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

# metribuzin

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## SUMMARY

Metribuzin is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise 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 one year a conclusion on the risk assessment to the EU-Commission.

Germany being the designated rapporteur Member State submitted the DAR on metribuzin in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 23 August 2004. Following a quality check on the DAR, the peer review was initiated on 3 September 2004 by dispatching the DAR for consultation of the Member States and the applicants Bayer CropScience and Feinchemie Schwebda. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 18 May 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 8 June 2006 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 a herbicide as proposed by the applicants which comprises broadcast spraying to control some grasses and broad-leaved weeds in potatoes. The maximum total dose is 1.05 kg metribuzin per hectare.
The representative formulated products for the evaluation were Sencor and Mistral both are water dispersible granule formulations (WG) containing 700 g/kg metribuzin.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25
* The list of endpoints in Appendix 1 (page 65) has been updated to correct the endpoint for acute toxicity to mammals.

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of metribuzin in soil water and air.
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.

Metribuzin has a moderate acute oral toxicity and low dermal and inhalation toxicity. It is neither a skin and eye irritant nor a skin sensitiser. The classification as R22 (Harmful if swallowed) has been proposed. The meeting considered that metribuzin potentially reached the requirement for classification as [R22/48] since in a number of studies, serious adverse effects were noted at doses of >50 mg/kg bw/day. The issue was flagged to ISPRA for consideration. Metribuzin did not exhibit a genotoxic and carcinogenic potential. A possible classification as R62/63 was considered and forwarded to ISPRA based on delays in skeletal ossification, considered to be related to decreased bodyweight, rather than developmental toxicity, and alterations in kidneys and ureter, together with the increased pup mortality in the multigeneration study. The ADI for metribuzin was established at 0.013 mg/kg bw/day, based on the NOAEL of 1.3 mg/kg bw/day from the chronic toxicity/carcinogenicity study in rats, with an assessment factor of 100. The AOEL and ARfD are 0.02 mg/kg bw/day, based on the overall NOAEL of 2 mg/kg bw/day and on the acute neurotoxicity, respectively, with an assessment factor of 100. The operator risk assessment is inconclusive since the re-calculations provided by the rapporteur Member State lack of transparency and were not made available for peer review in due time.

The metabolism of metribuzin has been investigated in potatoes, soybeans and wheat. Similar metabolic pathways were identified but different residue-amounts of parent and metabolites, depending on the crop, were observed. In potatoes about 60 % of the total residues were identified, with 20 % of the total residue being metribuzin. Three metabolites were present representing a global toxicological burden expected to be similar to that of the parent compound. Residue definitions are proposed for potatoes only. For monitoring purposes metribuzin and for risk assessment the sum of metribuzin, desamino-metribuzin, diketo-metribuzin and desaminodiketo-metribuzin, expressed as metribuzin. Residue definitions for other commodities should be dealt with at Member State level, taking into account the specific residue pattern of these commodities. Supervised residue trials according to the representative use demonstrate that residues are below the LOQ of 0.05 mg/kg for the parent compound and its metabolites. No residues are expected in rotational or succeeding crops.
Human and animal exposure to residues of metribuzin and its metabolites is therefore minimal and below the trigger toxicological end points.

Metribuzin is low to moderate persistent in soil under dark aerobic conditions. It forms the major metabolites diketo-metribuzin and desamino-diketo-metribuzin. Bound residues amounted up to 65.3 % AR after 71 d and $CO_2$ up to 38.9 % AR at the end of the study after 126 d. Desamino-diketo-

metribuzin is low to moderate persistent in soil under aerobic conditions. Metabolite diketo-metribuzin metabolite seems to be moderately persistent in soil under aerobic conditions ($DT_{50}$ = 29.9 – 48.6 d). However, fitting procedures, kinetic employed and goodness of fitting are not reported and assessed in the DAR. Therefore, values for this metabolite should be taken with caution. Metribuzin is highly persistent in soil under anaerobic conditions.

Four metabolites: desamino-metribuzin (max. 21.5 % AR), polar I (max 4.6 % AR), apolar I (max. 8.4 % AR) and apolar II (max. 5.3 % AR) reached the maximum at the end of the study of photolysis in soil (13 d). Major soil photolysis metabolite desamino-metribuzin needs to be addressed with respect of soil and ground water compartments.

PEC in soil of metribuzin, diketo-metribuzin and desamino-diketo-metribuzin were calculated by the rapporteur Member State for the worst case GAP and 90$^{th}$ percentile half lives.

Metribuzin may be classified as high to very high mobile in soil. Desamino-diketo-metribuzin is high mobile in soil. The experimentally derived $K_{oc}$ for metabolite diketo-metribuzin is necessary to finalise the ground water assessment.

Metribuzin is stable to hydrolysis in buffer solutions (pH 5, 6, 7 and 9) at 25 ºC. Photolysis may strongly contribute to the dissipation of metribuzin in water with half lives shorter than one day. Main photolysis metabolite is desamino-metribuzin (max. 83.8 % AR after 6 h). Metribuzin is proposed not to be ready biodegradable for classification purposes.

In water / sediment systems metribuzin was adsorbed to the sediment up to 13.6 –26 % AR and it dissipated from water phases with half lives of 31.1 to 52.6. In the whole systems it degrades with half lives of 47 – 50 d. Desamino-metribuzin was a major metabolite both in water (14.5 – 28. 7 % AR) and sediment (12.1 – 22.1 %). In one study a half life of 93 d in the whole system was proposed for this metabolite. In another study, half lives were estimated as 135.4 -284.1 d in the water and 87.6 – 90.6 d in the sediment. Mineralization was very low and non extractable radioactivity increased up to 38 % AR after 100 d.

The rapporteur Member State calculated $PEC_{SW}$ for metribuzin and desaminometribuzin based on spray drift loadings only. Run off and drain flow may need to be considered for the risk assessment, since from the calculations presented by one of the applicants these routes of entry to surface water may be as relevant or more than spray drift. For $PEC_{SED}$, the rapporteur Member State accepted the approach presented by one of the applicants. This calculation does not cover the worst case application rate of 1050 g / ha but $PEC_{SED}$ are actually not needed to finalize the aquatic risk assessment (driven by toxicity to Lemna and $PEC_{SW}$)

The rapporteur Member State produced new FOCUS GW calculations for metribuzin, diketo-metribuzin and desamino-diketo-metribuzin taking into consideration all available data from both applicants. In this calculation diketo-metribuzin exceeds the trigger 0.1 µg / L in one scenario and desamino-diketo-metribuzin in three scenarios of the nine FOCUS GW scenarios simulated. The meeting of MS experts identified a new data gap with respect to metabolite diketo-metribuzin for the necessary information (including experimentally derived Koc) to produce revised FOCUS GW assessment. Major soil photolysis metabolite desamino-metribuzin needs also to be addressed.

Relevance assessment for metabolite desamino-diketo-metribuzin and diketo-metribuzin may be then necessary. One of the applicants (Bayer) submitted a lysimeter study where leaching was investigated

after application of 5-$^{13}$C/$^{14}$C-metribuzin (applied at 500 g a.s / ha as WG 70 formulation). Metribuzin and diketo-metribuzin were below 0.01 µg / L. However, desamino-diketo-metribuzin amounted for 0.14 – 0.23 µg / L the first year and 0.09- 0.14 µg / L the second year. Two other metabolites were found in the leachate: 4-methyl-desamino-diketo-metribuzin (M17) and desmethylthio-metribuzin (U1). The meeting of MS experts identified a new data gap for the necessary information on metabolites 4-methyl-desamino-diketo-metribuzin and desmethylthio-metribuzin to undertake the FOCUS GW assessment and for the relevance assessment of metabolite desamino-diketo-metribuzin. Due to its properties, long range transport of metribuzin in the atmosphere is not expected.

A first tier high acute risk was identified for insectivorous and herbivorous birds and a high long-term risk to insectivorous birds and herbivorous mammals. The risk assessment for birds was refined by choosing the yellow hammer (*Emberiza citronella*) as representative of insectivorous birds and the grey partridge (*Perdix perdix*) as representative of herbivorous birds. Based on these refinements the risk to birds was considered to be low. It is noted by the EFSA that also the acute risk assessment was refined. For other active substances where a use in potato fields has been proposed the yellow wagtail (M*ontacilla flava*) has often been chosen as a focal species for insectivorous birds. In the PPR Panel opinion on metamidophos[3] it was concluded that yellow wagtails nest in potato fields and that some individuals may obtain close to 100% of their food within the treated field. It is therefore proposed by the EFSA that for a full assessment of the acute risk to birds also other bird species that might be relevant are considered at Member State level. The assessment of long-term risk to mammals was refined based on estimated $DT_{50}$ in green plant material and the risk was concluded to be low.

