formerly Bayer) source based on Tier I assessment, due to the presence of two new impurities.
The applicant has proposed generous limits for some of the impurities and was requested to revise the technical specification to remove the impurities not present at significant levels.
Two notifiers, Barclay and the Metamitron Task Force II, submitted information on their sources for equivalence check only. The RMS concluded that the Barclay source can be considered equivalent to the FSG source as there are no new impurities, and the Metamitron Task Force II source was considered not equivalent to the source of metamitron supported by a complete dossier in the review.
The specification for the technical material as a whole should be regarded as provisional for the moment.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of metamitron or the respective formulations. However, the following data gaps were identified:
- information on the commercial availability of starting materials, relevant for Task Force II source
- validation data for the analytical method used in the batch analysis, relevant for the Agan source

The main data regarding the identity of metamitron and its physical and chemical properties are given in appendix 1.

Adequate analytical methods based on HPLC-UV are available for the determination of metamitron in the technical material and in the representative formulations as well as for the determination of the respective impurities in the technical material (HPLC-UV, GC-FID and ICP-OES).
Sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that quality control measurements of the plant protection product are possible.

Metamitron was set as residue definition for monitoring purposes for food/feed of plant origin, air and for the environmental compartments. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed.

An LC-MS/MS analytical method is available to monitor residues of metamitron in plant matrices (sugar beet leaves and roots), with LOQ of 0.05 mg/kg. The German standard multi-residues method DFG S 19 for the determination of residues of metamitron and desamino-metamitron[3] in sugar beet was considered not applicable.
Adequate methods are available to monitor all compounds given in the respective residue definitions in environmental matrices.
Adequate HPLC-DAD methods are available to monitor residues of metamitron and desamino-metamitron in soil with LOQs of 0.05 mg /kg and in drinking and surface water with LOQs 0.1 µg /L.
A GC-NPD method is also available to monitor metamitron in drinking water and surface water with LOQ of 0.1 µg/L.
Residues of metamitron in air can be determined with HPLC-UV with LOQ of 0.019 mg/m^3.

Analytical methods for the determination of residues in body fluids and tissues are not required as metamitron is not classified as toxic or highly toxic.

2. Mammalian toxicology

Metamitron was discussed at a meeting of experts for mammalian toxicology (PRAPeR 54, round 11) in July 2008.
No detailed impurity profiles of the batches used in the different tests are available, therefore no conclusion on the equivalence of the batches used in the toxicological tests with the technical specification of metamitron can be drawn. The experts pointed out that the purity of the batches used in the toxicological tests and that of the technical specification of metamitron is very high.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Metamitron is absorbed rapidly (peak plasma levels are already attained 20-40 minutes after application) and almost completely absorbed based on excretion in urine (34-56%) and bile (55-65%). It is rapidly and evenly distributed between blood and various organs. Although higher tissue residues were found in the liver and the kidneys there is no evidence of a potential for accumulation. Excretion is rapid (more than 90% within 48 hrs via urine and faeces). Metamitron is rapidly and extensively metabolised since only less than 4.3% of metamitron have been recovered in excreta as such. Metabolism involves an initial desamination step followed by hydroxylation, oxidation and conjugation reactions. Major metamitron metabolites found in urine and faeces of rats are

[3] desamino-metamitron: 3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one

metamitron-triazinium acetic acid[4], metamitron-4-hydroxy-desamino[5], metamitron-3-hydroxy-desamino[6] and desamino-metamitron.

2.2. ACUTE TOXICITY

Metamitron is of moderate toxicity by the oral (LD_{50}= 1183 mg/kg bw) and of very low toxicity by the dermal route (LD_{50} > 5000 mg/kg bw). The experts discussed the data on inhalation toxicity and agreed that the relevant LC_{50} in rats was 3.17 mg/L suggesting a moderate inhalation toxicity of the substance. Metamitron was neither irritant to eyes nor to skin nor did it show any skin sensitising potential in a Magnusson & Kligman test with guinea pigs. Based on the data on acute effects a classification of metamitron as **Xn; R20 "Harmful; Harmful by inhalation"** and as **Xn; R22 "Harmful; Harmful if swallowed"** was proposed.

2.3. SHORT TERM TOXICITY

Subchronic effects of metamitron have been assessed in a 28-day and four 90-day dietary studies in rats, a 90-day feeding study in mice, two 90-day and a 1-year oral study in dogs and a 28-day dermal study in rabbits. The lowest relevant NOAELs in the rat and the mouse were set at 18.4 mg/kg bw/d and at 54.8 mg/kg bw/d respectively based on observations of clinical changes indicative of liver damage and liver histopathology in 90-day studies in both species. The relevant NOAEL in dogs was set at 3.6 mg/kg bw/d and was derived from changes in clinical chemistry in a 90-day study. In the second 90-day study and in the 1-year study in dogs also haematological effects were observed. A NOAEL of 50 mg/kg bw/d was set in the rabbit study based on clinical changes.

2.4. GENOTOXICITY

In total eight *in vitro* and five *in vivo* genotoxicity assays have been reported in this section. Taking into account the overall evidence and the absence of relevant findings in the multigeneration study (see section 2.6 Reproductive toxicity), the experts agreed to dismiss the findings of dominant lethality in one assay at high dose as not relevant and concluded that metamitron is not genotoxic.

2.5. LONG TERM TOXICITY

Long term toxicity of metamitron has been assessed in a 2-year dietary study in rats, an 18-month carcinogenicity study in mice and a 2-year dietary study in dogs (that has been reported in section 6.3. "Short term toxicity studies" of the DAR). In neither species tumours have been detected. Systemic NOAELs have been set at 4.9 mg/kg bw/d in the rat based on increased liver weight and histopathology and reduced haematocrit and haemoglobin (indicative of anaemia), at 7.1 mg/kg bw/d in the mouse, derived from increased liver weights and histopathology, and at 3.0 mg/kg bw/d in the dog based on increased cholesterol levels.

[4] Metamitron-triazinium acetic acid: 5-(carboxymethyl)-2-methylpyrido[2,1-*f*][1,2,4]triazin-9-ium-4-olate
[5] Metamitron-4-hydroxy-desamino: 6-(4-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one
[6] Metamitron-3-hydroxy-desamino: 6-(3-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one

2.6. REPRODUCTIVE TOXICITY

In this section of the DAR two two-generation studies, two developmental studies with rats and one with rabbits are reported.

While in the first two-generation study no evidence of reproductive toxicity was observed, in the second investigation reduced numbers of corpora lutea and implantations were seen at the highest dose (2500 ppm) based on which an overall reproductive NOAEL of 97.2 mg/kg bw/d was set. Based on observations of reduced bodyweight in parental animals and in pups in both studies and in addition reduced pup survival in the second study an overall parental and developmental NOAEL of 7.3 mg/kg bw/d was derived.

In the two rat developmental studies identical doses were employed and similarly in both studies, besides reduced body weight and food consumption, no specific effects on development could be detected, leading to a maternal and developmental NOAEL of 10 mg/kg bw/d and 100 mg/kg bw/d respectively in both studies.

In the rabbit the maternal NOAEL was set at 40 mg/kg bw/d based on reduced body weight development in dams. The experts agreed to set the developmental NOAEL at 160 mg/kg bw/d (the highest dose tested) based on the lack of relevant findings. The resorptions observed were dismissed as non relevant because they occurred in animals suffering from a significant weight loss during the treatment period.

2.7. NEUROTOXICITY

No specific studies with metamitron have been submitted. Metamitron does not provide any structural alerts for neurotoxicity. However, in single dose functional and pharmacological tests presented in section 6.8 of the DAR ("Further toxicological studies") some inconclusive evidence for effects on the central nervous system was seen.

2.8. FURTHER STUDIES

Metabolites

In the rat the oral LD_{50} of the metamitron metabolite desamino metamitron was 4325 mg/kg bw, that of metabolites metamitron-4-hydroxy[7] and metamitron-4-hydroxy-desamino was higher than 5000 mg/kg bw. Metabolite 3-methyl-4-amino-6-phenyl-1,2,4-triazine-5-one-oxide (found at levels lower than 3% in kidneys and urine) was positive in a bacterial mutagenicity assay.

EFSA Note: Desamino-metamitron is not only a rat but also a soil and a groundwater metabolite (for groundwater in one of the nine FOCUS scenarios a level of 1.44 µg/L was determined). Only an acute oral toxicity test is available for the metabolite. Its relevance according to guidance document Sanco/221/2000-rev. 10 – final has not been discussed at the meeting of experts.

[7] metamitron-4-hydroxy: 4-amino-6-(4-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one

However, taking into consideration the high amounts of desamino-metamitron detected in plasma, kidneys and liver of rats reported in section B. 6. 1 of the DAR (Absorption, Distribution, Metabolism and Excretion – Toxicokinetics) after application of metamitron, it can be assumed with reasonable confidence that the mammalian toxicity of the metabolite has been assessed also when evaluating the parent compound metamitron.

Pharmacological and functional investigations

A series of single dose functional and pharmacological investigations with rats, mice and dogs are reported. In rats, metamitron did not affect respiration or lung mechanics and did also not adversely impact urine volume, haemoglobin levels or coagulation parameters, but markedly increased renal electrolyte secretion. In another experiment with rats a weak natriuretic effect was confirmed. Metamitron did not affect neuromuscular transmission. Inconclusive results were obtained with regard to effects on intestinal motility. Metamitron did neither induce contractions nor did it influence induced spasms in the ileum of guinea pigs. In mice transient clinical signs (sedation, prone position, ptosis and piloerection) and reduced balance ability were observed. In anaesthetised dogs metamitron increased the blood pressure. Next to decreased body temperature metamitron also caused decreased motility and increased resting time in rats, based on which the experts agreed to set a NOAEL of 10 mg/kg bw.

2.9. MEDICAL DATA

According to the applicant no impairment of health or permanent lesions attributable to metamitron exposure among manufacturing personnel has been reported. In total seven poisoning incidents with metamitron, five of them in combination with other pesticidal substances, are described in the DAR. Overall, none of these cases were considered as serious. The symptoms observed included irritation in the mouth, laboured breathing, pyrexia, cough, emesis, vertigo, low blood pressure and headache.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

Although initially a lower value was proposed by the rapporteur the experts agreed to set an **ADI of 0.03 mg/kg bw/d** based on the NOAEL of 3 mg/kg bw/d obtained in the 2-year dog study applying a safety factor of 100.

The **AOEL was set at 0.036 mg/kg bw/d** based on the NOAEL obtained in a 90-day dog study applying a safety factor of 100.

The experts agreed to set an **ARfD of 0.1 mg/kg bw** and to base it on the maternal NOAEL of 10 mg/kg bw/d obtained in the rat developmental studies applying a safety factor of 100. The value is supported also by the NOAEL (10 mg/kg bw/d) obtained in single dose pharmacological/functional studies in rats.

2.11. Dermal absorption

Dermal absorption of metamitron was assessed in an *in vivo* rat percutaneous absorption assay combined with an *in vitro* dermal absorption test with human and rat skin membranes. The experts agreed that based on the excretion kinetics seen in the *in vivo* study also the residue at the application site had to be included, based on which the value for dermal absorption for the diluted product was increased from 15%, as initially proposed, to 20%. The value for the concentrate, however, remained unchanged at 1% as proposed by the rapporteur.

2.12. Exposure to operators, workers and bystanders

The representative for evaluation formulation is Goltix SC 700 a suspension concentrate that contains 700 g/L of metamitron. It is applied up to three times a year by spraying (tractor mounted, trailed or self-propelled field crop sprayer) on sugar and fodder beet for the control of grass weeds. The maximum application is 1.4 kg a.s./ha and the minimum spray volume is 200 L/ha.

Exposure assessments for operators, workers and bystanders employing the revised dermal absorption value for the spray diluted product (20% was agreed at the meeting of experts) have been provided with an addendum to the DAR.

Operator exposure

Operator exposures to metamitron when using Goltix SC 700 have been assessed using the German model and the UK POEM and are presented in percentages of the systemic AOEL of 0.036 mg/kg bw/d.

German model

Application	No PPE	PPE 1	PPE 2	PPE 3
Tractor mounted, trailed or self-propelled field crop sprayer	482%	455%	372%	34%

PPE 1: Gloves when handling the concentrate; PPE 2: Gloves when handling the concentrate and during application; PPE 3: Gloves when handling the concentrate. Coverall, gloves and sturdy footwear during application.

UK POEM

Application	No PPE	PPE 1	PPE 2
Tractor mounted, trailed or self-propelled field crop sprayer	2875%	2721%	446%

PPE 1: Gloves when handling the concentrate; PPE 2: Gloves when handling the concentrate and during application;

Worker exposure

Worker exposure was assessed according to EUROPOEM. The experts agreed that for the calculations a transfer factor of 2500 cm^2/person/h should be employed instead of the transfer factor of 5000 cm^2/person/h employed in the present calculation. A revised exposure assessment using the new value for dermal absorption and the agreed transfer factor of 2500 cm^2/person/h has been provided in the Addendum 6 to the DAR (September, 2008). This revised calculation predicts a level of exposure for unprotected workers of 73% of the systemic AOEL of 0.036 mg/kg bw/d after an exclusion period of 3 days.

Bystander exposure

No agreed model for assessment of exposure of unprotected bystanders exists. Three alternative estimates using different input parameters and approaches employing the agreed value for dermal absorption have been provided in the Addendum 4 to the DAR resulting in exposure values of 23%, 8% and 8% respectively of the systemic AOEL of 0.036 mg/kg bw/d.

3. Residues

Metamitron was discussed at the PRAPeR experts meeting for residues (PRAPeR 55, round 11) in July 2008.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The nature of the residues in plants following the use of metamitron was studied in sugar beet. [Phenyl-UL-^{14}C-] metamitron was applied at a rate of 1.54 kg a.s./ha each (1.3N) with the last application at BBCH 12-14. TRR were 74 mg/kg in forage sampled 2 days after the last application and 0.11-0.12 mg/kg in beet roots and 0.15-0.19 mg/kg in beet leaves sampled at maturity. 97%, 92% and 73% of the radioactive residues in forage, roots and leaves were extractable. In extracts of forage metamitron was identified as main radioactive component (65 mg/kg), besides desamino-metamitron (2 mg/kg), metamitron-N-glucoside[8] and its sulphate and bis-sulphate (2.4 mg, 1.0 mg/kg and 1.2 mg/kg respectively) and oxime-acid[9] (trace). In roots the only radioactive compound identified was sucrose which accounted for 65.1% of TRR. In leaves metamitron-N-glucoside and its sulphate and bis-sulphate (0.01 mg, 0.01 mg/kg and 0.04 mg/kg respectively) and oxime-acid (<0.01 mg/kg) and sucrose (0.03 mg/kg) were identified.

An additional metabolism study on sugar beet was submitted by the notifier. The RMS stated that the study was not regarded as acceptable and therefore it was not evaluated in the DAR.

[8] metamitron-N-glucoside: N-β-D-glucosyl-4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one
[9] oxime-acid: 2-hydroxyimino-2-phenyl-acetic acid or (2*Z*)-(hydroxyimino)(phenyl)ethanoic acid

The meeting of experts discussed if desamino-metamitron and the metamitron conjugates should be included in the residue definition. Desamino-metamitron was only observed in leaves 2 days after the last application, but not at maturity. The conjugates were not found in roots and their levels were not considered to be significant in the diets of livestock fed with mature leaves. Therefore, the meeting proposed the following residue definition for monitoring and risk assessment for root/tuber crops: metamitron only. It was noted that due to the proportion of metamitron conjugates observed in beet leaves at harvest, the residue definition should be reconsidered for further uses, especially on leafy crops. The residue definition is also pending the submission of a metabolism study on rotational crops which was requested by the experts meeting (see section 3.1.2).

A total of 28 residue trials on sugar beet, 12 carried out in Northern Europe and 16 in Southern Europe were submitted by the notifier to support the notified use of metamitron on sugar and fodder beet in Northern Europe. Only for four of the trials carried out in Northern Europe were acceptable validation data of the analytical methods used submitted. The expert meeting concluded that these trials indicating residues below the LOQ, and in addition trials performed in Southern Europe with residue trials below the LOQ, were sufficient to propose a MRL. However, a data gap was formulated for validation data for the method of analysis used in four further residue trials to confirm the validity and completeness of the residue trial data set. The evaluation of the eco-toxicological section also relied on this study.

No data on the effects of processing on the nature of the residues or on residue levels have been submitted nor are they required.

Storage stability studies show that metamitron is stable in sugar beet leaves and roots for at least 730 days under deep frozen conditions.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

No studies on the metabolism of metamitron in rotational crops have been provided by the notifier, only the findings of ‘preliminary tests’ (up to step 3, following draft guidance document 7524/VI/95 rev.2) which were used to justify the non-submission of data. Information presented in addendum 3 to the DAR (May 2008) show that the only residues in soil available for uptake by rotational crops are metamitron and desamino-metamitron. In case of crop failure, and taking into account the DT_{50} corrected value for 10 °C of 75 days, significant residues are expected to remain in soil up to sowing or planting time. Therefore, the meeting agreed on the need of a rotational crop metabolism study for metamitron.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Intake calculations for domestic animals included in the DAR show that intake of metamitron residues is expected to be <0.1 mg/kg of the total diet. Therefore, the submission of studies on the metabolism, distribution and expression of residue in livestock is not required.

On the basis of the results of four acceptable residue trials (residues in leaves below LOQ for PHI ≥103 days) the experts meeting proposed a re-entry period of 103 days. It was noted that the re-entry period could be reconsidered when the requested validation data for the analytical method used in four further residue trials is available. Withholding periods for animal feeding stuff in the case of thinning or crop failure were not discussed by the experts meeting. EFSA states that, in line with the decision concerning the re-entry period, tops should not be fed after thinning or crop failure. This might also be re-evaluated when the requested validation data are available.

3.3. CONSUMER RISK ASSESSMENT

The PRAPeR 55 toxicology meeting lowered the ADI. The RMS provided updated results for the consumer risk assessment in the list of endpoints. Calculations on the basis of the WHO European diet showed the highest intake for Cluster B (TMDI = 0.09% ADI). Based on the UK model the highest chronic and acute intake occurred for toddlers (9.3% of ADI and 3.9% of ARfD respectively).

3.4. PROPOSED MRLS

Based on data from four residue trials the MRL for sugar beet is proposed at the LOQ (0.05 mg/kg).

4. Environmental fate and behaviour

Metamitron was discussed by the Member State experts for environmental fate and behaviour in the PRAPeR meeting 52 in July 2008 on basis of the Draft Assessment Report (August 2007).

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Soil experiments (5 different soils, OC% 0.9-2.58%, pH 5.8-7.3) were carried out under aerobic conditions in the laboratory (20°C, 40% maximum water holding capacity (MWHC)) in the dark. The formations of residues not extracted were a sink for the applied [^{14}C-phenyl]-labelled metamitron (29.5-41.2% of the applied radioactivity (AR) after 100-120 days). Mineralisation to carbon dioxide of this radiolabel accounted for 23.3-57.4% AR after 100-120 days. The only major (>10% AR) extractable breakdown product present was desamino-metamitron (maximum occurrence 7.5-17.1% AR at 28-30 days). However, in one soil an unidentified minor metabolite (M3) occurred above 5% AR at two consecutive occasions (5.2% AR at day 1 and 5.8% AR at day 2). The behaviour of this compound was considered by the RMS to be transient in nature, but the meeting of experts considered it as a non-transient metabolite since it was found above 5% AR at two consecutive points in time. A data gap was therefore identified by the meeting to address the leaching potential of this degradation product based on worst case assumption.

No anaerobic soil degradation study was available; however anaerobic soil conditions would not be expected for the intended use applied for on sugar and fodder beet. In a laboratory soil photolysis study no new photodegradation products were identified (desamino-metamitron was found at a level < 5% AR, only). The rate of degradation in light exposed moist soil was higher than that in the moist dark control experiment, but the degradation by photolysis was not considered to be a process that significantly influences the dissipation of metamitron in soil.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The rate of degradation of metamitron was estimated from the results of the studies described in 4.1.1 and in 22 additional soils (at 23°C and 40% MWHC or at 20°C and 33 kPa soil moisture, pH 5-7.4). Results from 18 soils out of the 22 were questioned during the peer review as these old, non-guideline, non-GLP experiments (published scientific paper by Allen and Walker, 1987) were not designed for regulatory purposes and suffered from several shortcomings (for discussion see Report of PRAPeR Expert Meeting 52 Sub-group 1 of metamitron and addendum 4 to the DAR for re-evaluation of the data). As the degradation of metamitron in these 18 soils was significantly slower than the degradation observed in the 9 accepted experiments, the meeting of experts from Member States agreed to include these results in the risk assessment as a precaution until more details from these experiments or definite reasons for exclusions will be available. Consequently, a data gap was identified to obtain and evaluate all the relevant raw data of these experiments and consider the relevance of these to the assessment (note: the data were considered in the risk assessment in this conclusion and therefore the data gap only applies for refinement). Single first order (SFO) DT_{50} values were calculated to be 3.4-49.5 days (number of soils considered were 27). After the meeting of experts the RMS normalised these values to FOCUS reference conditions[10] (20°C and pF2 soil moisture content) (see Addendum 4 to the DAR). The range of single first order DT_{50} after normalisation was 2.2-45.5 (geometric mean that is appropriate for use in FOCUS modelling 19.0 days). The normalisation may not be strictly considered as peer-reviewed, however EFSA considers that the method of normalisation applied was in line with the relevant guidelines. The meeting of experts discussed and agreed that there was no evidence of a correlation of degradation of metamitron with pH.

The rate of degradation of the major soil degradation product, desamino-metamitron was estimated from the results of the studies with the parent compound, described in 4.1.1 and in 4 additional soils (at 20°C and 40% MWHC) where desamino-metamitron was applied as test substance. Single first order DT_{50} values were calculated to be 22.8-51.3 days (20°C, 40% MWHC, n=9). After normalisation to FOCUS reference conditions[11] (20°C and pF2 soil moisture content) this range of

[10] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.
[11] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

single first order DT_{50} became 22.8-45.2 (geometric mean that is appropriate for use in FOCUS modelling 30.5 days). No reliable degradation rate was determined for the minor non-transient soil degradation product, M3.

Though not formally triggered, a field dissipation study on four different soils in Germany where a formulation of metamitron was applied was provided. In each trial one spray application onto bare soil at a rate of 7.0 kg a.s./ha was applied. First order DT_{50} for metamitron and desamino-metamitron (by using ModelManager 1.1) were estimated to be in the range 6.6-22.0 days (DT_{90} 22-73.0 days) and 17.0-39.7 days (DT_{90} 56.5-131.9 days), respectively. However, the calculated dissipation rates were considered as uncertain since soil residues were found in the deepest sampled soil layer (15-30 cm for parent and 5-15 cm for desamino-metamitron), therefore not all material may have been recovered. Nevertheless it was discussed and agreed by the experts in the meeting that the appropriate decline value for PECsoil calculation of metamitron was the longest DT_{50} of 22 days from field dissipation experiments. For desamino-metamitron, only the initial PECsoil value was recalculated. Details of the calculations can be found in Addendum 4 to the DAR.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The adsorption/desorption of metamitron was investigated in 19 soils. $K_f$oc values were calculated from 15 soils and varied from 22.4 to 392 mL/g, (median 86.4 mL/g) indicating that metamitron exhibits very high to medium mobility in soil. Freundlich coefficients ranged from 0.66 – 0.95 (median 0.78). The acceptability of the three out of the 15 1/n values, which were less than 0.7 (0.66 or 0.67) was questioned during the peer review. The meeting of experts from the Member States discussed and agreed that the values are acceptable as the experiments, in which they were determined, were reliable. There was no evidence of a correlation of adsorption with pH.

The adsorption/desorption of desamino-metamitron was investigated in four soils. Calculated adsorption $K_f$oc varied from 66-139 mL/g (mean 102.5 mL/g) and the 1/n values ranged from 0.75 – 0.80 (mean 0.78). There was no indication of any relationship between adsorption and any soil characteristic including pH.

No information was available on adsorption/desorption or mobility in soils of the unidentified minor metabolite, M3.

The mobility of metamitron (non-radiolabelled) was assessed in 9 different soil types in non-aged laboratory column leaching studies, where the doses applied to the top of columns exceeded the maximum recommended field application rate. Following the leaching processes (48 hours), metamitron was detected in the leachate in 4 soils at levels between <2% and 9.07%. Desamino-metamitron was detected in the leachate from one soil up to 0.11% of the parent.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The aqueous hydrolysis of metamitron was investigated in 4 studies at different pH values and temperatures. One of these studies (Müller, 2002) was regarded by the peer review as more reliable than the other three studies therefore results only from this study are included in Appendix 1 of this conclusion. Based on the results of this single study performed at 30°C-60°C, metamitron was found to hydrolyse slowly at pH 4 and 7, the hydrolytic half-lives were calculated to be 353.2 and 479.6 days, respectively (results were extrapolated from higher temperatures to 20°C using Arrhenius relationship). The hydrolytic degradation was faster at pH 9 resulting in a DT_{50} of 8.5 days (at 20°C, using Arrhenius relationship). Five major hydrolysis products were formed: unidentified Substance 6 (maximum occurrence 17.7 %AR, pH 4), 3-methyl-6-phenyl-1,2,4,5-tetrazine (maximum occurrence 17.3% AR, pH 7), 2-methyl-5-phenyl-1,3,4-oxadiazole (maximum occurrence 18.6% AR, pH 9), benzonitrile (maximum occurrence 25.2% AR, pH 9), unidentified Substance 4 (maximum occurrence 18.6% AR, pH 9). Hydrolysis was considered to play a minor role in the dissipation of metamitron in water when compared to competing processes such as photolysis, biodegradation and partitioning to sediment, but could be significant in higher pH water bodies.

The aqueous photolysis of metamitron was investigated in natural river water (pH 7) under continuous artificial irradiation (xenon lamp) and in pure water under natural sunlight at latitude 51 °N in two separate studies. In the latter study the photolysis of the major metabolite desamino-metamitron was also investigated as well as in a separate study where continuous artificial irradiation (xenon lamp) was applied. Moreover quantum yield of metamitron and desamino-metamitron was determined. In the natural water study metamitron was found to photolyse rapidly (SFO DT_{50} 1.45 hours). The photolytic half-life of metamitron equated to summer sunlight at 50°N calculated from quantum yield was 0.47 hours. The photolytic degradation of the major metabolite, desamino-metamitron was calculated to be 18 days (SFO). A further polar compound was formed which peaked at 13.5% AR after 45 minutes in pure water and then declined, and was identified as N-acetylbenzoic acid hydrazide[12]. This compound was considered as transient, and on the basis of RMS opinion it is unlikely to be formed under real environmental conditions at significant levels when other competing routes are relevant (e.g. biodegradation or sorption to sediment). Calculated quantum yield of metamitron and desamino-metamitron was 1.62×10^{-2} and 5.78×10^{-5}, respectively. It was concluded by the peer review that photodegradation may be a significant route of degradation of metamitron in aquatic systems, particularly close to the surface of natural water bodies where indirect photolysis may be significant due to the presence of photosensitizers.

A ready biodegradability test (OECD 301D) indicated that metamitron is 'not readily biodegradable' using the criteria defined by the test.

[12] *N*-acetylbenzoic acid hydrazide: *N'*-acetylbenzohydrazide

Information on degradation of metamitron in water sediment systems was available from three different studies; two of them were considered as supporting information only. The relied on water-sediment study (2 systems studied at 20°C in the laboratory, water pH 7.96 and 8.04, sediment pH 7.24 and 7.43) demonstrated metamitron exhibited moderate persistence degrading in the total systems with estimated single first order DT_{50} of 10.8 and 11.4 days (DT_{90} 35.9-37.9 days).
Desamino-metamitron was the only major metabolite which peaked in both the sediment and water phase on day 58 reaching maximum levels of 54% AR in the water phase and 27.5 % in the sediment. The terminal metabolite, CO_2, was a minimal sink in the material balance, accounting for only 1% AR in both systems by the study end. Residues not extracted from sediment accounted for 23-26 % AR at study end. Because the pH of both systems was in alkaline range where contribution of hydrolysis to degradation may be enhanced, a data gap was identified for investigation of degradation of metamitron in acidic water/sediment system(s) to support the aquatic risk assessment for EU regions where acidic surface water bodies occur. This data gap was not considered essential to finalize the EU risk assessment.

FOCUS surface water modelling was evaluated up to step 3 for metamitron and step 2 for the metabolite desamino-metamitron in addendum 5. These calculations, included in addendum 5 and summarised in the list of endpoints, were prepared after the PRAPeR 52 meeting, but based on the input parameters agreed by the peer review.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The applied for representative use of spring applications to sugar beet and fodder bet was simulated using FOCUS PELMO 3.3.2 and FOCUS PEARL 2.2.2 using the following input parameters: metamitron single first order DT_{50} 19.0 days, K_{foc} 86.4 mL/g, 1/n=0.78; desamino-metamitron single first order DT_{50} 30.5 days, formation fraction from metamitron 50%, K_{foc} 102.5 mL/g, 1/n=0.78. Regarding the unidentified minor metabolite (M3) calculations using DT_{50} 2.6 days (calculations based on 4 data only using ModelMaker) and Koc 10 mL/g as input parameters were submitted (formation fraction applied was 5.8% based on the maximum occurrence in soil experiments). Neither the degradation, nor the adsorption data of M3 were regarded as reliable by the peer review. Therefore a data gap was identified for a new calculation using a Koc of zero and an appropriate combination of DT_{50} and formation fraction. After the meeting, during the conclusion writing procedure, the RMS expressed the opinion that the potential ground water contamination by M3 may be regarded as negligible on the basis of expert judgement and the known properties of this metabolite (the assumed short persistency and the chromatographic properties). In the simulations using PELMO, parent metamitron was calculated to be present in leachate leaving the top 1 m soil layer at 80th percentile annual average concentrations of <0.01 µg/L. Desamino-metamitron exceeded 0.1 µg/L at Piacenza FOCUS scenario, only. Using PEARL, both metamitron and desamino-metamitron exceeded the trigger of 0.1 µg/L at Piacenza; however the calculated results for the remaining eight scenarios were below 0.1 µg/L for both compounds. A description of the calculations in more detail can be found in addendum 4 to the DAR, which was not available to the meeting of experts; however the input parameters used in these simulations were the agreed values.