Metribuzin is very toxic to green algae and aquatic plants. For the most sensitive species, *Lemna gibba,* risk mitigation measures comparable to buffer zones of 15 m are required to meet the Annex VI trigger of 10. The risk to bees is low. An in-field risk to other non-target arthropods was identified. However, considering that the species of concern are leaf dwellers, that residues of metribuzin can be expected to disappear within a week and that the off-field risk is low, it was concluded that there is a potential for recovery within an ecologically relevant time period. The risk to earthworms, other soil macro-organism, soil micro-organisms and biological methods of sewage treatment is considered low. Risk mitigation comparable to a 5 m buffer zone is required to protect non-target plants outside the treated field.

**Key words: metribuzin, peer review, risk assessment, pesticide, herbicide**

[3] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from the Commission related to the evaluation of methamidophos in ecotoxicology in the context of Council Directive 91/414/EEC. The EFSA Journal (2004) 144, 1-50.
http://www.efsa.europa.eu/science/ppr/ppr_opinions/769_en.html

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## BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Metribuzin is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Germany as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Germany submitted the report of its initial evaluation of the dossier on metribuzin, hereafter referred to as the draft assessment report, to the EFSA on 23 August 2004. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the draft assessment report was distributed for consultation on 3 September 2004 to the Member States and the main applicants Bayer CropScience and Feinchemie Schwebda 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, representatives from Member States identified and agreed in an evaluation meeting on 18 May 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in September 2005. 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 with representatives from Member States on 8 June 2006 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 Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, 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 June 2005)
- the consultation report

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 19 June 2006)

Given the importance of the draft assessment report including its addendum (compiled version of June 2006 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

Metribuzin is the ISO common name for 4-amino-6-*tert*-butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one or 4-amino-6-*tert*-butyl-3-methylthio-1,2,4-triazin-5(4*H*)-one (IUPAC). Metribuzin belongs to the class of triazinone herbicides such as hexazinone and metamitron. It is a selective pre- and post-emergence herbicide acting primarily through root uptake. Its mode of action is by photosynthetic electron transport inhibition at the photosystem II receptor site

The representative formulated products for the evaluation were Sencor and Mistral both are water dispersible granule (WG) formulations containing 700 g/kg metribuzin. They are registered under different trade names in Europe.

The evaluation of the representative uses as a herbicide which comprises broadcast spraying to control some grasses and broad-leaved weeds in potatoes. The maximum total dose is 1.05 kg metribuzin per hectare.

## SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of metribuzin as manufactured should not be less than 930 g/kg, which is higher than the minimum purity given in the FAO specification 283/TC/S/F (1991) of 910 g/kg. The higher value relates to the submitted results of current batch analysis and not to any toxicological concern to increase the minimum purity.

According to the equivalence assessment of the different technical materials, the rapporteur Member State concluded that they cannot be regarded as chemically equivalent on the basis of a Tier I assessment. However, the different impurities and levels of impurities are not of toxicological concern (Tier II, Sanco/10597/2003 –rev.7 final2. An assessment of the ecotoxicological equivalence of the materials was conducted in an addendum but was not peer reviewed. Therefore for this reason a final conclusion on the equivalence of the two sources can not be made. The content of metribuzin in the representative formulation is 700 g/kg (pure).

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 metribuzin or the respective formulations.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of metribuzin in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data 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 definition, in food of plant origin (potato only) and surface water and air. The residue definitions for soil and ground water are not finalised. Depending on the final residue definition, it could be necessary to require further data. A method of analysis for products of animal origin is not required as no MRLs are proposed.

Residues in food can be determined with a multi-method (the German S19 method has been validated).
The methods of analysis for soil were GC-PND and HPLC-DAD for water they were HPLC-UV or DAD and for air HPLC-UV or GC-MS.

Methods for body fluids or tissues are not required as the active substance is neither classified as toxic or very toxic.

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material and some of the classification data.

# 2. Mammalian toxicology

Metribuzin was discussed in the EPCO expert meeting on toxicology in June-July 2005 (EPCO 28).

The rapporteur Member State indicated that the technical specifications from the two notifiers differed in the presence of one impurity. However, both notifiers submitted a full data package, with comparable results obtained with each. Therefore the two technical specifications were considered to be equivalent.

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

Metribuzin is rapidly and nearly completely absorbed after 36 hours from oral exposure, based on urinary and faecal excretion (40.4% and 51.8%, respectively) after oral and i.v. application. It is widely distributed with the highest concentrations in liver and kidney and the elimination half-lives in all tissues ranged between 18.4 and 33.6 hours. In general, more than 95% of the administered radioactivity was excreted via urine and faeces within 72 hours after dosing. Less than 0.1% of the orally administered radioactivity was excreted in expired air. Metabolism is extensive: main metabolites are desamino-metribuzin (DA)4, 6-tert-butyl-4,5-dihydro-1,2,4-triazin-5-one-3-mercapturic acid and t-BuOH-desamino-metribuzin.5

## 2.2. Acute toxicity

Metribuzin has a moderate acute oral toxicity (LD50 322 mg/kg bw) and low dermal and inhalation toxicity (LD50 > 5000 mg/kg bw and LC50 >2.0 mg/L, respectively). It is neither a skin and eye irritant nor a skin sensitiser. The classification as R22 (Harmful if swallowed) has been proposed.

## 2.3. Short term toxicity

The main target organs in short term toxicity studies were the liver and the kidney in rats, dogs and rabbits. In rats and rabbits the thyroid gland (changes in hormone levels) and in rats and dogs red blood cells were also affected at higher doses. An overall NOAEL of 2 mg/kg bw/day was derived.
The meeting considered that in a number of studies, serious adverse effects were noted at doses <50 mg/kg bw/day (dog, 3 month study at ~20 mg/kg bw/day and 1 year study at 50 mg/kg bw/day). The meeting considered that metribuzin potentially reached the requirement for classification as R 48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed". The issue was flagged to ISPRA for consideration.

## 2.4. Genotoxicity

Metribuzin did not exhibit a genotoxic potential in a range of in vivo and in vitro tests.

[4] desamino-metribuzin (DA, M01): 6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazine-5-(4H)-one
[5] t-BuOH-desamino-metribuzin (M05): 6-(1-hidroxy-1-methyl-ethyl)-3-methylsulfanyl-4H-[1,2,4]-triazine-5-one

## 2.5. LONG TERM TOXICITY

The liver was found to be the main target organ in rats, mice and dogs. In rats effects on thyroid (histology, T3 and T4 changes) were recorded, as after short-term exposure. The thyroid effects were interpreted in terms of a rodent-specific response due to liver enzyme induction. Neither functional impairment nor increased tumour incidence in the thyroid was noted. The overall NOAEL was set to 1.3 mg/kg bw/day, from the 2-year chronic toxicity/carcinogenicity studies in rat. Metribuzin did not show any evidence of a carcinogenic potential.

## 2.6. REPRODUCTIVE TOXICITY

The meeting discussed the multigeneration studies and developmental studies available and confirmed the NOAELs proposed by the rapporteur Member State (parental - offspring NOAELs 2.2 mg/kg bw/day, reproductive NOAEL 67 mg/kg bw/day, based on reduced body weight and food consumption at higher doses; developmental NOAEL <10 mg/kg bw/day and parental NOAEL <25 mg/kg bw/day). It was noted that there was no clear NOAEL for developmental toxicity, and that as a result an adequate margin of safety was required in the derivation of the reference doses.

The meeting discussed the potential classification of metribuzin in relation to reproductive/developmental endpoints. Delays in skeletal ossification were considered to be related to decreased bodyweight, rather than developmental toxicity. The increased pup mortality in the multigeneration study was considered, and the meeting concluded that this issue should be flagged to ISPRA for **possible classification as R62/63,** together with the alterations in ureter and kidney in rats, which could be potentially considered malformations.

## 2.7. NEUROTOXICITY

No specific neurotoxic effects were observed in acute and subchronic neurotoxicity studies in rats. The observed effects in the acute neurotoxicity study, i.e. decreased motor and locomotor activity, ptosis, oral staining and reduced body temperature at the dose of 5.2 mg/kg bw, were considered to be related to the general toxicity of this compound. The NOAEL for general toxicity was found to be >2 mg/kg bw, while it was 100 mg/kg bw/day and 70 mg/kg bw/day for acute and subchronic neurotoxicity, respectively.

## 2.8. FURTHER STUDIES

Metabolites

Plant and animal metabolites

The acute oral toxicity of the four main plant and animal metabolites t-BuOH-DADKmetribuzin, desamino-diketo-metribuzin (DADK)[6], desamino-metribuzin (DA) and diketo-metribuzin (DK)[7] was assessed. The respective $LD_{50}$ are > 2000 mg/kg, 700 mg/kg, 468 mg/kg and 266 mg/kg.