Information on ground water monitoring (from the National Institute of Public Health and Environmental Protection (RIVM) in the Netherlands) indicated that metamitron has potential to reach groundwater under vulnerable soils conditions. Under less vulnerable conditions residues were not found.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of metamitron (7.44×10^{-7} Pa at 25°C) means that metamitron would be classified under the national scheme of The Netherlands as very slightly volatile; indicating losses due to volatilisation might be expected to be minimal. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at 19.8 hours (assuming an atmospheric hydroxyl radical concentration of 5×10^5 radicals cm^{-3}) indicating the proportion of applied metamitron that did volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Metamitron was discussed in the meeting of the experts PRAPeR 53 in July 2008 on the basis of the draft assessment report, Addendum 3 from May 2008 and the Addendum 4 from August 2008. The representative use evaluated is the use as herbicide in sugar and fodder beets (3 applications, the first at 0.7 kg a.s./ha and the second and the third at 1.4 kg a.s./ha with an interval between applications of 6 -14 days).

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000 September 2002; Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The acute LD_{50} and short-term LD_{50} for birds were 1302 mg a.s./kg bw and >904 mg a.s./kg bw/d respectively. The first-tier risk assessment for birds resulted in acute and short-term TERs that were above the Annex VI trigger value, except for the acute risk for medium herbivorous birds TER_A = 9.1. The long-term (reproductive) NOEC was 81.5 mg a.s/kg bw /d. The first-tier long-term risk assessment resulted in TERs values of 1.24 and 1.93 for medium herbivorous and small insectivorous birds, respectively. Therefore, the first tier risk assessment indicates a low risk from acute exposure to insectivorous birds and from the short-term exposure to herbivorous/insectivorous birds. Further refinement is required to identify whether there is a low risk from acute exposure to herbivorous birds and from long-term exposure to herbivorous and insectivorous birds.

The refined risk assessment for herbivorous birds was based on the residue decline studies that were available in the DAR. From these residue studies a DT_{50} value for residues decline on beet leaves of 1.9 days was obtained. Based on this DT_{50}, the multiple application factor could be recalculated as MAF = 1.11, and the revised time weighted average factor f_{twa} was 0.41. The refined acute and long-term TERs values were 14.9 and 3.5 for medium herbivorous birds. The acute risk to birds was identified to be low, however, further assessment of the long-term risk was required.

The long-term risk for herbivorous and insectivorous birds was further refined in the DAR by assessing the risk to skylark, yellowhammer and the yellow wagtail as "focal species". The RMS proposal included refinements of the dietary consumption (PD) and the proportion of the diet obtained in the treated areas (PT). For sugar beet the median 90th percentile PT values were 0.94, 0.88 and 1.0 for the yellowhammer, the skylark and the yellow wagtail, respectively (Finch and Payne 2006). When feeding in freshly treated beet in spring and early summer, skylarks could consume on a dry weight basis 63% seedling, 21% weed seed and 16% invertebrates. For the yellowhammer the consumption was likely to be 80% insects and 20% weed seeds. Yellow wagtail can be assumed to consume 100% insects. The estimated TER_{lt} values were still below the Annex VI trigger value of 5 indicating a further refinement is needed.

The applicant suggested a further refinement for the herbivorous birds, which used a revised estimate of the mean daily exposure in consumed foliage / seeding based on a 21 day time weighted average (twa), calculated for a mean daily exposure level for the time period covering the first (day 1), second (day 6) and third (day12) applications, up to 21 days after the first application (= 9 days after last treatment) assuming a DT_{50} of 1.9 days for foliar residues. The RMS has recalculated an average "long-term" (21 days) foliar exposure level in line with the applicant suggestion. The overall time weighted average exposure level (covering the "long-term" 21 day period) was 21.53 mg a.s./kg (Addendum 3).

Assuming a daily food intake rate per unit body weight (FIR/bw) for medium herbivorous birds of 0.76, the above refined exposure estimate is equivalent to an intake level of 16.36 mg a.s./kg bw /day. If the derived bird reproductive NOEL of 81.5 mg /kg bw /day is compared to this refined exposure estimate, the TER_{lt} is 5.0. The estimated TER_{lt} values considering the refined exposure were above the Annex VI trigger value of 5, indicating that the long-term risk from metamitron exposure to herbivorous birds was assessed as low. The experts at the PRAPeR 53 agreed with the refinement proposed by the RMS in the Addendum 4.

It was also considered that although a 'low' long-term risk to insectivorous birds had not been demonstrated (long term TER for yellow wagtail = 4.1), a further refinement of the exposure estimate (in a similar way to that undertaken for foliar residues) may enable to conclude on a 'low' risk to insectivorous birds. This could be considered at Member State level for product re-registration following Annex I inclusion.

The acute LD_{50} for mammals was 644 mg/kg. The acute TER value in the first tier risk assessment was above the Annex VI trigger of 10, indicating that a low acute risk was expected for mammals.
The relevant end-point for the long- term toxicity to mammals was discussed at the PRAPeR 53. A NOAEL = 97.2 mg a.s./kg bw /d was proposed by the RMS from the multi-generation toxicity study in rats (Eiben 1998). Member State experts decided that at this concentration the percentage of reduction (up to 20%) in the bodyweight was considered as relevant. RMS proposed to use a second multi-generation toxicity study in rats (Suresh 1993) that used the same test material and different tested concentrations, and that could be combined with the previous study to choose a more relevant NOEC for reproduction (Addendum 4). The test concentration ranged from 50 to 2500 ppm. The meeting agreed that at 500 ppm (equivalent to 36.4 mg a.s./kg bw/d) no effects on the key reproductive parameters and no significant reductions in bodyweight were observed. The experts set the overall NOAEL appropriate for the long-term risk assessment to mammals at 36.4 mg a.s./kg bw/day.
The RMS suggests in the Addendum 4, based on the revised NOAEL= 36.4 mg a.s./kg bw/d as well as the refined considerations of foliar residue levels, that the long term risk to herbivorous mammals was considered to be acceptable (TER_{lt} =6.04).

No risk assessment for secondary poisoning was triggered for metamitron since the log $P_{ow} < 3$. A potential high acute risk to birds and mammals from intake of contaminated water from in-field puddles was identified. A data gap for the applicant was set to refine the risk to birds and mammals from the uptake of drinking water in-field puddle.

Based on the available data, the acute and short-term risk to birds and the acute and long-term risk to mammals were identified to be low. A refined bird risk assessment demonstrated a ‘low’ long-term risk to herbivorous species but not to insectivorous species.

5.2. RISK TO AQUATIC ORGANISMS

Based on the available information metamitron was considered to be very toxic to the aquatic organisms. Acute LC_{50}/EC_{50} values for fish, Daphnids and algae were >190, 5.77 and 0.4 mg a.s. /L, respectively. With regard to chronic toxicity, fish were more sensitive than aquatic invertebrates. The NOEC for reproductive effects in fish was 7 mg a.s./L for *Oncorhynchus mykiss*.

Fate experts during the PRAPeR 53 meeting identified a data gap for the applicant to provide a new predicted environmental concentration for all the environmental compartments (soil, ground water, surface water). RMS submitted the new PEC values for all compartments in the Addendum 4. No new TER values were provided with the updated PECsw values. EFSA recalculated the TERs when drafting the conclusions and the list of endpoints was updated accordingly. The outcome of the risk assessment with the new PECsw was not different from the risk assessment presented in the original DAR by the RMS. The new risk assessment is summarised below.

The first tier risk assessment indicated a low acute and chronic risk to fish. However, potential high acute and chronic risks were observed to aquatic invertebrates, algae and aquatic plants. The estimated TER values for Daphnids, algae and aquatic plants, based on the new FOCUS PEC_{sw} step 3 PECsw were above the Annex VI trigger value for all the representative scenarios, except for the R_3 Stream run-off scenario.
A microcosm study (Heimbach F. et al, 1999) was available to refine the risk for invertebrates. The outdoor microcosm study was performed in the Netherlands. No consistent treatment related effects on structural endpoints of phytoplankton (species composition, densities, chlorophyll-A level), periphyton (chlorophyll-A level) and macrophytes (% cover, final biomass, growth of *Myriophyllum spicatumin* in *in-situ* bioassay) were obtained at the highest test concentration. In addition, densities of the major zooplankton groups (Cladocera, Copepoda, Rotifera and Protozo) appear to be unaffected. Only the more pronounced effects on oxygen and pH levels at the higher tested concentration were considered to be ecologically relevant and based on this a NOAEC of 1120 µg a.s./L was proposed by the applicant. RMS suggests that, although the microcosm study included an assessment of the effects of metamitron exposure to a wide range of algae and aquatic invertebrate species, the number of the assessed macrophyte species was limited to three. RMS considered that an assessment factor of 3 should be applied to the microcosm. The estimated TER values based on the FOCUS Step 3 PECsw were above the Annex VI trigger values for all the representative scenarios.

No bioconcentration study with fish is triggered since the log P_{ow} of metamitron is < 3.

The first tier risk assessment indicated that the risk of the metabolite desamino-metamitron to aquatic organisms was assessed to be low.
In conclusion the acute and chronic risk to aquatic organisms from exposure to metamitron and the relevant metabolite desamino-metamitron is considered to be low.

5.3. RISK TO BEES

Acute contact toxicity studies were conducted with metamitron and the formulated Goltix 700 SC showing lower toxicity of the a.s. when formulated (LD_{50} > 100 µg a.s./bee and >200 µg a.s./bee respectively). The acute oral toxicity was tested with metamitron and with Goltix 700 SC, giving a LD_{50} > 97.2 and 123.3 µg a.s./bee, respectively. The oral and contact HQ values were below the Annex VI trigger of 50 indicating a low risk to bees from the representative uses evaluated.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with Goltix 700 SC and the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. The LR_{50} values were estimated to be > 21 L/ha. Laboratory tests with Goltix 700 SC were also conducted with the ground-dwelling predator *Pardosa spp* and with the foliar-dwelling predator *Coccinella septempunctata.*

The in field Hazard Quotient (HQ) values *A. rhopalosiphi* and *T. pyri* were calculated as < 0.22 and < 0.22, respectively. The off-field HQs were < 0.0045 and <0.0045 for *A. rhopalosiphi* and *T. pyri*, respectively. The results of the laboratory toxicity studies with *Pardosa spp* and *C. septempunctata* resulted in no significant adverse effects or effects well within the ESCORT 2 trigger of 50 %.
In conclusion, the risk of metamitron to non-target arthropods was assessed to be low.

5.5. RISK TO EARTHWORMS

The acute toxicity to earthworms was tested with technical metamitron. A 14-d LC_{50} of 914 mg a.s./kg soil was observed in Heimbach F. (1999). The chronic toxicity endpoint was NOEC = 28 mg a.s./kg dry soil. The acute toxicity to earthworms was also tested with the desamino-metamitron, for which a LC_{50} >500 mg a.s./kg dry soil was obtained.
Fate experts during the PRAPeR 53 meeting identified a data dap for the applicant to provide a new predicted environmental concentration for all the environmental compartments (soil, ground water, surface water). The RMS submitted in the Addendum 5 the new PEC values for all compartments.
The outcome of the risk assessment with the new PECsw was not different from the risk assessment presented in the original DAR by the RMS. (EFSA re-estimated the new TER values).
The acute and long-term TER values for metamitron were above the Annex VI trigger values and the acute TER value for the desamino-metamitron was also above the Annex VI trigger value.

In conclusion the acute and long-term risk to earthworms from exposure to metamitron and desamino-metamitron were considered to be low.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

No studies were required for metamitron since the field DT_{90} is 36.8 days in soil. However, since the field DT_{90} for desamino-metamitron was 103.4 days in soil, an assessment of the potential effects on soil macro-organisms from the exposure of this metabolite was conducted.
A 28 days reproduction toxicity study to *Folsomia candida* was conducted with the metabolite desamino-metamitron. A 28 day NOEC = 100 mg/kg dry soil was derived as endpoint. The long-term TER value estimated based on the maximum PECsoil, (TER_{lt} = 161) was above the Annex VI trigger value of 5, indicating that a low risk to soil macro-organisms was expected from the exposure of desamino-metamitron.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects exceeding 25 % on soil respiration and nitrification were observed in tests with the formulated Goltix 700 SC up to a concentration of 19.6 mg a.s./kg dry soil. The tested concentration is 5 times above the maximum PEC in soil, indicating a low risk to soil non-target micro-organisms for the representative uses evaluated.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

The effects of the formulation Goltix 700 SC on vegetative vigour and emergence were investigated in tests with four dicotyledon plant species (rape, carrot, soya bean, lettuce) and with three monocotyledon plant species (oat, onion and maize). The lowest ER_{50} values were observed for rape (pre-emergence exposure ER_{50} = 54.9 g a.s./ha) and for lettuce (post-emergence exposure ER_{50} = 171.6 g a.s./ha). The TERs concluded in the DAR were 0.83 (pre-emergence exposure) and 4.4 (post-emergence exposure) for rape and lettuce respectively based on PECs from spray drift at 1m distance. TERs were 4.1 (pre-emergence exposure) and 21.5 (post-emergence exposure) for rape and lettuce respectively based on the use of a 5 m non-spray buffer zone. Based on these initial results a refinement of the pre-emergence risk was required. The applicant presented in the DAR a procedure to refine the risk based on the re-calculation of the MAF taking into account the four reported field dissipation studies. A mean DT_{50} = 12.23 days was obtained from these studies. When this DT_{50} was used, the MAF value for the 2 applications at an interval of 12 days was 1.51, and at an interval of 6 the MAF was 1.71. These values were then used to derive refined accumulated spray drift exposure estimates at 1 and 5 metres. Using this refined spray drift exposure estimates, the refined TER values were 0.99 and 4.9 from spray drift at 1 m and 5m, respectively.

Furthermore, the applicant also presented a probabilistic risk assessment in the DAR, taking into account the species sensitivity distribution for the 7 plant species tested. The 5th percentile (Hazard Rate HR_5) was 35 g a.s./ha. A comparison of the HR_5 with the refined exposure rate results in a TER of 0.63 and 3.1 from spray drift at 1 and 5 metres, respectively.

In conclusion, a potential high risk was identified for metamitron to non-target plants. Risk mitigation measures, similar to a 5 m non-spray buffer zone, should be taken into account to address the risk.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Technical metamitron did not inhibit the respiration of activated sewage sludge at a concentration of 1000 mg a.s./L. It could be assumed that no undue effects to sewage treatment would occur, if the product is applied according to the GAP. Therefore the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definition for risk assessment: metamitron, desamino-metamitron

Definition for monitoring: metamitron

Water

Ground water

Definition for exposure assessment: metamitron, desamino-metamitron, unidentified minor metabolite (M3)

Definition for monitoring: metamitron (provisional, pending on the final assessment for the unknown minor metabolite (M3))

Surface water

Definition for risk assessment: metamitron, desamino-metamitron
Definition for monitoring: metamitron

Air

Definition for risk assessment: metamitron
Definitions for monitoring: metamitron

Food of plant origin

Definition for risk assessment: metamitron (root / tuber crops only), (provisional, pending on the submission of metabolism studies on rotational crops)
Definition for monitoring: metamitron (root / tuber crops only), (provisional, pending on the submission of metabolism studies on rotational crops)

Food of animal origin

Definition for risk assessment: not required
Definition for monitoring: not required

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
metamitron	Low to moderate persistence Single first order DT_{50} 2.2-45.5 days (20°C, pF2 soil moisture)	A 28-d LC_{50} of 914 mg a.s./kg soil The risk to earthworms is low.
desamino-metamitron	Moderate persistence Single first order DT_{50} 22.8-45.2 days (20°C, pF2 soil moisture)	A LC_{50} >500 mg a.s./kg dry soil The risk to earthworms is low

Ground water

Compound (name and/or code)	**Mobility in soil**	**> 0.1 µg / L 1m depth for the representative uses** (at least one FOCUS scenario or relevant lysimeter)	**Pesticidal activity**	**Toxicological relevance**	**Ecotoxicological activity**
metamitron	Very high to medium mobility $K_f$oc 22.4 to 392 mL/g	Yes 1 scenario from 9 (Pearl)	Yes	Yes	Yes
desamino-metamitron	High to medium mobility $K_f$oc 66 to 139 mL/g	Yes; 1 scenario from 9 (Pearl and Pelmo)	No	No	No
unidentified minor metabolite (M3)	No information	Data GAP - available information is non reliable	No information available	No information available.	No information available

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
metamitron	The 48 h EC50 for *Daphnia magna* = 7.0 mg a.s./L The risk of metamitron to aquatic organisms is low.
desamino-metamitron	The 48 h EC50 for *Daphnia magna* = 745 mg metabolite /L The risk of desamino-metamitron to aquatic organisms is low.

Air

Compound (name and/or code)	Toxicology
Metamitron	Metamitron is of moderate inhalation toxicity (LC_{50} = 3.17 mg/L) A classification as Xn; R20 “Harmful; Harmful by inhalation” is proposed.

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Information on the commercial availability of starting materials, (relevant for Task Force II source, relevant for all representative uses evaluated, date of submission unknown, data gap identified by experts at PRAPeR Meeting 51(June 2008); refer to chapter 1)
- Validation data for the analytical method used in the batch analysis (relevant for the Agan source, for all representative uses evaluated, date of submission unknown, data gap identified by RMS confirmed by the experts at PRAPeR Meeting 51(June 2008); refer to chapter 1)
- Validation data for method of analysis used to determine residues of metamitron and desamino-metamitron in sugar beet (Hoenzelaers, R. and Schulz, J. 1995) in accordance with SANCO/3029/99 rev.4 (relevant for all representative uses evaluated; data gap identified by PRAPeR 55 meeting (July 2008); date of submission: September, October 2008; refer to chapter 3)
- Metabolism study on rotational crops (relevant for all representative uses evaluated; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3)
- Investigation of degradation of metamitron in acidic water/sediment system(s) (relevant for uses evaluated in areas with acidic surface waters; not essential for EU risk assessment; data gap identified by PRAPeR 52 meeting (July 2008); date of submission unknown; refer to chapter 4.2.1)
- Obtain and evaluate the relevant raw data of the study by Allen and Walker, 1987 and consider the relevance of these data to the assessment (relevant for all representative uses evaluated; data gap identified by PRAPeR 52 meeting (July 2008); date of submission unknown; refer to chapter 4.1.2)
- A new calculation of the leaching potential (FOCUS PECgw) of the unidentified minor metabolite (M3) using a Koc of zero and an appropriate combination of DT_{50} and formation fraction (relevant for all representative uses evaluated; data gap identified by PRAPeR 52 meeting (July 2008); date of submission unknown; refer to chapter 4.1.1 and 4.2.2)
- A data gap was identified for further refinement of the long term risk to insectivorous birds (relevant for all representative uses evaluated; data gap identified in the DAR ; submission date proposed by the notifier: unknown ; data gap was identified by the RMS in the DAR; refer to point 5.1)
- The risk to birds and mammals from the uptake of drinking water in-field puddle water should be refined. (relevant for all representative uses evaluated; data gap identified in the DAR ; submission date proposed by the notifier: unknown ; refer to point 5.1)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprise pre- and post-emergence applications with conventional tractor-mounted spraying devices to control annual grasses and broad-leaved weeds in sugar and fodder beet, in Northern Europe, up to growth stage of BBCH 18, up to maximum 3 treatments per year, with application rates of maximum 700 g a.s./ha for the first application, and maximum 1400 g a.s./ha for the succeeding applications, with an interval between applications of 6-14 days.

The representative formulated product for the evaluation was "Goltix SC 700", a suspension concentrate (SC) containing 700 g/l of metamitron, registered under different trade names in Europe.

The specification for the technical material as a whole should be regarded as provisional for the moment.

Adequate analytical methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant origin and environmental matrices. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

Metamitron is absorbed rapidly and almost completely. It is evenly distributed and has no potential for accumulation. It is rapidly excreted and also quickly and extensively metabolized. Metabolism involves an initial desamination step followed by hydroxylation, oxidation and conjugation reactions. Metamitron is of moderate oral and inhalation, and of very low dermal toxicity. It is neither a skin nor an eye irritant nor a skin sensitizer. Based on the data on acute toxicity a classification as **Xn; R20 "Harmful; Harmful by inhalation"** and **Xn; R22 "Harmful; Harmful if swallowed"** is proposed.

In short term tests with rodents, liver effects (clinical changes and pathology) were predominant. In dogs in addition, also haematological effects were observed. The lowest relevant short-term NOAEL of 3.6 mg/kg bw/d was obtained in a 90-day dog study. Metamitron is not genotoxic. Metamitron was not tumourigenic in chronic studies with rats and mice and dogs. The lowest chronic NOAEL of 3.0 mg/kg bw/d was derived from increased cholesterol levels detected in a 2-year dog study.

In one of two multigeneration studies conducted, reduced corpora lutea and implantations were observed at doses already toxic to the dams. Neither in rats nor in rabbits were specific developmental effects observed. In single dose pharmacological tests metamitron induced behavioural changes in rats.

The acceptable daily intake (ADI) was set at 0.03 mg/kg bw/d based on a NOAEL of 3 mg/kg bw/d obtained in a 2-year dog study applying a safety factor of 100. The acceptable operator exposure level (AOEL) was set at 0.036 mg/kg bw/d based on a NOAEL of 3.6 mg/kg bw/d obtained in a 90-day dog study. The ARfD was set at 0.1 mg/kg bw based on a maternal NOAEL of 10 mg/kg bw/d obtained in a rat developmental study that was supported by NOAELs obtained in single dose pharmacologic and functional studies in rats. Only when gloves were used when handling the concentrate and when gloves, coverall and sturdy footwear were worn during application of the formulation, operator exposure resulted in a value below the AOEL in the German model (34%). In the UK POEM the AOEL was exceeded in all scenarios. Exposure of an unprotected worker amounted to 73% of the systemic AOEL. Maximum exposure of bystanders accounted for 23% of the AOEL.

The metabolism of metamitron was investigated in sugar beet. Sucrose was the only identified radioactive compound in roots. The experts meeting decided that metabolites found in forage and leaves should not be included in a provisional residue definition for monitoring and risk assessment for root/tuber crops, as their levels were considered not to be significant in the diets of livestock. Therefore the proposed residue definition for monitoring and risk assessment for root/tuber crops is metamitron only. The residue definition is pending the submission of a metabolism study on rotational crops which was requested by the experts meeting on the basis of the stability of metamitron in soil.

The expert meeting concluded that four residue trials carried out in Northern Europe with acceptable validation data of the analytical methods indicating residues below the LOQ, and in addition trials performed in Southern Europe with residues also below the LOQ, were sufficient to propose a MRL. However, a data gap was formulated for validation data for the method of analysis used in four further residue trials to confirm the validity and completeness of the residue trial data set. Metamitron residues have been shown to be stable under freezing conditions.

As residues found in beet roots and leaves at maturity are below the LOQ, processing studies and metabolism studies in livestock are not required. However, the experts meeting proposed a re-entry period after application of metamitron and EFSA notes that tops should not be fed after thinning or crop failure. These suggestions could be reconsidered after submission of validation data for the method of analysis used in further residue trials.

On the basis of the calculations carried out by the RMS, chronic and acute intake of residues of metamitron after application according to the notified cGAP are not expected to exceed the ADI and ARfD respectively.

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level with the exception that further data are necessary to address the groundwater exposure potential of the unidentified metabolite M3. For the applied for intended uses, the potential for groundwater exposure by the active substance metamitron and the metabolite desamino-metamitron above the parametric drinking water limit of 0.1 µg/L, is low. However, for both metamitron and desamino-metamitron, in geoclimatic regions represented by Piacenza FOCUS groundwater scenarios, contamination of groundwater above the 0.1 µg/L limit cannot be excluded.

After a refined process, the acute, short-term and long-term risk of metamitron to herbivorous birds and the acute and long-term risk to mammals were considered to be low. The acute and short-term risk to insectivorous birds was considered to be low but a low long-term risk to insectivorous birds had not been demonstrated. No risk assessment for secondary poisoning was triggered for metamitron since the log $P_{ow} < 3$. A potential high risk to birds and mammals from intake of contaminated water from in-field puddle water was identified. Metamitron is very toxic to aquatic invertebrates, algae and to higher aquatic plants. The TERs based on FOCUS PEC_{sw} step 3 were above the Annex VI trigger value for all the representative scenarios, except for the R_3 run-off scenario. Based on the results of the microcosm study a NOAEC of 1120 µg a.s./L was proposed by the applicant. The RMS suggests applying an uncertainty factor of 3 to the microcosm NOAEC. The estimated TER values based on the FOCUS Step 3 PECsw were above the Annex VI trigger values for all the representative scenarios. Based on this it could be concluded that the acute and chronic risk of metamitron and of desamino-metamitron to aquatic organisms were low.
The lowest ER_{50} values for the non-target plants were observed for rape (ER_{50} = 54.9 g a.s./ha, pre-emergence exposure) and for lettuce (ER_{50} = 171.6 g a.s./ha, post-emergence exposure). The refined TER values for pre and post-emergence were respectively 0.99 and 4.4 from spray drift at 1 m and 4.9 and 21.5 from spray drift at 5 m. A potential high risk was identified from metamitron exposure to the off-crop non-target plants, therefore risk mitigation measures, similar to a 5 m non-spray buffer zone, were required to identify a low risk.
The risk to bees, non-target arthropods, earthworms, soil macro and micro-organisms and biological methods of sewage treatment was assessed as low.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- Personal protective equipment is needed for operators (refer to point 2.12).
- For use beyond root crops (for example for leafy crops) a further assessment would be required (refer to section 3.1).
- Re-entry period of 103 days for livestock after application of metamitron on sugar beet (refer to point 3.2).
- Sugar beet tops should not be fed after thinning or crop failure (refer to point 3.2).
- A 5 m non-spray buffer zone to protect the non-target plants or other appropriate risk mitigation measures (refer to point 5.8).

Critical areas of concern

- Residue definition for food of plant origin pending outstanding rotational crop study.
- The potential groundwater contamination by the unknown minor soil metabolite, M3 can not be finalised.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

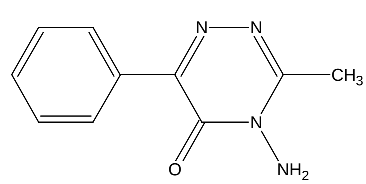
(Abbreviations used in this list are explained in appendix 2)

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	metamitron
Function (*e.g.* fungicide)	herbicide

Rapporteur Member State	United Kingdom
Co-rapporteur Member State	—

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	4-amino-4,5-dihydro-3-methyl-6-phenyl-1,2,4-triazin-5-one
Chemical name (CA) ‡	4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one
CIPAC No ‡	381
CAS No ‡	41394-05-2
EC No (EINECS or ELINCS) ‡	255-349-3 (EINECS)
FAO Specification (including year of publication) ‡	FAO specification 381/TC/S/F (1992) in FAO document AGP:CP/313, Rom, 1994. Minimum purity 960 g/kg Water maximum content 5 g/kg
Minimum purity of the active substance as manufactured ‡	980 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{10}H_{10}N_4O$
Molecular mass ‡	202.2 g/mol
Structural formula ‡	

Appendix 1 – list of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	166 °C (99.8%)
Boiling point (state purity) ‡	None observed between melting and decomposition
Temperature of decomposition (state purity)	250 °C (99.4%)
Appearance (state purity) ‡	Yellow to beige crystalline powder (98-99.4%)
Vapour pressure (state temperature, state purity) ‡	7.44×10^{-7} Pa at 25°C (99.9%)
Henry's law constant ‡	8.95×10^{-8} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	1.77 g/L at 25 °C (pH 5) (99.8%)
	1.68 g/L at 25 °C (pH 7) (99.8%)
	Solutions at pH 9 not stable
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20°C in g/L (99.4%) n-Heptane < 0.1 Xylene 2 Dichloromethane 33 2-Propanol 18 1-Octanol 6 Polyethylene glycol 71 Acetone 37 Ethylacetate 20 Acetonitrile 35 Dimethyl sulphoxide > 250
Surface tension ‡ (state concentration and temperature, state purity)	68 mN/m at 20°C (1 g/L) (99.4%)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 0.85 at 21 °C (not pH dependent) (99.8%)
Dissociation constant (state purity) ‡	Molecular structure precludes dissociation
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Methanol solution: λ_{max} (nm); ε ($L.mol^{-1}.cm^{-1}$) 311.1 11789 Purity of batch and pH of solution not specified

Appendix 1 – list of endpoints

Flammability ‡ (state purity)	Not highly flammable (99.4%) No self ignition below 400 °C (99.4%)
Explosive properties ‡ (state purity)	Not explosive (99.4%)
Oxidising properties ‡ (state purity)	Not oxidising (99.4%)

Appendix 1 – list of endpoints

Summary of representative uses evaluated (metamitron)*

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 as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	g as/hL min max	water L/ha min max	g as/ha min max		
Sugar and fodder beet	UK	Goltix SC 700	F	Grass weeds, particularly annual meadow grass, and broadleaved weeds	SC	700 g/L	Spraying	1st application: pre- or post-emergence (BBCH 10) 2nd application: post-emergence 3rd application: post-emergence (latest BBCH of crop 18)	3	6 – 14 days	175 – 350 350 – 700 350 – 700	200 – 400 200 – 400 200 – 400	700 1400 1400	Covered by the time between the last application and harvest	

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse 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. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(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) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

Appendix 1 – list of endpoints

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC/GC-FID/ICP-OES
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Metamitron (root / tuber crops only), (provisional, pending on the submission of metabolism studies on rotational crops)
Food of animal origin		Not required
Soil		Metamitron
Water	surface	Metamitron
	drinking/ground	Metamitron (provisional, pending on the toxicological profile of desamino-metamitron and on the final assessment for the unknown minor metabolite)
Air		Metamitron

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Metamitron: LC-MS/MS (LOQ = 0.05 mg/kg for sugar beet leaves and roots for both metamitron and desamino-metamitron)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required
Soil (analytical technique and LOQ)	Metamitron and desamino-metamitron: HPLC-DAD (LOQ = 0.05 mg/kg for both metamitron and desamino-metamitron))

Appendix 1 – list of endpoints

Water (analytical technique and LOQ)	Metamitron and desamino-metamitron: HPLC-DAD (LOQ = 0.1 µg/L for drinking and surface water) (for both metamitron and desamino-metamitron) Metamitron: GC-NPD (LOQ = 0.1 µg/L for drinking and surface water)
Air (analytical technique and LOQ)	Metamitron: HPLC – UV (LOQ = 0.019 mg/m^3)
Body fluids and tissues (analytical technique and LOQ)	Not required

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	None

Appendix 1 – list of endpoints

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Rapidly (peak plasma levels are attained 20-40 minutes after a low dose and slightly higher 1-8 h after a high dose.) and almost completely absorbed (91-105% in bile cannulation studies) 34-56% in urine and 55-65% in bile
Distribution ‡	Rapidly distributed evenly between blood and various organs, with the highest concentrations in liver and kidneys
Potential for accumulation ‡	No evidence of any tissue accumulation
Rate and extent of excretion ‡	Rapid > 90% over 48 hours
Metabolism in animals ‡	Metamitron is extensively and rapidly metabolised with a fast initial desamination, followed by several hydroxylation, conjugation and oxidation reactions; only small amounts of Metamitron (< 4.3 %) is recovered in excreta. Major metabolites in urine and faeces were Metamitron-triazinium-acetic-acid, Metamitron-4-hydroxy-desamino, Metamitron-3-hydroxy-desamino and Metamitron-desamino;
Toxicologically relevant compounds ‡ (animals and plants)	Metamitron
Toxicologically relevant compounds ‡ (environment)	Metamitron

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1183 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 5000mg/kg bw	
Rat LC_{50} inhalation ‡	3.17 mg/L (4 hours, nose only)	**R20**
Skin irritation ‡	Not irritating to skin	
Eye irritation ‡	Not irritating to eyes	
Skin sensitisation ‡	Not sensitising to skin (M&K)	

Appendix 1 – list of endpoints

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Primarily hepatotoxicity and haematological effects	
Relevant oral NOAEL ‡	Dogs: 90-day 3.6 mg/kg bw/day Rats: 90-day 18.4 mg/kg bw/day Mouse: 54.8 mg/kg bw/day	
Relevant dermal NOAEL ‡	50 mg/kg bw/day in 28-day dermal toxicity study in rabbits (5 days/ week)	
Relevant inhalation NOAEL ‡	No data	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Overall, not genotoxic in a range of in vitro and in vivo genotoxicity studies.	