The toxicological properties of the metabolite desaminodiketo-metribuzin were also investigated in a subacute gavage study in rats: the NOAEL was established at 5 mg/kg bw/d based on clinical signs

[6] desamino-diketo-metribuzin (DADK, M03): 6-(1,1-dimethylethyl)-1,2,4-triazine-3,5(2H,4H)-dione

[7] diketo-metribuzin (DK, M02): 4-amino-6-(1,1-dimethylethyl)-1,2,4-triazine-3,5(2H,4H)-dione

observed at 30 and 150 mg/kg bw/d; no genotoxic potential was found. Desaminodiketo-metribuzin was negative in the genotoxicity tests.

Groundwater metabolites

The toxicological significance of the groundwater metabolites diketo-metribuzin, desmethylthio-metribuzin[8] (U1) and 4-methyl-desamino-diketo-metribuzin[9] (M17) was considered. Diketo-metribuzin is a significant rat metabolite, and is of higher acute oral toxicity than metribuzin. No data was available for desmethylthio-metribuzin (U1) and 4-methyl-desamino-diketo-metribuzin (M17), which are not rat metabolites. A new data requirement was therefore set for the notifier(s) to address their potential toxicity.

In summary, based on the assessment of metabolites in groundwater, the following data gaps were identified:

- assessment of the acute toxicity, genotoxicity and reproductive toxicity potential of metabolite U1;
- assessment of the genotoxic and reproductive toxicity potential of DK-metribuzin;
- assessment of the reproductive toxicity potential of DADK-metribuzin;

In case the FOCUS trigger is exceeded, there might be the need of addressing genotoxicity and reproductive toxicity potential of DA-metribuzin and M17 metabolite

## 2.9. MEDICAL DATA

The routine medical examinations of plant personnel which have been performed since 1976 did not indicate any specific adverse effects on the health of employees.

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

ADI

The ADI for metribuzin was established at 0.013 mg/kg bw/day, based on the NOAEL of 1.3 mg/kg bw/day from the chronic toxicity/carcinogenicity study in rats, with an assessment factor of 100.

AOEL

The AOEL for metribuzin is 0.02 mg/kg bw/day, based on the overall short term NOAEL of 2 mg/kg bw/day, with an assessment factor of 100.

ARfD

The ARfD for metribuzin is 0.02 mg/kg bw/day, based on the NOAEL of 2 mg/kg bw/day from the acute neurotoxicity study, with an assessment factor of 100.

[8] desmethythio-metribuzin: 4-amino-6-(1,1-dimethylethyl)-1,2,4-triazine-5(4H)-one
[9] 4-methyl-desamino-diketo-metribuzin: 4-methyl-6-(1,1-dimethylethyl)-1,2,4-triazine-3,5(2H,4H)-dione

## 2.11. DERMAL ABSORPTION

No data was available for Mistral and therefore a default value of 100% was allocated by the experts. For Sencor, values of 50% for the concentrate and 70% for the dilution were derived, based on *in vivo* rat data corrected by *in vitro* rat/human data, by a factor of 1.5-1.8 and 1.7-3 for the concentrate and the diluted formulation, respectively.

## 2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Metribuzin is intended to be used as a pre- and post-emergence selective herbicide in potatoes. The maximum application rate for Mistral is 0.525 kg/ha in pre-emergence and 0.35 kg/ha in post-emergence, in 200-400 L water/ha; for Sencor the maximum application rate is 1.05 kg/ha in 200-700 L water/ha.
Both notifiers support a 70 % WG preparation (Bayer CropScience: Metribuzin WG 70; Feinchemie: Mistral) with metribuzin as the only active substance proposed to be applied.

DAR
According to the assessment in the DAR (50% default dermal absorption) the operator exposure for the BCS formulation exceeded the AOEL even when PPE is worn (136%, German model). On the basis of an exposure study with fenthin-hydroxide in potatoes, the exposure would represent the 47.5% of the AOEL with the use of PPE.

For the Feinchemie formulation (Mistral), according to the assessment in the DAR (50% default dermal absorption), the estimated operator exposure is below the AOEL (68%, German model) when PPE such as gloves during mixing/loading and application and standard protective garment during application is worn.

Worker and bystander exposure were considered to be below the AOEL.

Recalculations according to the EPCO outcomes
The rapporteur Member State was asked to re-calculate operator, worker and bystander exposure on the basis of the EPCO meeting's outcomes, with regard to the dermal absorption values. Further, it was asked to provide an explanation on the representativeness and rational for the use of the field study.
In June 2006 the rapporteur Member State submitted a revised list of end points with the results of the operator exposure assessment. No addendum was submitted and calculations are not presented. According to the proposal made by the rapporteur Member State, the estimated operator exposure for application of Mistral in post-emergence (application rate 0.35 kg/ha) would be 86% of the AOEL with the use of PPE (gloves during mixing/loading and application and garment and sturdy footwear during application); the estimated exposure would be 75% of the AOEL with use of PPE for the re-entry workers and 20.5% of the AOEL for bystanders.

However, the operator risk assessment should be considered as inconclusive due to the lack of transparency and since the calculations were not made available for peer review in due time.

EFSA note: an addendum with the re-calculated operator, worker and bystander risk assessment was made available after the last EWG in addendum 7 (June 2006), but not peer reviewed.

# 3. Residues

EPCO expert meeting on residues in September 2005 (EPCO 34).

## 3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

### 3.1.1. PRIMARY CROPS

The metabolism of metribuzin has been investigated in wheat, soybeans and potatoes. The product was applied either in pre-emergence of the crop (soybean and potatoes) or in post-emergence (wheat). It can be considered that the information provided is appropriate for the supported representative use in potatoes. The studies demonstrated that the metabolic pathway is qualitatively similar in all crops investigated. The metabolism of metribuzin proceeds via the following pathways:

- Desamination (formation of metabolite desamino-metribuzin (M01 or DA)
- hydroxylation at the ter-butyl side chain (formation of metabolite M09)[10]
- hydrolytic or aminolytic cleavage of the thioalkyl moiety (formation of metabolites diketo-metribuzin (M02 or DK) and desamino-diketo-metribuzin (M03 or DADK)
- conjugation
- combination of the here above mentioned reactions (formation of metabolites M04, M05 and M08)[11,12,13]
- total breakdown of the triazinone ring and incorporation of the $^{14}C$ into glucose and fructose.

In a separate translocation experiment with grapes it was shown that only trace amounts of the radioactivity applied was translocated.

The residue pattern observed in these metabolism studies show different residue-amounts of parent and metabolites, depending on the crop. In potatoes about 60 % of the total residues were identified, with 20 % of the total residue being metribuzin. Three metabolites accounted together for an amount comparable to that of the parent compound (metabolites desamino-metribuzin, diketo-metribuzin and desamino-diketo-metribuzin). In soybeans only 1.2 % of the parent substance was found while the total identified amount was 55.9 % of the residues. In wheat grain and straw 9.3 % and 24.2 % respectively of the residues were identified, with parent compound representing about 15-20 % of the material identified. Because the crops tested showed varying ratio's of parent to metabolites no conclusion could be drawn for a residue definition applicable to all crop groups. In particular the parent compound may not be an appropriate choice as indicator compound of the residue situation in

[10] M09: 4-amino-6-(2,2-dimethylethyl-ethanol)-3-methylthio)-1,2,4-triazin-5-(4H)-one
[11] M04: 6-(2,2-dimethyl-ethanol)-1,2,4-triazine-3,5(2H,4H)-dione
[12] M05: 6-(2,2-dimethyl-ethanol)-3-(methylthio)-1,2,4-triazine-5-(4H)-one
[13] M08: 4-amino-6-(2,2-dimethyl-ethanol)-1,2,4-triazine-3,5(2H,4H)-dione

certain crops. Therefore as the representative crop is potatoes the following residue definition applies to potatoes only. For monitoring purposes metribuzin and for risk assessment the sum of metribuzin, metabolite desamino-metribuzin, metabolite diketo-metribuzin and metabolite desamino-diketo-metribuzin, expressed as metribuzin. The inclusion of metabolites in the residue definition for risk assessment is based on the fact that the information provided does not authorise to exclude that they cause the same toxic effects as the parent compound. Therefore these metabolites are considered to be characterised by the same toxicological end points as the parent compound (ADI and ARfD). A conversion factor of 2 has been proposed for conversion of monitoring residue levels of metribuzin to levels for risk assessment purposes.

The magnitude of metribuzin residues was examined in 16 supervised residue trials in the North of Europe of these 5 were analysed for the risk assessment residue definition. In the South of Europe 8 supervised trials were carried out where only metribuzin was analysed for. Nine trials in the North and 2 in the South were considered reflecting the proposed PHI of 42 days. However the experts in EPCO 34 September 2005 considered the other trials with longer PHI representative of the common use of the product. In all these trials residues of metribuzin were consistently below the Limit of Quantification of the method of analysis (0.05 or 0.04 mg/kg, depending on the trial). Similarly levels of metabolites analysed in 5 of the Northern trials were not detectable. The rapporteur Member State and the expert meeting (EPCO 34) concluded that sufficient information was available for the purpose of setting a MRL and for risk assessment purposes. Freezer storage stability of metribuzin and its metabolites desamino-metribuzin, diketo-metribuzin and desamino-diketometribuzin was examined in potato tubers. The results demonstrate that the residues of metribuzin are stable when stored at -5°C or below for at least 24 months.