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

Target/critical effect ‡	Rat and mouse: Hepatotoxicity and haematological effects suggestive of anaemia Dog: increased cholesterol	
Relevant NOAEL ‡	Dog: 104 weeks 3.0 mg/kg bw/day Rat: 2-year 4.9 mg/kg bw/day Mouse: 18-month 7.1 mg/kg bw/day	
Carcinogenicity ‡	Not carcinogenic in rats and mice	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: reduced bw Reproduction: reduced number of corpora lutea and implantations Offspring: reduced survival and bw	
Relevant parental NOAEL ‡	7.3 mg/kg bw/day	
Relevant reproductive NOAEL ‡	97.2 mg/kg bw/day	
Relevant offspring NOAEL ‡	7.3 mg/kg bw/day	

Appendix 1 – list of endpoints

Developmental toxicity

Developmental target / critical effect ‡	Rat: Maternal: reduced bw and food consumption Developmental: no effects Rabbit: Maternal: reduced bw and food consumption Developmental: no effects	
Relevant maternal NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 40 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 100 mg/kg bw/day Rabbit: 160 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡ Repeated neurotoxicity ‡ Delayed neurotoxicity ‡	Some inconclusive indications in investigative work. NOAEL: 10 mg/kg day, no specific neurotoxicity study performed.	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	A number of effects was seen in a series of functional and pharmacological investigations were carried out with Metamitron. The NOAEL was 10 mg/kg bw.
Studies performed on metabolites or impurities ‡	Desamino-metamitron: acute oral LD50 = 4325 mg/kg bw. Metamitron-4-hydroxy: acute oral LD50 > 5000 mg/kg bw. Metamitron-4-hydroxy-desamino: acute oral LD50 > 5000 mg/kg bw 3-methyl-4-amino-6-phenyl-1,2,4-triazine-5-one-oxide: positive in abacterial reverse mutation test.

Appendix 1 – list of endpoints

Medical data ‡ (Annex IIA, point 5.9)

	Reports on clinical cases, poisoning incidents, manufacturing plant employees and epidemiological investigations were provided. These do not indicate any specific issues arising from the use of Metamitron

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw/day	2 year dietary study in dogs	X100
AOEL ‡	0.036 mg/kg bw/day	90-day oral toxicity study in dogs	X100
ARfD ‡	0.1 mg/kg bw	Maternal effects in rat developmental study supported by single dose pharmacological and functional studies in rats	X100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Goltix SC 700)	1% for the concentrate and 20% for the spray solution based on *in vivo* and *in vitro* data

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Operator exposure estimates using the German model predict that the use of 'Goltix SC 700' through tractor-mounted or trailed field crop sprayers will result in a level of systemic exposure to metamitron for an operator wearing gloves when handling the concentrate and coveralls and gloves and sturdy footwear during application equivalent to 34% of the AOEL of 0.036 mg/kg bw/day proposed in this evaluation. The corresponding UK POEM estimates predict a level of systemic exposure for an operator wearing gloves when handling the concentrate and when handling contaminated surfaces during application equivalent to 446% of the AOEL.

Appendix 1 – list of endpoints

Workers	Worker exposure estimates using the EUROPOEM re-entry model and residue decline data predict a level of systemic exposure to metamitron for an unprotected worker inspecting crops treated with 'Goltix SC 700' equivalent to 73% of the proposed AOEL after an exclusion period of 3 days.
Bystanders	Worst case estimates of bystander exposure to metamitron vapour based on published surrogate data, predict a level of systemic exposure by this route equivalent to 23% of the AOEL. Estimates of bystander exposure to spray drift, based on a simulated bystander exposure study for field crop sprayers, predict a level of systemic exposure to metamitron for an unprotected bystander equivalent to 8% of the AOEL. Estimates based on published spray drift deposition values and published EPA residential exposure data, predict a level of systemic exposure to metamitron for children in areas contaminated by spray drift fallout equivalent to 8% of the AOEL.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Metamitron	Harmful, R20/22 Harmful by inhalation and if swallowed

Appendix 1 – list of endpoints

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

Plant groups covered	Root vegetables (sugar beet roots)
Rotational crops	No studies have been submitted. Rotational crop metabolism studies are required.
Metabolism in rotational crops similar to metabolism in primary crops?	No studies have been submitted on the metabolism in rotational crops. These studies are required.
Processed commodities	No data submitted or required
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No data submitted or required
Plant residue definition for monitoring	Metamitron (root /tuber crops only) (a)
Plant residue definition for risk assessment	Metamitron (root /tuber crops only) (a)
Conversion factor (monitoring to risk assessment)	None

(a) Provisional: pending submission of metabolism studies on rotational crops.

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

Animals covered	No data submitted or required.
Time needed to reach a plateau concentration in milk and eggs	No data available – not required
Animal residue definition for monitoring	No data available – not required
Animal residue definition for risk assessment	No data available – not required
Conversion factor (monitoring to risk assessment)	No data available – not required
Metabolism in rat and ruminant similar (yes/no)	No data available – not required
Fat soluble residue: (yes/no)	No data available – not required

Appendix 1 – list of endpoints

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

	No data have been submitted by the notifier on the metabolism of metamitron in rotational crops. The findings of ‘preliminary tests’ (up to Step 3, according to Lundehn guideline 7524/VI/95 Rev 2 – Appendix C) were provided. However, these data are not sufficient to negate the need for rotational crop metabolism studies to support the use in all MS. Depending upon the results of rotational crop metabolism studies, rotational crop residue trials maybe required.

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

	Residues of metamitron and desamino-metamitron in sugar beet leaves and roots were stable for up to 730 days of freezer storage.

Appendix 1 – list of endpoints

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	No data available – not required	No data available – not required	No data available – not required
Liver	No data available – not required	No data available – not required	No data available – not required
Kidney	No data available – not required	No data available – not required	No data available – not required
Fat	No data available – not required	No data available – not required	No data available – not required
Milk	No data available – not required		
Eggs		No data available – not required	

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Sugar beet	Northern	4 x < 0.05 mg/kg	To prove validity of 4 further residue trials: Validation data required for the method of analysis used in study Hoenzelaers, R. and Schulz, J. (1995).	0.05	0.05	0.05

(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 representative use
(c) Highest residue

Appendix 1 – list of endpoints

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

ADI	0.03 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	Highest intake occurred for cluster B: 0.09 % of the ADI.
TMDI (% ADI) according to national (to be specified) diets	Based on the UK model the highest intake occurred for toddlers: 9.3% of the ADI
IEDI (WHO European Diet) (% ADI)	Not relevant
NEDI (specify diet) (% ADI)	Not relevant
Factors included in IEDI and NEDI	-
ARfD	0.1 mg/kg bw
IESTI (% ARfD)	Refer to NESTI (UK) – see below
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Based on UK model the highest intake occurred for toddlers: 3.9 % of the ARfD.
Factors included in IESTI and NESTI	Variability factor = 1

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Not relevant as residues were <0.1 mg/kg in the harvestable crop				

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

Sugar beet	0.05 mg/kg*

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Appendix 1 – list of endpoints

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

Mineralization after 100 days ‡	*23.3-57.4* % after *100-120* d, [^{14}C-phenyl]-label (n[13]= *5*)
Non-extractable residues after 100 days ‡	29.5-*41.2* % after *100-120* d, [^{14}C-phenyl]-label (n= *5*)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	Desamino-metamitron – max. 7.5 – 17.1 % at 28 – 30 d (n= 5) Unidentified metabolite, code: M3 (minor) - 5.2% and 5.8% at day 1 and day 2

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

Anaerobic degradation ‡	Argued case therefore no data submitted
Soil photolysis ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Desamino-metamitron – *4.7* % at *21* d continuous exposure (80.07 W/m^2, 300-400 nm)(n= 1) [^{14}C-phenyl] label

[13] n corresponds to the number of soils.

Appendix 1 – list of endpoints

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

Laboratory studies ‡

Parent	Aerobic conditions						
Study reference	Soil type	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Gilges 2002	Sandy loam[1]	6.3	20 °C / 40 %	15.7 /52.2	12.5	0.977	SFO
Sneikus 2002	Silt[1]	6.7	20 °C / 40 %	26.7 / 88.7	25.5	0.919	SFO
Sneikus & Brumhard , 2002	Loamy sand[1]	6.2	20 °C / 40 %	21.1 / 70.1	21.1	0.988	SFO
	Silt loam[1]	7.3	20 °C / 40 %	3.4 / 11.3	2.2	0.982	SFO
Fischer, H., 1994 & amendment 1994	Loamy sand[1]	5.8	20 °C / 40 %	34.2 / 113.6	34.2	0.983	SFO
Schneider, E., 1992	Sand[2]	5.5	23 °C / 40 %	7.1 / 23.6	8.9	0.995	SFO
	Sandy loam[2]	5.5	23 °C / 40 %	8.4 / 27.9	8.5	0.955	SFO
	Loamy sand[2]	5.54	23 °C / 40 %	11.0 / 36.5	13.8	0.989	SFO
	Silt loam	6.2	23 °C / 40 %	7.4 / 24.6	8.9	0.915	SFO
Allen and Walker 1987	clay loam[2]	6.8	20°C / 33kPa*	49.5**	44.5	0.979	1st order linear regression
	clay[2]	7.2	20°C / 33kPa*	34.7**	22.6	0.995	1st order linear regression
	clay loam[2]	6.0	20°C / 33kPa*	25.7**	23.7	0.961	1st order linear regression
	clay[2]	7.0	20°C / 33kPa*	36.5**	25.0	0.988	1st order linear regression
	sandy clay loam[2]	7.3	20°C / 33kPa*	10.7**	8.2	0.950	1st order linear regression

Appendix 1 – list of endpoints

	sandy clay loam[2]	7.4	20°C / 33kPa*	16.5**	15.4	0.987	1st order linear regression
	clay loam[2]	7.3	20°C / 33kPa*	23.9**	20.8	0.999	1st order linear regression
	sandy clay loam[2]	6.5	20°C / 33kPa*	27.7**	27.7	0.997	1st order linear regression
	sandy clay loam[2]	6.6	20°C / 33kPa*	24.8**	21.5	0.991	1st order linear regression
	clay loam[2]	6.8	20°C / 33kPa*	49.5**	44.4	0.961	1st order linear regression
	silty clay loam[2]	5.0	20°C / 33kPa*	40.8**	36.9	0.990	1st order linear regression
	sandy loam[2]	6.4	20°C / 33kPa*	20.4**	20.4	0.957	1st order linear regression
	sandy clay loam[2]	6.4	20°C / 33kPa*	23.9**	23.9	0.961	1st order linear regression
	clay loam[2]	6.4	20°C / 33kPa*	43.3**	33.0	0.979	1st order linear regression
	clay[2]	6.8	20°C / 33kPa*	40.8**	28.7	0.967	1st order linear regression
	sandy clay loam[2]	6.6	20°C / 33kPa*	28.9**	28.9	0.946	1st order linear regression
	sandy loam[2]	6.3	20°C / 33kPa*	25.7**	16.4	0.972	1st order linear regression
	sandy clay loam[2]	6.6	20°C / 33kPa*	21.0**	21.0	0.987	1st order linear regression
Geometric mean/median					**19.0/21.5**		

*-actual moisture in study
** - DT50 only

Appendix 1 – list of endpoints

[1] according to USDA soil classification
[2] according to UK soil classification

Desamino-metamitron	Aerobic conditions							
Soil type	X	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam[2]		6.3	20 °C / 40 %	37.2 / 123.6	0.2	29.7	0.986	SFO
Silt[2]		6.7	20 °C / 40 %	39.3 / 130.6	0.5	37.5	0.955	SFO
Loamy sand[2]		6.2	20 °C / 40 %	30.7 / 102.0	0.2	30.7	0.992	SFO
Silt loam[2]		7.3	20 °C / 40 %	51.3 / 170.4	0.1	33.3	0.981	SFO
Loamy sand[2]		5.8	20 °C / 40 %	24.7 / 82.1	0.4	24.7	0.951	SFO
Sand[2]		6	20 °C / 40 %	46.3 / 153.7	na	45.2	0.9699	SFO
Loamy sand[2]		6.1	20 °C / 40 %	22.8 / 75.8	na	22.8	0.8515	SFO
Sandy loam[2]		6.6	20 °C / 40 %	28.4 / 94.2	na	23.8	0.9567	SFO
Sandy loam[1]		6.4	20 °C / 40 %	40.9 / 135.9	na	32.6	0.952	SFO
Geometric mean/median						30.5/30.7		

na: not applicable
[1] according to USDA soil classification
[2] according to UK soil classification

Appendix 1 – list of endpoints

Field studies ‡

Metamitron	Aerobic conditions								
Soil type (German KA4 soil classification)	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand bare soil	Germany		5.7	0-30	10.7	35.5	0.9302	-	1st order
Loamy sand bare soil	Germany		6.2	0-30	6.6	22.0	0.9838	-	1st order
Clay loam bare soil	Germany		6.2	0-30	22.0	73.0	0.9952	-	1st order
Sandy loam bare soil	Germany		6.2	0-30	9.6	32.0	0.9765	-	1st order
Geometric mean/median					11.1/10.2	36.8/33.8		-	
Desamino-metamitron	Aerobic conditions								
Soil type	Location		pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand bare soil	Germany		5.7	0-30	37.3	123.9	0.987	-	1st order
Loamy sand bare soil	Germany		6.2	0-30	37.3	123.8	0.997	-	1st order
Clay loam bare soil	Germany		6.2	0-30	17.0	56.5	0.996	-	1st order
Sandy loam bare soil	Germany		6.2	0-30	39.7	131.9	0.989	-	1st order
Geometric mean/median					31.1/ 37.3	103.4/ 123.9		-	