Due to the very low residue level in the raw agricultural commodity when metribuzin is used according to GAP for the supported representative use, no residues are expected in processed commodities.

### 3.1.2. SUCCEEDING AND ROTATIONAL CROPS

In several laboratory studies the degradation behaviour of metribuzin in soils was investigated. For metribuzin, the calculated $DT_{50}$ values were in the range from 5.2 to 22.4 days, whereas the DT90 ranged from 17.6 to 80.7 days. For desamino-diketo-metribuzin, the calculated $DT_{50}$ values ranged from 20.6 to 28.8 days indicating a DT90 value of approx. 100 days. The metabolism studies showed, that metribuzin is not accumulated in the plant. If after 100 days, less than 10% of residues is present, further testing can be dispensed with, if it is known that the residues are not accumulated in the plant. Additional studies on grapes showed, that metribuzin and its soil metabolites are not taken up or translocated by the plants. It was therefore concluded that it is highly unlikely that any significant residues of metribuzin and its metabolites will be present as residues in rotational crops.

### 3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

As no significant residues are expected to be present in products intended for livestock consumption, metabolism studies are not in principle required. However, a goat metabolism study was submitted and evaluated, but no residue definition for animal products needs to be proposed.

This lactating goats study showed that in muscle and fat the residue of parent metribuzin is the major substance. In milk metribuzin is also present but metabolite sulfamate-metribuzin (M15)[14] is the main compound found. Metribuzin is not fat-soluble (log POW at 22 °C is 1.7) and during the biotransformation it forms even more polar conjugates. Based on the supervised residue trial data in potatoes no residues above the LOQ occur. Therefore, no residues are to be expected in animal products and no livestock feeding studies are required.

### 3.3. CONSUMER RISK ASSESSMENT

The chronic dietary exposure assessment has been based on the Theoretical Maximum Daily intake (TMDI) calculation of WHO using the WHO typical European diet for adult consumers and the German national diet (VELS-model) for the 4-6 year old girl. Residues in potatoes were taken to be at 0.05 mg/kg which using the conversion factor of 2 gives a relevant residue level for risk assessment of 0.1 mg/kg. The calculated intakes using the WHO model were 4.52 % of the ADI and 1.97 % using the German VELS-model.

The acute exposure to residues of metribuzin and its metabolites in potatoes has been assessed according to the WHO model for conducting National Estimates of Short Term Intakes (NESTI) calculations. Large portion consumption data from the national German VELS-model and from the national UK-model intakes were used. Calculations were carried out considering a residue level of 0.1 mg/kg in composite samples of treated potatoes (Level of the proposed MRL multiplied by the conversion factor of 2). NESTI calculated in that basis were 24 % and 76.9 % of the ARfD (UK infant had the highest intake) for the German and UK models respectively.

### 3.4. PROPOSED MRLS

Based on the available database, a MRL of 0.05* mg/kg for potatoes is proposed to cover the representative use reported for this crop.

## 4. Environmental fate and behaviour

Metribuzin was discussed in the meeting of MS experts on fate and behaviour in the environment EPCO 31 on basis of the DAR, the addendum 1 to Vol. 3, rev 1 and the updated list of end points.

### 4.1. Fate and behaviour in soil

#### 4.1.1. Route of degradation in soil

Route of degradation of metribuzin in soil under dark aerobic conditions at 20 ºC was investigated in one study with four soils (pH 6.4 – 7.6, clay 5 – 12.9 %, OC 0.97 – 1.55 %; 48 % MWHC) using 5-

[14] M15: sulfamate-metribuzin

$^{13}C/^{14}C$-metribuzin and with one soil (pH 5.7[15], clay 12.1 %, OC 2.32 %; 40 % MWHC) using 6-$^{14}C$-metribuzin. Main transformations metribuzin undergoes under these conditions are desamination and substitution of the thioether group by a ketone to deal the major metabolites **diketo-metribuzin** (DK, M02; max. 9.7 % AR after 7-21 d) and **desamino-diketo-metribuzin** (DADK, M03; max. 16.7 % AR after 21 d). Bound residues amounted up to 65.3 % AR after 71 d and $CO_2$ up to 38.9 % AR at the en of the study after 126 d.

Two degradation studies in soil under dark anaerobic conditions with 5-$^{13}C/^{14}C$-metribuzin are available. Same metabolites identified in aerobic degradation studies were found in these studies.

Photolysis in soil was investigated in one study under natural sunlight in Stilwell, Kansas, USA (38.8 ºN) from May 30, 1989 through June 30, 1989. Temperature was maintained below 30 ºC in the irradiated and dark control module. Four metabolites **desamino-metribuzin** (DA, max. 21.5 % AR), polar I (max 4.6 % AR), apolar I (max. 8.4 % AR) and apolar II (max. 5.3 % AR) reached the maximum at the end of the study (13 d). These metabolites were either not found (apolar I and II) or found at very low levels (desaminometribuzin and polar I) in the dark control. During the preparation of the conclusion, EFSA proposed that consistence with previous assessments would require to address the major photolysis metabolite desamino-metribuzin with respect to potential contamination of soil and ground water. The rapporteur Member State disagreed with EFSA proposal based on the fact that metabolite/degradate formation rates in soil photolysis studies do reflect the unrealistic conditions of the study (thin soil layer of only 1 mm thickness was exposed to strong sunlight) rather than realistic conditions on arable fields and the absence of concurrent biodegradation (substantiated by a calculated half life of 1254 d for metribuzin in the dark control). In the rapporteur Member State's opinion the photolysis studies should be assessed qualitatively. EFSA agrees that, as already seen in similar situations; the guidance photolysis study in soil does not represent realistic conditions and should not be considered quantitatively but only qualitatively. However, qualitative assessment of the level observed for the major photolysis metabolite (21.5 % AR) and the representative uses proposed (which includes pre-emergence spraying on Southern EU fields) does not allow to exclude that desamino-metribuzin will reach 10 % of applied metribuzin in molar bases under realistic conditions of use. Therefore, EFSA confirms that major soil photolysis metabolite desamino-metribuzin needs to be addressed with respect of soil and ground water compartments. Weather this assessment will need further experimental data to be generated may be the subject of a separated analysis. The fact that desamino-metribuzin is found also as a minor soil metabolite under dark aerobic conditions and that it has been identified as a metabolite of metribuzin in different organism should be taken into consideration in the respective ground water and ecotoxicological assessments.

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

Rate of degradation of metribuzin in soil under dark aerobic conditions was investigated in the same studies employed to investigate the route of degradation. Additionally, degradation in soil under dark

[15] pH not found in the DAR and provided by the rapporteur Member State in their comments to the conclusion.

aerobic conditions was investigated in a non labelled study at a higher application rate (520 µg / Kg soil ≈ 525 g a.s. / ha) with four soils (pH 6.0 – 6.6, clay 2.5 – 10.9 %, OC 0.6 – 3.5 %; 40 % MWHC). In these studies, metribuzin shows to be low to moderate persistent in soil ($DT_{50}$ = 5.3 – 17.7 d).

Rate of degradation of [5-$^{14}$C]desamino-diketo-metribuzin was investigated under dark aerobic conditions at 20 ºC in one study with three soils (pH 6.9 – 8.5, clay 5.0 – 34.7 %, OC 0.97 – 1.60; 45 – 54 % MWHC). According this study desamino-diketo-metribuzin is low to moderate persistent in soil ($DT_{50}$ = 9.1 – 22.1 d).

Rate of degradation of metabolite diketo-metribuzin was determined with the data in the studies performed with the labelled parent compound. This metabolite is moderately persistent in soil under aerobic conditions ($DT_{50}$ = 29.9 – 48.6 d). However, fitting procedures, kinetic employed and goodness of fitting are not reported and assessed in the DAR. At the time of writing the conclusion, EFSA required the rapporteur Member State to clarify the kinetic procedure employed to obtain these values. The rapporteur Member State informed EFSA that no records were available and that it was not possible to provide the information on time to be included in this conclusion. Therefore, these values should be taken with caution. A footnote has been added in the list of end points to indicate that the reliability of these values can not be confirmed.

In the study performed in soil under dark anaerobic conditions metribuzin showed to be highly persistent ($DT_{50}$ = 109 d).