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No data submitted – none required

Appendix 1 – list of endpoints

Laboratory studies ‡

Parent	Anaerobic conditions – Not studied						
Soil type	X[14]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean/median							

Met 1	Anaerobic conditions – Not studied							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean/median								

[14] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Appendix 1 – list of endpoints

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent Metamitron							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Borstel, loamy sand[2]	1.08	5.1			0.933	86.4	0.8048
LUFA 3A, sandy silt loam[2]	2.60	7.1			1.413	54.4	0.7019
LUFA 2.2, sandy loam[2]	2.30	6.2			1.292	56.2	0.8204
Parabraunerde Soest, silt loam[2]	1.86	6.0			1.190	64.0	0.8305
Lufa 2.1, sand[2]	0.6	5.8			1.82	303	0.67
Lufa, clay[2]	0.9	7.4			1.04	116	0.85
Parabraunerde A_p, silt loam[2]	1.1	7.1			1.54	140	0.75
Parabraunerde B_t, silty clay loam[2]	0.3	6.7			0.36	120	0.95
Braunerde, sandy silt loam[2]	0.8	5.5			1.49	186	0.75
Greenhouse, sandy silt loam[2]	1.5	6.3			5.88	392	0.67
Lufa 2.1, sand[2]	0.7	5.7	0.54	77.1	-	-	-
Lufa 2.3, sandy loam[2]	1.34	6.4	1.21	90.3	-	-	-
Lufa F3, sandy silt loam[2]	1.2	7.3	1.59	132.5	-	-	-
BBA 2.2, loamy sand[2]	1.56	5.6			0.384	24.6	0.7667
Hetendorf, loamy sand[2]	2.25	5.0			1.511	67.2	0.7791
Karlsdorf, loamy sand[2]	0.84	5.7	0.193	22.9	-	-	-
Dossenheim, clay loam[2]	1.68	7.5			0.376	22.4	0.6563
Borstel, sandy loam[1]	1.15	6.3			1.43	124	0.8003
Laacherhof, sandy loam[1]	1.35	6.9			1.07	79	0.7917
Arithmetic mean/median					1.45/1.29	122.3/86.4	0.77/0.78
pH dependence, Yes or No			No				

[1] according to USDA soil classification
[2] according to according to UK classification

Appendix 1 – list of endpoints

Metabolite Desamino-metamitron							
Soil Type (USDA soil classification)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
BBA 2.1, sand	0.59	5.8			0.802	136	0.8008
BBA 2.2, loamy sand	2.48	6.3			1.703	69	0.7766
Laacherhof, sandy loam	1.8	6.4			2.507	139	0.7899
Höfchen, silt	2.62	7.2			1.729	66	0.7545
Arithmetic mean/median					1.685/1.716	102.5/102.5	0.7805/0.7833
pH dependence (yes or no)			No				

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

Column leaching ‡	Eluation (mm): *400 mm* Time period (d): *2* d
	Leachate: max 2.82 – 9.07% active substance in leachate in 1 soil out of 9 tested (3 reps). Remaining soils <*2*% active substance, Max. 0.06 – 0.11% desamino-metamitron in leachate of 1 soil out of 9 tested (3 reps).
Aged residues leaching ‡	Non submitted
Lysimeter/ field leaching studies ‡	Not submitted

Appendix 1 – list of endpoints

PEC (soil) (Annex IIIA, point 9.1.3)

Metamitron Method of calculation	DT_{50} (d): 22 days Kinetics: SFO Field or Lab: representative worst case from field studies.
Application data	Crop: sugar beet Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: Pre-emergence therefore no crop interception (1st application), 20% 2nd and 3rd applications in spring (April/May) Number of applications: *3* Interval (d): *6 d* Application rate(s): *700, 1400 &1400* g as/ha

	1st application (pre or early post emergence)		2nd application (post-emergence)		3rd application (post-emergence BBCH 18)	
Days after application	PECsoil (mg/kg)	Time weighted average (mg/kg)	PECsoil (mg/kg)	Time weighted average (mg/kg)	PECsoil (mg/kg)	Time weighted average (mg/kg)
0	0.933	0.933	2.266	2.266	3.369	3.369
1	0.904	0.919	2.196	2.231	3.264	3.316
2	0.876	0.905	2.128	2.196	3.163	3.265
4	0.823	0.877	1.998	2.129	2.970	3.165
7	0.749	0.838	1.817	2.033	2.702	3.023
14	0.600	0.755	1.458	1.832	2.167	2.724
28	0.386	0.620	0.938	1.505	1.394	2.238
50	0.193	0.470	0.469	1.141	0.697	1.696
100	0.040	0.284	0.097	0.688	0.144	1.023

Appendix 1 – list of endpoints

Metabolite I, Desamino-metamitron Method of calculation	Molecular weight relative to the parent: 187.2/202.2 Calculation based on total soil loading of parent corrected for molecular weight difference, crop interception and maximum formation (assumed Met I is formed at a maximum of 17.1 % of the applied dose)

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.620		-	
Plateau concentration	Not required			

Appendix 1 – list of endpoints

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4: 353.2 d at 20°C (1st order) Substance 6, (unid.): 17.7 %AR (192 h, 60°C)
	pH 7: 479.6 d at 20°C (1st order) 3-methyl-6-phenyl-1,2,4,5-tetrazine: 17.3% AR (193 h, 60°C) 2-methyl-5-phenyl-1,3,4-oxadiazole: 13.1% AR (193 h, 60°C) Substance 6, (unid.): 15.1 %AR (139 h, 60°C)
	pH 9: 8.5 d at 20°C (1st order) 2-methyl-5-phenyl-1,3,4-oxadiazole: 18.6% AR (35 h, 40°C) benzonitrile: 25.2 %AR (168 h, 40°C) Substance 4 (unid.): 18.6% AR (35 h, 40°C)
Photolytic degradation of active substance ‡	DT_{50} (under test conditions): 1.45 h, river water, pH 7 (continuous irradiation) Xenon lamp, 456 Wh/m2, λ 300-800 nm, Natural light, 50°N; DT_{50} 0.47 h (pure water surface in summer sunlight from quantum yield) Major metabolite: Desamino-metamitron: 92.4% AR (24 h)
Photolytic degradation of metabolites above 10 % ‡	Desamino-metamitron DT50: 18 d, pH 7 (continuous irradiation from xenon arc lamp - 290 - 800 nm)
Quantum yield of direct phototransformation in water at Σ > 295 nm	Metamitron: 1.62 x 10^{-2} mol.Einstein $^{-1}$ Desamino-metamitron: 5.78 x 10^{-5} mol.Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	Substance considered not ready biodegradable.

Appendix 1 – list of endpoints

Degradation in water / sediment

Parent	Distribution (eg max in water *109%* after *0* d. Max. sed 47% after *100* d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Waldwinkel	7.96	7.24	20	10.80/35.87	0.977	9.62/31.94	0.986	nc	nc	SFO
Rückhaltebecken	8.04	7.43	20	11.41/37.91	0.979	11.55/38.37	0.978	nc	Nc	SFO
Geometric mean				11.1/36.88		10.54/35.01				

nc not calculated

Metabolite: desamino-metamitron	Distribution: Max in water *54%* after 58 d.; Max. sed 27.5% after 58 d									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Geometric mean/median										

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Waldwinkel	7.96	7.24	1% after 100 d	23%, 100 d	23% 100 d
Rückhaltebecken	8.04	7.43	1% after 100 d	26% after 100 d	26% after 100 d

Appendix 1 – list of endpoints

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent: Metamitron Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: 1.1 Molecular weight (g/mol): 202.2 Water solubility (mg/L): 1680 (20°C) K_{OC} (L/kg): 86.4 (median of 15 soils) 1/n: 0.78 DT_{50} soil (d): *19* days (Lab. In accordance with FOCUS SFO) DT_{50} water/sediment system (d): 11.41 (representative worst case from sediment water studies) DT_{50} water (d): 1000 DT_{50} sediment (d): 11.41 Crop interception (%): 0%
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: FOCUS SWASH 1.1 FOCUS MACRO 4.4.2 FOCUS PRZM SW 3.21.b FOCUS TOXSWA 2.1.2 Vapour pressure: 3.01×10^{-7} Koc: 86.4 (median of 15 soils) 1/n: 0.78
Application rate	Crop: sugar beets Crop interception: 0% Number of applications: Step 1 & 2 = 1 Step 3 = 3 Interval (d): *6* Application rate(s): *3500* g as/ha (step 1 & 2) Step 3: pre-emergence: 700 g as/ha (0% interception) at emergence: 1400 as/ha (20% interception) post emergence: 1400 as/ha (20% interception) Application window: 2 weeks before, 2 weeks after of the emergence

Appendix 1 – list of endpoints

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0	1080.0	-	903.87	-
	1	1010.0	1040	874. 02	888.95
	2	951.92	1010	822.46	868.46
	4	842.93	954.77	728.29	821.44
	7	702.38	875.80	606.85	7554.71
	14	458.91	723.92	396.50	642.47
	21	299.84	607.20	259.06	523.95
	28	195.90	516.45	169.26	445.71
	42	83.63	388.26	72.26	335.13
	50	51.42	336.74	44.42	290.66
	100	2.46	176.42	2.12	152.29

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h				
	24 h				
	2 d				
	4 d				
	7 d				
	14 d				
	21 d				
	28 d				
	42 d				

Appendix 1 – list of endpoints

FOCUS STEP 2 Scenario	Day after overall maximum	PEC$_{SW}$ (µg/L)		PEC$_{SED}$ (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0 h	391.09	-	328.40	-
	24 h	389.68	390.39	317.05	322.72
	2 d	387.07	389.38	314.92	319.35
	4 d	381.89	386.93	310.70	316.08
	7 d	374.25	383.12	304.48	312.44
	14 d	357.00	374.34	290.46	304.93
	21 d	340.56	365.80	277.08	297.86
	28 d	324.87	357.51	264.31	291.05
	42 d	295.62	341.68	240.52	278.11
	50 d	280.11	333.06	227.90	271.08
	100 d	200.00	285.44	162.72	232.28

FOCUS STEP 3 Scenario	Water Body	Day after overall maximum	PEC$_{SW}$ (µg/L)		PEC$_{SED}$ (µg/kg)	
			Actual	TWA	Actual	TWA
D3 Ditch		0 h	5.331		1.848	
D4 pond		0 h	0.568		1.086	
D4 stream		0 h	4.525		0.452	
R1 pond		0 h	1.139		1.815	
R1 stream		0 h	14.847		3.594	
R3 stream		0 h	48.261		7.561	

Appendix 1 – list of endpoints

Metabolite: Desamino-metamitron Parameters used in FOCUSsw step 1 and 2	Molecular weight: 187.2 Water solubility (mg/L): 399.9 (25°C) Soil or water metabolite: Soil Koc (L/kg): 102.5 (arithmetic mean 4 soils) DT_{50} soil (d): *30.5* days (geometric mean. In accordance with FOCUS SFO) DT50 water/sediment system (d): 1000 (FOCUS default) DT_{50} water (d): 1000 (FOCUS default) DT_{50} sediment (d): 1000 (FOCUS default) Maximum occurrence observed: (% molar basis with respect to the parent) (Whole system) Water: 54% Sediment: 92.4%
Parameters used in FOCUSsw step 3 (if performed)	Not performed

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	193.16	-	143.10	-
	24h	179.09	186.12	154.73	148.91
	2d	168.52	179.94	145.60	149.52
	4d	149.23	169.31	128.93	143.31
	7d	124.34	155.21	107.43	132.40
	14d	81.24	128.24	70.19	109.95
	21d	53.08	107.55	45.86	92.35
	28d	34.68	91.47	29.96	78.60
	42d	14.81	68.76	12.79	59.13
	50	9.10	59.64	7.86	51.29
	100	0.44	31.24	0.38	26.88

Appendix 1 – list of endpoints

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h				
	24 h				
	2 d				
	4 d				
	7 d				
	14 d				
	21 d				
	28 d				
	42 d				
Southern EU	0 h	67.20	-	54.18	-
	24 h	66.59	66.89	53.81	53.99
	2 d	66.14	66.63	53.45	53.81
	4 d	65.26	66.16	52.73	53.45
	7 d	63.95	65.49	51.68	52.92
	14 d	61.00	63.98	49.30	51.70
	21 d	58.19	62.52	47.03	50.52
	28 d	55.51	61.10	44.86	49.37
	42 d	50.52	58.39	40.82	47.18
	50	47.86	56.92	38.68	45.99
	100	34.17	48.78	27.62	39.42

Appendix 1 – list of endpoints

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PELMO 3.3.2; PEARL 3.3.3 Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: Sugar beets Metamitron DT50: *19* d, (geomean lab studies)(normalisation to pF2, 20 °C with Q10 of 2.2). K_{FOC}: median *86.4*, $^{1}/_{n}$= *0.78 (15 soils)* Metabolites: Desamino-metamitron DT50: 30.5 d (geomean lab studies) K_{FOC} : arithmetic mean 102.5, 1/n = 0.78 (4 soils) Formation fraction: 0.5 (highest calculated from lab aerobic soil metabolism study).
Application rate	No. of applications: 3 Application interval (d): 6 Application rate: pre-emergence: 700 g as/ha (0% interception) at emergence: 1400 as/ha (20% interception) post emergence: 1400 as/ha (20% interception) Time of application (March to May):

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

	Scenario	Parent Metamitron (µg/L)	Metabolite desamino-metamitron (µg/L)
PELMO / Sugar beet	Châteaudun, irrigated	<0.001	<0.001
	Hamburg	<0.001	<0.001
	Jokioinen	<0.001	<0.001
	Kremsmünster	<0.001	<0.001
	Okehampton	<0.001	<0.001
	Piacenza, irrigated	0.002	0.139
	Porto	<0.001	<0.001
	Sevilla, irrigated	<0.001	<0.001
	Thiva, irrigated	<0.001	<0.001

Appendix 1 – list of endpoints

	Scenario	Parent Metamitron (µg/L)	Metabolite desamino-metamitron (µg/L)
PEARL / Sugar beet	Châteaudun, irrigated	<0.001	0.022
	Hamburg	<0.001	0.014
	Jokioinen	<0.001	<0.001
	Kremsmünster	<0.001	0.006
	Okehampton	<0.001	0.008
	Piacenza, irrigated	0.139	1.440
	Porto	<0.001	<0.001
	Sevilla, irrigated	<0.001	<0.001
	Thiva, irrigated	<0.001	<0.001

$PEC_{(gw)}$ From lysimeter / field studies - Non submitted

Parent	1st year	2nd year	3rd year
Annual average (µg/L)			

Metabolite X	1st year	2nd year	3rd year
Annual average (µg/L)			

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

Direct photolysis in air ‡	DT_{50} of *19.8* hours derived by the Atkinson model (version AOPWIN v1.88). OH (24 h) concentration assumed: 5 x 10^5 cm^{-3}