PEC in soil of metribuzin, diketo-metribuzin and desamino-diketo-metribuzin were calculated by the rapporteur Member State using the common soil dilution approach for the worst case GAP (pre-emergence, 1.05 Kg a.s. /ha). However, 90$^{th}$ percentile half lives were used instead of worst case. This deviation from common practice was discussed in the meeting of MS experts. The meeting agreed that this is not the common used approach for the EU risk assessment but that in this particular case the impact on the calculated $PEC_S$ will be negligible. Therefore, no new calculations were required to finalize the EU risk assessment.

### 4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Three studies with a total of eighth batch soil adsorption / desorption experiments are available for metribuzin. Seven of these experiments were considered valid. Metribuzin may be classified as high to very high mobile in soil ($K_{oc}$ = 24.3 – 106.0 mL / g). Adsorption / desorption in soil of metabolite desamino-diketo-metribuzin was investigated in one study with four soils. This metabolite is high mobile in soil ($K_{oc}$ = 60.3 – 116.8 mL / g). The meeting of MS experts identified the need for experimental derived $K_{oc}$ for metabolite diketo-metribuzin.

## 4.2. Fate and behaviour in water

### 4.2.1. Surface water and sediment

Metribuzin is stable to hydrolysis in buffer solutions (pH 5, 6, 7 and 9) at 25 ºC. At elevated temperatures (50 – 70 ºC) some degradation was observed in the experiments performed at pH 9. Half life extrapolated at 20 ºC and pH 9 would be 1317 d.

Aqueous photolysis was investigated and quantum yield calculated in different studies performed with natural or artificial light by both applicants. All these studies consistently demonstrated that

photolysis may contribute to the dissipation of metribuzin in water with half lives shorter than one day. Main photolysis metabolite is **desamino-metribuzin** (DA, max. 83.8 % AR after 6 h).
Ready biodegradability test is not available for metribuzin. Metribuzin is considered not to be ready biodegradable for classification purposes.
Dissipation of 6-$^{14}$C-metribuzin in water sediment was investigated in one study with two dark water / sediment systems ($pH_{WATER}$ 7.8 – 8.3; $pH_{SED}$ 7.13-7.15) at 20 ºC. Both systems exhibited very similar behaviour. Metribuzin was adsorbed to the sediment up to 26 % AR after two weeks. It dissipated from water phases with a half life of 41 d and degrades in the whole systems with half lives of 47 – 50 d. Desaminometribuzin was a major metabolite both in water (14.5 – 22. 3 % AR) and sediment (15.0 – 22.1 %). From data in this study a half life of 93 d for desaminometribuzin was proposed assuming formation and degradation according first order kinetics. Observation of the fitting curve indicates that reliability of this value is limited due to the deviation of the fitted curve form actual data points and to the fact that there is not decrease of the amount of desaminometribuzin during the whole experiment. Mineralization was very low with a maximum of 1.8 % AR after 201 – 202 d. Non extractable radioactivity increased up to 23 – 28 % AR at the end of the study (201-202 d).
In another study, dissipation of 5-$^{14}$C-metribuzin was investigated in two dark water / sediment systems ($pH_{SED}$ 5.4-7.4) at 20 ºC. Metribuzin was adsorbed to the sediment to levels of 13.6 – 19.0 % AR after one or two weeks. It dissipated from water phase with half lives of 31.1 and 52.6 d and from the sediment with half lives of 20 d. Desamino-metribuzin reached maximum amounts of 21.8 -28.7 % AR in the water and 12.1 – 21.2 % AR in the sediment at the end of the study (100 d). Half lives were estimated as 135.4 -284.1 d in the water and 87.6 – 90.6 d in the sediment. Mineralization was low (2.1 – 3.5 % after 100 d) and a considerable amount of unextractable residues were formed in the sediment (21.9 – 38 % AR after 100 d).
The rapporteur Member State calculated $PEC_{SW}$ for metribuzin and desamino-metribuzin based on spray drift loadings only with worst case assumptions with respect to application rate (1050 g / ha) and half lives. These values were used for the risk assessment presented in the DAR. However, run off and drain flow may need to be considered for the risk assessment, since from the calculations presented by one of the applicants (based on a non standard approach) these routes of entry to surface water may be as relevant or more with respect to its potential contamination. For $PEC_{SED}$, the rapporteur Member State accepted the approach presented by one of the applicants based on standard spray drift loadings and non standard estimation of run off and drainflow. This calculation does not cover the worst case application rate of 1050 g / ha but $PEC_{SED}$ are actually not needed to finalize the aquatic risk assessment (driven by toxicity to Lemna and $PEC_{SW}$)

### 4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

Both applicants presented FOCUS PELMO (v. 1.1.1 or v.2.2.2) calculations of the 80$^{th}$ percentile annual average concentration of metribuzin in the leachate at 1 m depth for the nine FOCUS GW scenarios. However, in both cases application of the product every third year was assumed. The rapporteur Member State considered that this does not corresponds to the first tier approach used for the EU risk assessment and produced new calculations for metribuzin, diketo-metribuzin and

desamino-diketo-metribuzin. Median half lives were used for metribuzin ($DT_{50}$ = 9.6 d) and diketo-metribuzin ($DT_{50}$ = 42.3 d) and geometric mean for desamino-diketo-metribuzin ($DT_{50}$ = 14.3 d) (the calculations of the rapporteur Member State make use of all available data from both notifiers). For diketo-metribuzin a $K_{oc}$ = 98.6 L / kg was assumed, based on a PcKocWin v. 1.66 estimation. In this calculation diketo-metribuzin exceeds the trigger 0.1 µg / L in one scenario and desamino-diketo-metribuzin in three scenarios. The meeting of MS experts identified a new data gap with respect to metabolite diketo-metribuzin for the necessary information (including experimentally derived Koc) to produce revised FOCUS GW assessment. Major soil photolysis metabolite desamino-metribuzin needs also to be addressed. Relevance assessment for metabolite desamino-diketo-metribuzin and diketo-metribuzin will be then necessary.

One of the applicants (Bayer) submitted a lysimeter study with two undisturbed soil cores where leaching was investigated for two years after application of 5-$^{13}C/^{14}C$-metribuzin (applied at 500 g a.s / ha as WG 70 formulation). Potatoes were followed by winter wheat and winter barley. The radioactive residue in the leachate was analyzed for metribuzin and its main soil metabolites. Product was applied to potatoes on the first experimental season. Metribuzin and diketo-metribuzin were below 0.01 µg / L. However, desamino-diketo-metribuzin amounted for 0.14 – 0.23 µg / L the first year and 0.09- 0.14 µg / L the second year. Two other metabolites were found in the leachate: **4-methyl-desamino-diketo-metribuzin**[16] (M17, at levels of 0.05 – 0.06 µg / L the first year and 0.06 – 0.07 µg / L the second year) and **desmethylthio-metribuzin**[17] (U1, at levels of 0.05 µg / L and 0.09 – 0.1 µg / L). The relevance of the lysimeter study with respect to the EU risk assessment was discussed by the meeting of MS experts. The meeting identified a new data gap for the necessary information on metabolites 4-methyl-desamino-diketo-metribuzin and desmethylthio-metribuzin to undertake the FOCUS GW assessment (pre-emergence application of 1.05 kg a.s. / ha should be modelled) and for the relevance assessment of metabolite desamino-diketo-metribuzin.

### 4.3. Fate and behaviour in air

Vapour pressure of metribuzin was estimated to be $1.21 \cdot 10^{-4}$ Pa at 20 ºC and Henry Law constant was calculated to be $2.0 \cdot 10^{-5}$ Pa m3 mol-1. The photo-oxidative degradation in the atmosphere was calculated to be 21 h. Therefore, long range transport of metribuzin in the atmosphere is not expected.

## 5. Ecotoxicology

Metribuzin was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 32) in September 2006.

The two specifications of the technical material presented by the two applicants differ in their content of two impurities. The rapporteur Member State assessed the equivalence of the two sources from an ecotoxicological point of view in addendum 1 of August 2005. No specific differences between the tests presented by the two applicants in their toxicity towards algae, aquatic invertebrates, fish, and

[16] 4-methyl-desamino-diketo-metribuzin: 4-methyl-6-(1,1-dimethylethyl)-1,2,4-triazine-3,5(2H,4H)-dione
[17] desmethythio-metribuzin: 4-amino-6-(1,1-dimethylethyl)-1,2,4-triazine-5(4H)-one

earthworms were noted. Due to the lack of comparable data, no comparison of the toxicity of the two specifications was possible for terrestrial plants, birds, arthropods and other soil organisms than earthworms. In addendum 5 of March 2006, the rapporteur Member State presents an assessment for these groups of organisms based on a weight of evidence approach. The assessment has not been peer reviewed, but the EFSA agrees to the rapporteur Member State conclusion that that the ecotoxicological profile of the different specifications of technical metribuzin is not determined by their content of those impurities. The specifications can thus be considered equivalent with respect to ecotoxicity.