PEC (air)Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$	
Maximum concentration	negligible

Appendix 1 – list of endpoints

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: desamino-metamitron Surface Water: desamino-metamitron Sediment: desamino-metamitron Ground water: desamino-metamitron, Unidentified metabolite M3 Air: none

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)	Groundwater sampling programme in Netherlands for analysis of 18 pesticides including metamitron. Feb ’85 – Oct ’87: upper 1-2 m of groundwater sampled from vulnerable soils. Residues of metamitron >LOD (range 0.06 – 0.73 µg/L) found in 8 out of 12 samples. 1988: groundwater sampling extended to less vulnerable soils to a depth of 6 m below groundwater level. No observations above LOD (<0.05 - <0.01 µg/L) in 19 groundwater samples below potato cultivation and 8 samples from bulb cultivation areas.
Air (indicate location and type of study)	None

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate for R53

Appendix 1 – list of endpoints

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

Species	Test substance	Time scale	End point (mg a.s. or metabolite /kg bw /day)	End point (mg a.s. /kg feed)
Birds ‡				
Japanese quail (*Coturnix coturnix japonica*)	Technical metamitron	Acute	LD50 (male) = 1358 LD50 (female) = 1302	-
Bobwhite quail (*Colinus virginianus*)	Technical metamitron	Short-term	LD50 = >904	LC50 >5000 mg a.s. /kg diet
Mallard duck (*Anas platyrhynchos*)	Technical metamitron	Short-term	LD50 = >1586	LC50 >5000 mg a.s. /kg diet
Bobwhite quail (*Colinus virginianus*)	Technical metamitron	Long-term	NOAEL = 81.5	NOAEC 1000
Mammals ‡				
Rat	Technical metamitron	Acute	LD50 (male) = 1183 LD50 (female) = 1482	-
Mouse	Technical metamitron	Acute	LD50 (male) = 691 LD50 (female) = 644	-
Rat	'Goltix SC 700'	Acute	LD50 = 200-2000 (precise value not calculable)	-
Rat	Desaminometamitron	Acute	LD50 = 4325	-
Rat	Technical metamitron	Long-term	Ecological NOAEL = 36..4 (male) & 53.8 (female)	Ecological NOAEC = 500

Appendix 1 – list of endpoints

Additional higher tier studies ‡
Foliar residue studies: Details for a UK foliar residue decline field study indicate that following a spray application of 'Goltix SC 700' metamitron residues declined rapidly. The apparent short foliar half-life of metamitron is also supported by the results of four German residue field studies in which, following spray applications of formulated metamitron, the high initial (day 0) measured residues of metamitron were found to be reduced to non-significant levels (i.e. ≤ 0.1 mg/kg) at the subsequent analysis made in each trial 14-16 days after treatment. The evidence is considered sufficient to support use of a DT50 of 1.9 days in the refined risk assessment (in place of a default '1st tier' value of 10 days). Based on the available 'day 0' (initial) metamitron foliar residue data from one UK site and from five sites in Germany, the generic acute and long-term residue per unit dose values (RUDs) used in the first tier risk assessment can also be refined. Using these data, the 'refined' acute RUD is 74 (based on maximum residue levels) and the long-term RUD is 48 (based on mean residue levels). The 21 day time averaged C_{res} level is calculated to be 21.53 mg a.s./kg foliage. The long term risk assessment for herbivorous birds and mammals can be refined using this refined exposure value. Various published studies on bird behaviour and feeding preferences: The evidence is sufficient to support the assumption that in relation to the long-term consumption of invertebrates, the invertebrate component of the diet for the skylark and yellowhammer will consist (by weight) of approximately 75% 'large' invertebrates (>4mm body length) and 25% 'small' invertebrates (≤4mm body length). For the yellow wagtail, the evidence supports a long-term consumption estimate of 50% (by weight) of 'large' invertebrates and 50% of 'small' invertebrates.

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

Crop and application rate: Sugar beet and fodder beet – three applications of 700, 1400 and 1400 g a.s./ha, sprayed at a minimum application interval of 6 days.

Indicator species/Category	Time scale	ETE Mg /kg bw /day	TER[1]	Annex VI Trigger
Tier 1 (Birds)				
Medium herbivore	Acute	143.5	**9.1**	10
Small insectivore	Acute	75.7	17.2	10
Medium herbivore	Short-term	79.95	>11.3	10
Small insectivore	Short-term	42.22	>21.4	10
Medium herbivore	Long-term	65.56	**1.24**	5
Small insectivore	Long-term	42.22	**1.93**	5

Appendix 1 – list of endpoints

Indicator species/Category	Time scale	ETE Mg /kg bw /day	TER[1]	Annex VI Trigger
Higher tier refinement (Birds)				
Medium herbivore	Acute	87.40	14.9	10
Medium herbivore	Long-term	16.36	3.5	5
Skylark	Long-term	50.54 (assuming PT=0.99, 95% CI of 90th percentile) 44.92 (assuming PT=0.88, 90th percentile)	**1.6** **1.8**	5
Yellowhammer	Long-term	17.58 (assuming PT=1.0, 95% CI of 90th percentile) 16.53 (assuming PT=0.94, 90th percentile)	**4.6** **4.9**	5
Yellow wagtail	Long-term	20.06 (assuming PT=1.0 based on no available data)	**4.1**	5
Tier 1 (Mammals)				
Medium herbivore	Acute	52.86	12.2	10
Medium herbivore	Long-term	15.61	**2.3**	5
Higher tier refinement Mammals				
Medium herbivore	Long-term	6.02	**6.04**	5

[1].TERs included in bold indicate a breaching of the Annex VI trigger

Appendix 1 – list of endpoints

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 (Test type)	End point	Toxicity (mg a.s. /L unless indicated otherwise)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss (rainbow trout)	Technical metamitron (>98% purity)	96 hr (static), acute.	Mortality, EC_{50}	>190 (nominal)
Oncorhynchus mykiss (rainbow trout)	Technical metamitron (>98% purity)	21 d (semi-static with daily renewal), prolonged toxicity test.	Growth NOEC	7.0 (nominal)
Oncorhynchus mykiss *(rainbow trout)*	'Goltix SC 700' (690g /l metamitron)	96 hr (static)	Mortality, EC_{50}	>200 mg product /l ≡ >114 a.s. /l (nominal)
Oncorhynchus mykiss *(rainbow trout)*	Desamino-metamitron (99.5% purity)	96 hr (static)	Mortality, EC_{50}	>1000 mg (nominal)
Aquatic invertebrates				
Daphnia magna	Technical metamitron (99% purity)	48 h (static)	Immobilisation, EC_{50}	5.7 (mean measured)
Daphnia magna	Technical metamitron (99% purity)	21 d (semi-static, renewal 3 times per week), reproductive toxicity test	Reproduction, NOEC	10 (nominal)
Daphnia magna	Goltix SC 700 (57.4 w/w metamitron)	48 h (static)	Immobilisation, EC_{50}	170 mg product /l ≡ 97.6 mg a.s./l (nominal)
Daphnia magna	Desamino-metamitron (99% purity)	48 h (static)	Mortality, EC_{50}	745 mg metabolite / l (nominal)

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg a.s. /L unless indicated otherwise)
Sediment dwelling organisms				
Chironomus riparius (dipteran midge)	Desamino-metamitron (99.5% purity)	28 d (static spiked water) emergence & development study.	NOEC	100 mg metabolite /l (initial nominal)
Algae				
Pseudokirchneriella subcapitata formerly *Selanastrum capricornutum* (green alga)	Metamitron (technical: purity 99.3%)	72 h (static) Growth inhibition	Biomass E_bC_{50} Growth rate E_rC_{50}	0.4 (initial measured) 1.8 (initial measured)
Pseudokirchneriella subcapitata formerly *Selanastrum capricornutum* (green alga)	'Goltix SC 700' (724.1 g/l metamitron)	72 h (static) Growth inhibition	Biomass E_bC_{50} Growth rate E_rC_{50}	0.82 mg product/l ≡ 0.49 mg a.s./l (nom.) 3.38 mg product/l ≡ 2.01 mg a.s./l (nom.)
Pseudokirchneriella subcapitata formerly *Selanastrum capricornutum* (green alga)	Desamino-metamitron (99% purity)	72 h (static) Growth inhibition	Biomass E_bC_{50} Growth rate E_rC_{50}	25.1 mg metabolite /l (nominal) 73.5 mg metabolite /l (nominal)

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg a.s. /L unless indicated otherwise)
Higher plant				
Lemna gibba	a.s. (technical: purity 98.8%)	7 day (semi-static with renewal on days 3 & 5) Growth inhibition	Biomass E_bC_{50} Growth rate E_rC_{50}	0.4 mg a.s./l (mean measured) 0.8 mg a.s./l (mean measured)
Lemna minor	a.s. (technical: purity 98.6%)	14 day (semi-static with renewal on days 2, 5, 7, 9, & 12) Growth inhibition	Biomass E_bC_{50} Frond no. EC_{50}	0.38 mg a.s./l (mean measured) 0.45 mg a.s./l (mean measured)

Microcosm or mesocosm tests:

After a single application of 'Goltix SC 700' to outdoor mesocosm enclosures containing phytoplankton, zooplankton and macrophyte communities, significant treatment related effects were observed at the 2 highest test concentrations (i.e. 1120 and 4480 µg a.s./L), but only for physical-chemical endpoints related to the community metabolism (pH and dissolved oxygen concentration), with these effects at 1120 µg a.s./L being slight and transient (day 2 reductions of 0.5 in pH & of 30% in oxygen levels, with no effects when next assessed on day 5). No consistent treatment-related effects on structural endpoints of phytoplankton (species composition, densities, chlorophyll-a level), periphyton (chlorophyll-a level) and macrophytes (% cover, final biomass, growth of *Myriophyllum spicatum* in *in situ* bioassays) were obtained at up to the highest test concentration. In addition, densities of the major zooplankton groups appeared to be unaffected. Only the more pronounced effects on oxygen and pH levels at 4480 ug a.s. /L (i.e. reductions on day 2 compared with day 0 in oxygen levels by 80% and a pH drop from 9.2. to 7.5, with recovery by day 15) are considered to be ecologically relevant, and on this basis the **study NOAEC** (no observed ecologically adverse effect concentration) is 1120 µg a.s. /L or **1.12 mg a.s. /l (nominal)**.

It is noted that exposure in the study differs from the proposed use in not including repeat exposure. However, given the low level and rapid reversibility of effects at the NOAEC, the effects of metamitron exposure at or below this concentration are considered unlikely to be significant increased by repeat exposure. Although effects on a wide range of aquatic invertebrates and algae species were assessed in the study, effects on only three species of higher aquatic plants were assessed – which may not be fully representative of the range of sensitivity of higher aquatic plants to metamitron. To take account of the uncertainty involved in extrapolating the results of the mesocosm study to the field situation, an uncertainty factor of 3 has been applied by the RMS to the study NOAEC.

Appendix 1 – list of endpoints

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

FOCUS Step 1

Crop and application rate: Sugar beet and fodder beet – three applications of 700, 1400 and 1400 g a.s./ha, sprayed at a minimum application interval 6 days, use in Northern and Southern Europe.

Test substance	Organism	Time scale & endpoint measured	Toxicity end point value (mg a.s. or metabolite/l) #	Maximum PEC (mg a.s. or metabolite/l)	TER[1]	*Annex VI Trigger*
Metamitron (technical)	*Oncorhynchus mykiss* (rainbow trout)	Acute: 96h LC50	> 190	1.08	>175.9	*100*
Metamitron (technical)	*Oncorhynchus mykiss*	Chronic: 21d NOEC	7.0	1.08	**6.5**	*10*
Metamitron (technical)	*Daphnia magna* (water flea)	Acute: 48h EC50	5.7	1.08	**5.3**	*100*
Metamitron (technical)	*Daphnia magna*	Chronic: 21d NOEC	10.0 **	1.08	**9.3**	*10*
Metamitron (technical)	*Pseudokirchneriella subcapitata* (green alga)	Chronic: 72h EbC50	0.4	1.08	**0.4**	*10*
Metamitron (technical)	*Lemna minor*	Chronic: 14d EbC50	0.38	1.08	**0.4**	*10*
Desamino-metamitron (metabolite)	*Oncorhynchus mykiss*	Acute: 96h LC50	>1000	0.924	>1082.3	*100*
Desamino-metamitron (metabolite)	*Daphnia magna*	Acute: 48h EC50	745	0.924	806.3	*100*
Desamino-metamitron (metabolite)	*Pseudokirchneriella subcapitata*	Chronic: 72h EbC50	25.1	0.924	27.2	*10*
Desamino-metamitron (metabolite)	*Chironomus riparius* (dipteran midge)	Chronic: 28d NOEC*	100	0.924	108.2	*10*
'Goltix SC 700'	*Oncorhynchus mykiss*	Acute: 96h LC50	>114	1.08	>105.6	*100*
'Goltix SC 700'	*Daphnia magna*	Acute: 48h EC50	97.6	1.08	**90.4**	*100*
'Goltix SC 700'	*Pseudokirchneriella subcapitata*	*Chronic: 72h EbC50*	*0.49*	*1.08*	***0.5***	*10*

[1].TERs included in bold indicate a breaching of the Annex VI trigger
Formulation related endpoints converted to equivalent amounts of a.s.
* Spiked water study, with TER based on comparison of no effects following an initial (maximum)

Appendix 1 – list of endpoints

concentration in water with the FOCUS Step 1 initial (maximum) PECsw.
** It is recognised that the 21 day NOEC of 10.0 mg a.s. /l is higher than the 48h EC50 of 5.7 mg a.s./l reported in a *Daphnia* acute toxicity study, which is attributed to differences in sensitivity of the tested strains.

FOCUS Step 2

Crop and application rate: Sugar beet and fodder beet – three applications of 700, 1400 and 1400 g a.s./ha, sprayed at a minimum application interval of 6 days, use in Northern (N) and Southern (S) Europe.

Test substance	Organism	Time scale & endpoint measured	Toxicity end point value (mg a.s. or metabolite /L)#	Surface water $PEC_{max.}$ (mg a.s. /l)	TER[1]	*Annex VI Trigger*
Metamitron (technical)	*Oncorhynchus mykiss*	Chronic: 21d NOEC	7.0	0.210 (N) 0.391 (S)	33.3 17.9	*10*
Metamitron (technical)	*Daphnia magna* (water flea)	Acute: 48h EC50	5.7	0.210 (N) 0.391 (S)	**27.1 14.6**	*100*
Metamitron (technical)	*Daphnia magna*	Chronic: 21d NOEC	10.0	0.210 (N) 0.391 (S)	47.6 25.6	*10*
Metamitron (technical)	*Pseudokirchneriella subcapitata* (green alga)	Chronic: 72h EbC50	0.4	0.210 (N) 0.391 (S)	**1.9 1.0**	*10*
Metamitron (technical)	*Lemna minor*	Chronic: 14d EbC50	0.38	0.210 (N) 0.391 (S)	**1.8 0.9**	*10*
'Goltix SC 700'	*Daphnia magna*	Acute: 48h EC50	97.6	0.210 (N) 0.391 (S)	464.7 249.6	*100*
'Goltix SC 700'	*Pseudokirchneriella subcapitata*	*Chronic: 72h EbC50*	*0.49*	0.210 (N) 0.391 (S)	**2.3 1.25**	*10*

[1].TERs included in bold indicate a breaching of the Annex VI trigger
Formulation related endpoints converted to equivalent amounts of a.s.