## 5.1. Risk to terrestrial vertebrates

Valid toxicity studies are available to assess risk to terrestrial vertebrates from exposure to metribuzin. No bird acute toxicity study with the formulation is available. However the data available from the toxicology section does not indicate that the toxicity to mammals of the formulation is higher than expected from the content of metribuzin. Therefore, no further toxicity studies with birds are considered necessary.

The representative evaluated use of metribuzin is as herbicide in potato. The risk to birds and mammals was assessed based on exposure to metribuzin by intake of contaminated insects, vegetation (weeds) and possibly earthworms as well as contaminated drinking water. Two scenarios of exposure was considered; single pre-emergence application of 1.05 kg a.s./ha and single post-emergence application of 0.35 kg a.s./ha.

The first tier risk to generic species, representing insectivorous and herbivorous birds as well as herbivorous mammals was assessed according to the scenario 'leafy crops' in SANCO/ 4145/2000. In the pre-emergence scenario, the product is applied to bare soil and therefore only insectivorous birds were considered. The acute TER values for both insectivorous and herbivorous birds are below the Annex VI trigger (7.1 and 2.9). The long-term TER value for insectivorous birds is 0.9 and thus also below the trigger. For herbivorous mammals the long-term TER is below the trigger (TER=1.1).

The rapporteur Member State proposed to refine the assessment for birds by assuming the grey partridge (*Perdix perdix*) as representative for herbivorous birds in arable farmland[18]. The proportion of diet obtained in the treated area (PT) was set to 0.5 based on literature data[19]. The fraction of food type in diet (PD) for grey partridge was refined to 62% green plant material, 34% seeds and 4% insects based on data from the work of Dwenger *et al.*[20] No contamination of seeds was assumed. The yellowhammer (*Emberiza citronella*) was chosen by the rapporteur Member State as focal species representing insectivorous birds. Refinement of the PT factor to 0.5 was based on available

[18] Glutz von Blotzheim, U. *et al.* (1994), *Perdix perdix* (Linné 1758) – Rebhuhn. Handbuch der Vögel Mitteleuropas, Aula Verlag, Wiesbaden, vol. 14/III, 1997, p. 247-281

[19] Glänzer, U. *et al.*(1993), Rebhuhn-Forschung in Baden-Würtenberg mit Schwerpunkt im Strohgäu bei Ludwigsburg. Beihefte zu den Veröffenlichungen für Naturschuts und Landschaftspflege in Baden- Würtenberg, 70, 1993, 1-108

[20] Dwenger, R. *et al.* (1991), Das Rebhuhn *Perdix perdix*. A. Ziemsen Verlag, Wittenberg 1991

descriptive information on habitat use in the literature. The PD factor was refined based on literature data (82% large insects, 12% small insects, 6% cereals)[21]. Feed intake rate (FIR/bw) for insectivorous birds was calculated in accordance with Appendix 1 to the guidance document for birds and mammals (SANCO/4145/2000). Based on these refinements the risk to birds was considered to be low.

It is noted by the EFSA that also the acute risk assessment was refined with the focal species mentioned above. For other active substances, where a use in potato fields has been proposed, the yellow wagtail (*Motacilla flava*) has often been used as a focal species for insectivorous birds. In the PPR Panel opinion on metamidophos[22] it was concluded that yellow wagtails nest in potato fields and that some individuals may obtain close to 100% of their food within the treated field. It is therefore proposed by the EFSA that for a full assessment of the acute risk to birds also other bird species that might be relevant are considered at Member State level. Even though metribuzin is an herbicide, toxic effects including mortality was observed in the acute study with bobwhite quail. A risk assessment using the yellow wagtail as focal species with a diet composed of a mixture of large and small insects was provided by the rapporteur Member State in addendum 6 of May 2006, but has not been peer reviewed.

The assessment of long-term risk to mammals was refined based on estimated $DT_{50}$ in green plant material. Given a $DT_{50}$ of 1.13 days a refined TER value of 37.7 was obtained and hence the risk was concluded to be low.

No assessment of the risk from intake of contaminated drinking water was presented in the DAR. The EFSA proposes that such an assessment is done, or that a solid argumentation why the risk is can be considered to be low is given.

The $logP_{ow}$ for metribuzin <3 and hence the potential for bioaccumulation and secondary poisoning is considered as low.

## 5.2. Risk to aquatic organisms

Based on the available acute toxicity data, metribuzin is classified as very toxic to aquatic organisms, with an $EC_{50}$ of 0.02 mg/L for *Scenedesmus subspicatus* and an $EC_{50}$ of 0.00079 mg/L for *Lemna gibba*, the most sensitive species tested. Based on data for *S. subspicatus*, the formulations 'Sencor WG' and 'Mistral' were not more toxic than expected based on the content of metribuzin.

[21] Glutz von Blotzheim and Bauer (1997), *Emrezia citronella* (Linné 1758)_Goldammmer, Handbuch der Vögel Mitteleuropas, Aula Verlag, Wiesbaden, vol. 14/III, 1997, p. 1432-1485.

[22] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from the Commission related to the evaluation of methamidophos in ecotoxicology in the context of Council Directive 91/414/EEC. The EFSA Journal (2004) 144, 1-50. http://www.efsa.europa.eu/science/ppr/ppr_opinions/769_en.html

The first tier TER values were calculated based on $PEC_{sw}$ from spray drift assuming an application rate of 1.05 kg a.s./ha. For the most sensitive species *Lemna gibba* risk mitigation measures comparable to buffer zones of 15 m are required to meet the Annex VI trigger of 10. Since run-off and drainage might contribute to contamination of surface water the risk to the aquatic environment should be re-assessment at member State level taking also these routes of entry into account.

An available mesocosm study was discussed by the Member State experts. The rapporteur Member State proposed that a safety factor of 10 should be applied to the NOAEC derived in the study since it had some shortcomings such as insufficient replication and lack of species diversity for the most sensitive group of algae. Since an assessment based on the mesocosm result would lead to TER values quite similar to those based on laboratory data, the meeting proposed that the risk assessment is based on first tier data.

Metribuzin was detected in sediment at concentrations >10% of applied after 14 days in the water/sediment studies. However, since NOEC for *Daphnia* is >0.1 mg/L and the concentration in sediment was declining until end of the water/sediment study no further concern for sediment dwelling organism is considered necessary. A study on *Chironomus riparius* with the more stable metabolite desamino-metribuzin (DA) showed a low toxicity.

The metabolite desamino-metribuzin (DA) was detected in water and sediment above 10% of the applied amount in the water/sediment study. Studies are available showing 3 orders of magnitude lower toxicity to green algae and *Lemna gibba* compared to metribuzin, and similar toxicity to fish and aquatic invertebrates. Hence the risk from this metabolite is considered to be low.

The $logP_{ow}$ for metribuzin and its major metabolite DA is <3 and hence the potential for bioaccumulation and secondary poisoning is considered as low.

## 5.3. Risk to bees

The oral and contact toxicity to bees was tested with metribuzin technical and the formulations 'Metribuzin 70 WG and 'Mistral'. The oral and contact HQ quotients based on an application rate of 1.05 kg a.s/ha are below the trigger of 50. Two cage tests under semi field conditions confirm the low risk to bees.

## 5.4. Risk to other arthropod species

Tests on terrestrial arthropods were conducted with the formulations 'Mistral WG 70' or 'Sencor WG 70'. Hazard quotients (HQ) for in-field and off-field were calculated based on the $LR_{50}$ values obtained for *A. rhopalosiphi* and *Typhlodromus pyri*, obtained in glass plate tests. For the off-field assessment a drift rate of 2.77% at 1 m of the maximum application rate 1.05 kg a.s./ha were considered. A vegetation distribution factor of 5 and correction factor of 10 were applied for the off-field calculations. In-field HQ values were 16 and 14.4 for the two species respectively and hence clearly above the ESCORT II trigger of 2. The off-field HQ values of 0.89 and 0.81 are below the

trigger thus indicating a low risk outside the treated field. The vegetation distribution factor was discussed in the meeting with Member State experts and it was agreed that a factor of 10 as proposed in ESCORT II should be used for reasons of consistency between substances evaluated. Since the factor of 5 is worse case, this is however of minor importance for the conclusion of the off-field risk. HQ values calculated with a vegetation distribution factor of 10 are reported in addendum 5 of March 2006.

Additional laboratory tests using the lacewing, *Chrysoperla carnea,* the ground dwelling beetle, *Poecilius cupreus,* and the spider *Pardosa* spp. showed no significant effects. For *Coccinella septempunctata* an $LR_{50}$ of 385 g a.s./ha was determined. Extended laboratory studies on natural substrates with *A. rophalosiphi, T. pardosa* and *C. septempunctata* verifies the in-field risk. In an aged residue test with *T. pyri* 25% effect on mortality and 45% effect on reproduction was observed with 14 days ageing. After 28 days the effect on mortality had declined to 7.8% and no effect was observed on reproduction. Considering that the species of concern are leaf dwellers, that residues of metribuzin can be expected to disappear within a week (see 5.1) and the off-field risk is low, the Member State experts agreed that there is a potential for recovery within an ecologically relevant time period.

## 5.5. Risk to earthworms

The acute toxicity of metribuzin to earthworms is slight. The acute TER calculated based on initial $PEC_{soil}$ assuming a maximum application rate of 1.05 kg a.s./ha and no interception is 305 and thus well above the Annex VI trigger of 10. The $DT_{90}$ in soil is <100 days and only three applications are proposed. However, two studies on reproduction effects with the product Metribuzin WG 70 are available. In one of the studies effects on body weight were observed at 3.5 kg a.s./ha but no effects on offspring number. In the other study no significant effects on adults or offspring were observed at the highest concentration tested, 5.25 kg a.s./ha. The member state experts agreed that the NOEC of 5.25 could be considered as reliable. The resulting long-term TER is 5 which just meet the Annex VI trigger.

The acute TER values for the soil metabolites desamino-diketo-metribuzin (DADK) and diketo-metribuzin (DK) are >4450 and >7150 respectively, indicating a low acute risk. $DT_{50}$ for desamino-diketo-metribuzin (DADK) was determined to be in the range of 9 to 22 days in the soil degradation study, with a maximum concentration of 16.7% of applied after 21 days and thereafter decreasing. diketo-metribuzin (DK) was detected at a maximum concentration of 9.7% of applied after 21 days with $DT_{50}$ values indicating that the metabolite is not highly persistent. In light of the lower acute toxicity for the metabolites DADK and DK compared to metribuzin, no further studies are considered necessary. However, the risk from the photolysis metabolite desamino-metribuzin (DA), needs to be addressed since it cannot be excluded based on available data that this metabolite will appear as a major metabolite in soil under certain conditions.

## 5.6. Risk to other soil non-target macro-organisms

Since the $DT_{90}$ in soil for metribuzin is <100 days, additional studies on soil macro-organisms are not required according to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). Results from studies on reproduction of *Folsomia candida* with the soil metabolites desamino-diketo-metribuzin (DADK) and diketo-metribuzin (DK) detected in soil indicate that the risk from these metabolites to other soil macro-organisms is low. However, the risk from the photolysis metabolite, desamino-metribuzin (DA), needs to be addressed since it cannot be excluded based on available data that this metabolite will appear as a major metabolite in soil under certain conditions.

## 5.7. Risk to soil non-target micro-organisms

Metribuzin and the soil metabolite desamino-diketo-metribuzin (DADK) showed no effects >25% on soil respiration and nitrogen transformation after 28 days compared to the control. The metabolite diketo-metribuzin (DK) was only tested for effects on nitrogen transformation but showed no effects >25%. Since this metabolite appears already at day 0 and reached its peak between days 7 and 21 with decreasing levels thereafter it was probably present also in the study with metribuzin. Furthermore, the member state experts had no further concern since nitrate production rate in treated soil did not differ significantly from the control. However, the risk from the photolysis metabolite, desamino-metribuzin (DA), needs to be addressed since it cannot be excluded based on available data that this metabolite will appear as a major metabolite in soil under certain conditions.

## 5.8. Risk to other non-target-organisms (flora and fauna)

*Brassica napus* was the most sensitive species out of 10 tested for effects on seedling emergence and vegetative vigour. The $EC_{50}$ was determined to 12.3 g a.s/ha. In a study on vegetative vigour using the formulation 'Mistral' (70% WG) *Beta vulgaris* was more sensitive than *Brassica napus* ($EC_{50}$ 6.3 g a.s./ha).TER values calculated based on the lowest $EC_{50}$ and drift rates at different distances from the treated field indicate that the risk to terrestrial plants in the off-crop area is high. However, since data on 10 species were tested for seedling emergence and 13 for vegetative vigour a $HC_5$ from a species sensitive distribution was calculated. The lowest value was obtained was 10.87 for vegetative vigour. Since this value is above the drift rate calculated for 5 m, a buffer zone of 5 m would be sufficient to protect non-target plants off-field. The member state expert agreed that in line with the current guidance no uncertainty factor is required.

The soil metabolite desamino-diketo-metribuzin (DADK) might leach into ground water and reach concentrations >0.1 mg/L. Results from a test on herbicidal activity indicates that this metabolite can be classified as non relevant with respect to herbicidal activity.

## 5.9. Risk to biological methods of sewage treatment

Data from two available tests with formulations containing metribuzin demonstrate that metribuzin inhibits the respiratory activity of micro-organisms in sewage treatment plants at high concentrations ($EC_{50}$ 761/ml). However considering the concentration predicted for surface water the risk to biological methods of sewage treatment is low.

# 6. Residue definitions

**Soil**

Definitions for risk assessment: metribuzin, diketo-metribuzin, desamino-diketometribuzin and desamino-metribuzin (major photolysis metabolite).

Definitions for monitoring: metribuzin, desamino-metribuzin (pending to be addressed and assessed)

**Water**

**Ground water**

Definitions for exposure assessment: metribuzin, diketo-metribuzin, desamino-diketo-metribuzin, desmethyl-thio-metribuzin (U1), 4-methyl-desamino-diketo-metribuzin (M17) and desamino-metribuzin (major photolysis metabolite).

Definitions for monitoring: metribuzin, diketo-metribuzin (pending assessment), desamino-diketo-metribuzin (pending assessment), desmethyl-thio-metribuzin (U1) (pending assessment), 4-methyl-desamino-diketo-metribuzin (M17) (pending assessment) and desamino-metribuzin (major photolysis metabolite, pending assessment).

**Surface water**

Definitions for risk assessment: metribuzin, desamino-metribuzin

Definitions for monitoring: metribuzin

**Air**

Definitions for risk assessment: metribuzin

Definitions for monitoring: metribuzin

**Food of plant origin**

Definitions for risk assessment: sum of metribuzin, DA-metribuzin, DK-metribuzin and DADK-metribuzin, expressed as metribuzin

Definitions for monitoring: metribuzin

**Food of animal origin**

Definitions for risk assessment: no definition defined or required for the supported representative use.

Definitions for monitoring: no definition defined or required for the supported representative use.

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

**Soil**

| Compound (name and/or code) | Persistence | Ecotoxicology |
|---|---|---|
| Metribuzin | low to moderate persistent in soil ($DT_{50}$ = 5.3 – 17.7 d) | See 5.5 – 5.7 |
| Diketo-metribuzin (DK) | moderately persistent in soil under ($DT_{50}$ = 29.9 – 48.6 d)* | The risk to soil organisms was assessed in the DAR and considered to be low |
| Desamino-diketo-metribuzin (DADK) | low to moderate persistent in soil ($DT_{50}$ = 9.1 – 22.1 d) | The risk to soil organisms was assessed in the DAR and considered to be low |
| Desamino-metribuzin (DA) (major photolysis metabolite) | No data, needs to be assessed | No information available |

* Degradation parameters for diketo-metribuzin (DK), obtained from laboratory degradation in soil studies performed with the parent compound should be taken with caution since fitting procedures, kinetic employed and goodness of fitting are not reported and assessed in the DAR.

**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 relevance |
|---|---|---|---|---|---|
| Metribuzin | High to very high mobile ($K_{oc}$ = 24.3 – 106.0 mL / g) | FOCUS GW: No<br>Lysimeter: No (worst case application rate not covered) | Yes | Yes | Relevant |

| 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 relevance |
|---|---|---|---|---|---|
| Diketo-metribuzin (DK) | No data available | FOCUS: Yes (with estimated Koc, further modelling necessary)<br>Lysimeter: No (worst case application rate not covered) | No | $LD_{50}$ 266 mg/kg bw (Harmful if swallowed)<br>Genotoxicity and reproductive toxicity potential to be assessed | Not relevant. Studies available showing low toxicity to green algae, *Lemna gibba* and *Chironimus ripatius*. |
| Desamino-diketo-metribuzin (DADK) | High-mobile ($K_{oc}$ = 60.3 – 116.8 mL / g) | FOCUS: Yes, trigger of 0.1 µg / L exceeded in 3 of 9 scenarios.<br>Lysimeter: yes (worst case application rate not covered) | No | $LD_{50}$ 700 mg/kg bw (Harmful if swallowed)<br>28-d oral, rat: NOAEL: 5 mg/kg bw/d<br>No genotoxic potential *in vitro*<br>Reproductive toxicity potential to be assessed | Not relevant. Studies available showing lower toxicity to green algae and *Lemna gibba* and similar toxicity to fish and aquatic invertebrates. |
| Desmethyl-thio-metribuzin (U1) | No data available, data needed | FOCUS GW: No data available, data needed<br>Lysimeter: yes (worst case application rate not covered) | No data available | The acute toxicity, genotoxicity and reproductive toxicity potential to be assessed | No data available |
| 4-methyl-desamino-diketo-metribuzin (M17) | No data available, data needed | FOCUS GW: No data available, data needed<br>Lysimeter: No (worst case application rate not covered) | No data available | In case the 0.1 µg/L trigger is exceeded, there might be the need of addressing acute toxicity, genotoxicity and reproductive toxicity potential | No data available |

| 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 relevance |
|---|---|---|---|---|---|
| Desamino-metribuzin (major soil photolysis metabolite) | No data available, data needed. | No data available, data needed. | No data available | In case the 0.1 µg/L trigger is exceeded, there might be the need of addressing genotoxicity and reproductive toxicity potential | Not relevant. Studies available showing lower toxicity to green algae and *Lemna gibba* and similar toxicity to fish and aquatic invertebrates. |