Appendix 1 – list of endpoints

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Crop and application rate: Sugar beet and fodder beet – three applications of 700, 1400 and 1400 g a.s./ha, sprayed at a minimum application interval of 6 days, use in Northern and Southern Europe.

Test substance	Scenario[1]	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point value (mg a.s. /L)	Maximum PEC* (mg a.s. /L)	TER	Annex VI trigger
Metamitron (technical)	D3	Ditch	*Daphnia magna* (water flea)	Acute: 48h EC50	5.7	0.005331	1069.2	100
	D4	Pond				0.000568	10035.2	100
	D4	Stream				0.004525	1259.7	100
	R1	Pond				0.001139	50004.4	100
	R1	Stream				0.014847	383.9	100
	R3	Stream				0.048261	118.1	100
Metamitron (technical)	D3	Ditch	*Pseudokirch-neriella subcapitata* (green alga)	Chronic: 72h EbC50	0.4	0.005331	75.0	10
	D4	Pond				0.000568	704.2	10
	D4	Stream				0.004525	88.4	10
	R1	Pond				0.001139	351.2	10
	R1	Stream				0.014847	26.9	10
	R3	Stream				0.048261	**8.3**	10

Appendix 1 – list of endpoints

Test substance	Scenario[1]	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point value (mg a.s. /L)	Maximum PEC* (mg a.s. /L)	TER	Annex VI trigger
Metamitron (technical)	D3	Ditch	*Lemna minor*	Chronic: 14d EbC50	0.38	0.005331	71.3	10
	D4	Pond				0.000568	669.0	10
	D4	Stream				0.004525	83.9	10
	R1	Pond				0.001139	333.6	10
	R1	Stream				0.014847	25.6	10
	R3	Stream				0.048261	**7.8**	10

[1] drainage (D1-D6) and run-off (R1-R4)

Note: The above TERs are derived from the use of the available laboratory data, with an acceptable risk identical in 5 out of 6 of the assessed relevant full scenarios. The results of a field mesocosm study indicates an NOAEC of 1120 µg a.s./. A comparison of this NOAEC with the FOCUS Step 3 PECsw values indicates an acceptable risk for all assessed scenarios.

Higher Tier refinement – Microcosm (Step 3PECsw– 5m)

Scenario	Water body Type	Toxicity EndPoint	PEC (mg a.s./L)	TER	Annex VI trigger
D3	Ditch	NOAEC = 1120 µg/L	0.005331	211	10
D4	Pond		0.000568	1972	10
D4	Stream		0.004525	247.5	10
R1	Pond		0.001139	983.3	10
R1	Stream		0.014847	75	10
R3	Stream		0.048261	23.2	10

Appendix 1 – list of endpoints

Bioconcentration		
	Metamitron	Desamino-metamitron
$\log P_{OW}$	0.85-0.96	1.43-2.46
Bioconcentration factor (BCF)[1]	-	-

[1] only required if log P_{OW} >3.

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

Test substance	Acute oral toxicity (48h LD_{50} µg a.s. /bee)	Acute contact toxicity (48h LD_{50} µg a.s./bee)
Metamitron ‡	>97.2	> 100.0
'Goltix SC 700' (690g a.s./l) ‡ #	123.3	> 200.0

Toxicity of 'Goltix 700 SC' expressed in terms of levels of active substance exposure

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

Crop and application rate: Sugar beet and fodder beet, maximum individual application of 1400 g metamitron /ha.

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Oral	< 14.4	50
a.s.	Contact	< 14.0	50
Preparation	Oral	11.4	50
Preparation	Contact	< 7.0	50

Appendix 1 – list of endpoints

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

Laboratory tests with standard sensitive species:

Species	Test Substance	End point	Effect (LR_{50})
Typhlodromus pyri ‡	'Goltix SC 700'	Mortality	LR50 = > 21 litres product /ha (≡ > 14383 g a.s./ha)
Aphidius rhopalosiphi ‡	'Goltix SC 700'	Mortality	LR50 = > 21 litres product /ha (≡ > 14383 g a.s./ha)

Hazard quotients for other arthropod species (Annex IIIA, point 10.5)

Crop and application rate: Sugar beet and fodder beet – three applications of 1, 2 and 2 litres 'Goltix SC 700' /ha (700, 1400 and 1400 g a.s. /ha), sprayed at a minimum application interval of 6 days. Accumulative predicted exposure rate (based on default MAF of 1.9) ≡ 4.7 litres 'Goltix SC 700' /ha (3290 g a.s./ha)

Test substance	Species	Effect: LR_{50}	HQ in-field	HQ off-field (at 1 metre[1])	Trigger
'Goltix SC 700'	*Typhlodromus pyri*	> 21 litres product /ha	< 0.22	< 0.0045	2
'Goltix SC 700'	*Aphidius rhopalosiphi*	>21 litres product /ha	< 0.22	< 0.0045	2

[1] Estimated assuming an accumulated in-field dose ≡ 4.7 litres 'Goltix SC 700' /ha (3290 g a.s./ha) with 2.01% spray drift exposure at 1 metre (overall 90th percentile spray drift values for three applications, ref. Rautmann et al 2001)

Appendix 1 – list of endpoints

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	ESCORT 2 Trigger value
Pardosa spp	Adult	'Goltix SC 700'; quartz sand; 14 day exposure.	5 litres product /ha (exposure to initial residues)	Corrected mortality (%) Feeding activity (% reduction)	0% mortality 8% reduction	50 % (at in-field exposure rate)
Coccinella septempunctata	Larvae	'Goltix SC 700'# glass plate substrate, exposure up to adult emergence	2.0-6.1 litres product /ha (exposure to initial residues)	% corrected mortality (M) & % reduction in reproduction (R) 2.0 l product /ha 5.1 l product /ha 6.1 l product /ha	12(M), 32(R) 5(M), 33(R) 10(M), 68(R)	50 % (at in-field exposure rate)

Appendix 1 – list of endpoints

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7):

Test organism	Test substance	Time scale	End point
Earthworms			
Eisenia fetida	Technical metamitron (99% purity) ‡	Acute, 14 days	LC_{50} 914 mg a.s./kg d.w. soil
Eisenia fetida	Desamino-metamitron (99.4% purity) ‡	Acute, 14 days	$LC_{50corrected}$ > 500 mg a.s. /kg d.w. soil [1]
Eisenia fetida	'Goltix SC 700' (690.2 g metamitron / litre) ‡	Chronic, 8 weeks (reproductive toxicity study)	NOEC 28 mg a.s. /kg d.w. soil[2]
Other soil macro-organisms			
Folsomia candida, (Collembola)	Desamino-metamitron (99.4% purity) ‡	Chronic, 28 days (reproductive toxicity study)	NOEC 100
Soil micro-organisms			
Nitrogen mineralisation	'GOLTIX SC 700' (690 g/L metamitron)‡	28 day study	Effects on nitrogen transformation processes by day 28 at 19.5 mg a.s./kg d.w. soil < ±25% of the control [3]
Nitrogen mineralisation	Desamino-metamitron (99.4% purity). ‡	56 day study	Effects by day 42 on nitrogen transformation at 21.73 mg metabolite /kg dw soil <±25% of the control [3]
Carbon mineralisation	'GOLTIX SC 700' (690 g/L metamitron)‡	28 day study	Effects on soil respiration at 19.5 mg a.s./kg d.w. soil throughout the study < ±25% of the control [3]
Field studies			
Not required			

[1] Since the maximum estimated Log P_{OW} values of desamino-metamitron is above 2 and testing was conducted in an artificial soil containing 10% organic matter, an EPPO correction factor of 2 was applied to the toxicity endpoint
[2] Calculated from the applied rate per unit area - considering a soil depth of 5 cm and a density of 1.5 g/cm^3
[3] Test doses compares with maximum soil PECs from the proposed use of 3.74 mg a.s. /kg dw soil and 0.62 mg desamino-metamitron /kg dw soil.

Appendix 1 – list of endpoints

Toxicity/exposure ratios for soil organisms:

Crop and application rate: Sugar beet and fodder beet – three applications of 700, 1400 and 1400 g a.s. /ha, sprayed at a minimum application interval of 6 days.

Test organism	Test substance	Time scale & endpoint	Maximum soil PEC (mg a.s. or metabolite /kg dry soil)	TER	Trigger
Earthworms					
Eisenia fetida	Technical metamitron	Acute LC50	3.77	271	10
Eisenia fetida	'Metamitron 700 SC' (≡ 'Goltix SC 700')	Chronic NOEC	3.37	8.3	5
Eisenia fetida	Desamino-metamitron (soil metabolite)	Acute LC50	0.62	>806	10
Other soil macro-organisms					
Folsomia candida, (Collembola)	Desamino-metamitron (soil metabolite)	Chronic NOEC	0.62	161	5

Appendix 1 – list of endpoints

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

Preliminary screening data:

Not required for herbicides

Laboratory dose response tests:

Most sensitive species	Test substance	ER_{50} Post-emergence exposure	ER_{50} Pre-emergence exposure	Exposure[1] (g/ha)[2]	TER	Trigger
Lettuce (based on post-emergence exposure effects in vegetative vigour test) ‡	'Goltix 700 SC'	171.6 g a.s./ha (effects on shoot fresh weight – the most sensitive measured effect)	-	38.78 g a.s. /ha (at 1 metre) # 7.98 g a.s. /ha (at 5 metres) # (Post-emergence exposure)	4.4 21.5	5 5
Rape (based on pre-emergence exposure effects in seedling emergence & growth test) ‡	'Goltix 700 SC'	-	54.9 g a.s./ha (effects on shoot fresh weight – the most sensitive measured effect)	55.30 g a.s. /ha (at 1 metre) ## 11.28 g a.s. /ha (at 5 metres) ## (Pre-emergence exposure)	0.99 4.9	5 5

Assumes 2.77% and 0.57% spray drift exposure at 1 and 5 metres respectively from a single application at the maximum dose of 1400 g a.s./ha (90th percentile spray drift values for a single application, ref: Rautmann et al 2001)

Assumes 2.01% and 0.41% spray drift exposure at 1 and 5 metres respectively and a refined accumulated in-field PER of 2751 g a.s./ha (overall 90th percentile spray drift values for three applications, ref. Rautmann et al 2001)

Appendix 1 – list of endpoints

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	End point
Activated sludge bacterial respiratory inhibition study with technical metamitron (98.4% purity)	EC50 6400 mg a.s. /litre

Ecotoxicologically relevant compounds

Compartment	
soil	Metamitron, desamino-metamitron
water	Metamitron.
sediment	Desamino-metamitron
groundwater	-

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50, R53.

	RMS/peer review proposal
Preparation	R50, R53.

APPENDIX 2 – ABBREVIATIONS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
approx	approximate
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
AV	avoidance factor
BCF	bioconcentration factor
BOD	biological oxygen demand
bp	boiling point
bw	body weight
c	centi- (x 10^{-2})
°C	degree Celsius (centigrade)
cGAP	critical good agricultural practice
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
cm	centimetre
d	day
DAD	Diode array detection
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
ECD	electron capture detector
EDI	estimated daily intake
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union

Appendix 2 – abbreviations

F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FAO	Food and Agriculture Organisation of the United Nations
FIA	fluorescence immuno assay
FID	flame ionisation detector
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
f(twa)	time weighted average factor
g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GS	growth stage
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare
HDT	highest dose tested
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
ICP-OES	inductively coupled plasma optical emission spectroscopy
ID	ionisation detector
IEDI	international estimated daily intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
k	kilo
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole)

Appendix 2 – abbreviations

	(see also H)13
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
LOQ	limit of quantification (determination)
LT	lethal threshold
m	metre
M	molar
MAF	multiple application factor
µm	micrometer (micron)
MC	moisture content
µg	microgram
mg	milligram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
mm	millimetre
mN	milli-Newton
mol	Mol
MOS	margin of safety
mp	melting point
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MWHC	maximum water holding capacity
n	normal (defining isomeric configuration)
NAEL	no adverse effect level
nd	not detected

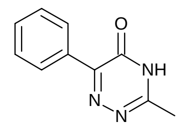
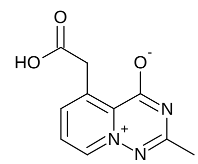
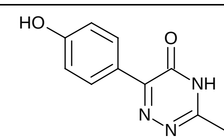
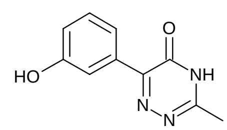
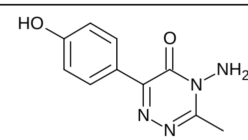
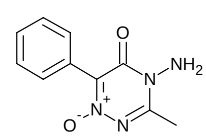
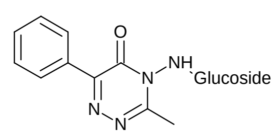
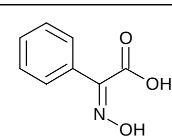
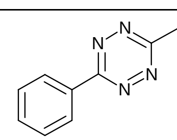
Appendix 2 – abbreviations

NEDI	no effect daily intake (mg/kg body wt/day)
NEL	no effect level
NERL	no effect residue level
NESTI	national estimated short term intake
ng	nanogram
NIR	near-infrared-(spectroscopy)
nm	nanometer
NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NPD	nitrogen-phosphorus detector or detection
OC	organic carbon content
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{Sed}	predicted environmental concentration in sediment
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PNEC	predicted no effect concentration
P_{ow}	partition coefficient between n-octanol and water
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
r	correlation coefficient
r^2	coefficient of determination
RH	relative humidity

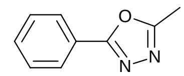
Appendix 2 – abbreviations

RL_{50}	residual lifetime
RPE	respiratory protective equipment
RUD	residue per unit dose
s	second
SC	suspension concentrate
SF	safety factor
SOP	standard operating procedure
sp	species (only after a generic name)
STMR	supervised trials median residue
t	tonne (metric ton)
$t_{1/2}$	half-life (define method of estimation)
TC	technical material
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TK	technical concentrate
TMDI	theoretical maximum daily intake
TWA	time weighted average
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
wk	week
wt	weight
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
desamino-metamitron	3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one	
metamitron-triazinium acetic acid	5-(carboxymethyl)-2-methylpyrido[2,1-*f*][1,2,4]triazin-9-ium-4-olate	
metamitron-4-hydroxy-desamino	6-(4-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one	
metamitron-3-hydroxy-desamino	6-(3-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one	
metamitron-4-hydroxy	4-amino-6-(4-hydroxyphenyl)-3-methyl-1,2,4-triazin-5(4*H*)-one	
	3-methyl-4-amino-6-phenyl-1,2,4-triazine-5-one-oxide	
metamitron-N-glucoside	*N*-*β*-D-glucosyl-4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one	
oxime-acid	(2*Z*)-(hydroxyimino)(phenyl)ethanoic acid	
	3-methyl-6-phenyl-1,2,4,5-tetrazine	

Appendix 3 – used compound code(s)

Code/Trivial name	Chemical name	Structural formula
	2-methyl-5-phenyl-1,3,4-oxadiazole	
N-acetylbenzoic acid hydrazide	*N*'-acetylbenzohydrazide