**Surface water and sediment**

| Compound (name and/or code) | Ecotoxicology |
|---|---|
| Metribuzin (water and sediment) | See 5.2 |
| Desamino-metribuzin (water and sediment) | Studies available showing 3 orders of magnitude lower toxicity to green algae and *Lemna gibba* compared to metribuzin, and similar toxicity to fish and aquatic invertebrates. |

**Air**

| Compound (name and/or code) | Toxicology |
|---|---|
| Metribuzin | Low toxicity via inhalation ($LC_{50}$ 2.045 mg/L) |

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

- The ecotoxicological equivalence of the two sources should be assessed (relevant for all representative uses evaluated; an assessment is available in addendum 1 (August 2005) and addendum 5 (March 2006); addendum 5 has not been peer reviewed; refer to chapter 5)
- Depending on the final residue definition, it could be necessary to require further data (refer to chapter 1).
- Re-calculations operator, worker and bystander risk assessment (relevant for all representative uses, data gap identified during the EPCO experts' meeting; calculations were made available after the evaluation meeting in addendum 7 (June 2006), but not peer reviewed; refer to point 2.12).
- Assessment of the acute toxicity, genotoxicity and reproductive toxicity potential of metabolite U1. Assessment of the genotoxic and reproductive toxicity potential of DK-metribuzin. Assessment of the reproductive toxicity potential of DADK-metribuzin. In case the FOCUS trigger is exceeded, there might be the need of addressing genotoxicity and reproductive toxicity potential of DA-metribuzin and M17 metabolite (relevant for all representative uses; data gap identified during the EPCO experts' meeting for metabolites DK, U1, M17, and by EFSA while drafting the conclusion for DA-metribuzin and DADK metribuzin; refer to point 2.8).
- The necessary information (including experimental derived $K_{oc}$) for soil metabolite diketo-metribuzin needs to be produced to finalize the ground water assessment (relevant for all representative uses evaluated; date of availability not known; refer to point 4.2.2).
- The necessary information (including experimental derived $K_{oc}$) for the leachate metabolites found in the lysimeter study 4-methyl-desamino-diketo-metribuzin and desmethyl-metribuzin (relevant for all representative uses; date of availability not known; refer to point 4.2.2).
- Potential ground water contamination by the major soil photolysis metabolite desamino-metribuzin needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA while drafting the conclusion; date of availability not known; refer to points 4.2.2).
- The risk to soil organisms from exposure to the metabolite desamino-metribuzin (DA) needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA while drafting the conclusion; date of availability not known; refer to points 5.5 – 5.7).

## CONCLUSIONS AND RECOMMENDATIONS

### Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide as proposed by the applicants which comprises broadcast spraying to control some grasses and broad-leaved weeds in potatoes. The maximum total dose is 1.05 kg metribuzin per hectare.

The representative formulated products for the evaluation were Sencor and Mistral both are water dispersible granule formulations (WG) containg 700 g/kg metribuzin.

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of metribuzin in soil water and air.
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.

Metribuzin has a moderate acute oral toxicity and low dermal and inhalation toxicity. It is neither a skin and eye irritant nor a skin sensitiser. The classification as R22 (Harmful if swallowed) has been proposed. The meeting considered that metribuzin potentially reached the requirement for classification as [R22/48] since in a number of studies, serious adverse effects were noted at doses of >50 mg/kg bw/day. The issue was flagged to ISPRA for consideration. Metribuzin did not exhibit a genotoxic and carcinogenic potential. A possible classification as R62/63 was considered and forwarded to ISPRA based on delays in skeletal ossification, considered to be related to decreased bodyweight, rather than developmental toxicity, and alterations in kidneys and ureter, together with the increased pup mortality in the multigeneration study. The ADI for metribuzin was established at 0.013 mg/kg bw/day, based on the NOAEL of 1.3 mg/kg bw/day from the chronic toxicity/carcinogenicity study in rats, with an assessment factor of 100. The AOEL and ARfD are 0.02 mg/kg bw/day, based on the overall NOAEL of 2 mg/kg bw/day and on the acute neurotoxicity, respectively, with an assessment factor of 100. The operator risk assessment is inconclusive since the re-calculations provided by the rapporteur Member State lack of transparency and were not made available for peer review in due time.

The metabolism of metribuzin has been investigated in potatoes, soybeans and wheat. Similar metabolic pathways were identified but different residue-amounts of parent and metabolites, depending on the crop, were observed. In potatoes about 60 % of the total residues were identified, with 20 % of the total residue being metribuzin. Three metabolites were present representing a global toxicological burden expected to be similar to that of the parent compound. Residue definitions are proposed for potatoes only. For monitoring purposes metribuzin and for risk assessment the sum of metribuzin, desamino-metribuzin, diketo-metribuzin and desamino-diketo-metribuzin, expressed as metribuzin. Residue definitions for other commodities should be dealt with at Member State level, taking into account the specific residue pattern of these commodities. Supervised residue trials according to the representative use demonstrate that residues are below the LOQ of 0.05 mg/kg for the parent compound and its metabolites. No residues are expected in rotational or succeeding crops.
Human and animal exposure to residues of metribuzin and its metabolites is therefore minimal and below the trigger toxicological end points.

Under aerobic conditions in soil, metribuzin shows to be low to moderate persistent ($DT_{50}$ = 5.3 – 17.7 d) and yields the major metabolites diketo-metribuzin (DK, M02; max. 9.7 % AR after 7-21 d) and desamino-diketo-metribuzin (DADK, M03; max. 16.7 % AR after 21 d).

Bound residues amounted up to 65.3 % AR after 71 d and $CO_2$ up to 38.9 % AR at the end of the study after 126 d. The same metabolites were found under anaerobic conditions but metribuzin is highly persistent ($DT_{50}$ = 109 d) under these conditions.

According a study performed with desamino-diketo-metribuzin under aerobic conditions this metabolite is low to moderate persistent in soil ($DT_{50}$ = 9.1 – 22.1 d).

Rate of degradation of metabolite diketo-metribuzin was determined with the data in the studies performed with the labelled parent compound. This metabolite is moderately persistent in soil under aerobic conditions ($DT_{50}$ = 29.9 – 48.6 d). However, fitting procedures, kinetic employed and goodness of fitting are not reported and assessed in the DAR. Therefore, these values should be taken with caution.

Photolysis in soil was investigated in one study under natural sunlight. Four metabolites desamino-metribuzin (max. 21.5 % AR), polar I (max 4.6 % AR), apolar I (max. 8.4 % AR) and apolar II (max. 5.3 % AR) reached the maximum at the end of the study (13 d). These metabolites were either not found (apolar I and II) or found at very low levels (desamino-metribuzin and polar I) in the dark control. EFSA agrees with the rapporteur Member State that photolysis study in soil does not represent realistic conditions and should not be considered quantitatively but only qualitatively. However, qualitative assessment of the level observed for the major photolysis metabolite (21.5 % AR) and the representative uses proposed (which includes pre-emergence spraying on Southern EU fields) does not allow to exclude that desamino-metribuzin will reach 10 % of applied metribuzin equivalents under realistic conditions of use. Therefore, major soil photolysis metabolite desamino-metribuzin needs to be addressed with respect of soil and ground water compartments. Weather this assessment will need further experimental data to be generated may be the subject of a separated analysis. The fact that desamino-metribuzin is found also as a minor soil metabolite under dark aerobic conditions and that it has been identified as a metabolite of metribuzin in different organism should be taken into consideration in the respective ground water and ecotoxicological assessments.

PEC in soil of metribuzin, diketo-metribuzin and desamino-diketo-metribuzin were calculated by the rapporteur Member State using the common soil dilution approach for the worst case GAP (pre-emergence, 1.05 Kg a.s. /ha). However, 90$^{th}$ percentile half lives were used instead of worst case. The meeting of MS experts agreed that in this particular case the impact on the calculated $PEC_S$ will be negligible. Therefore, no new calculations were required to finalize the EU risk assessment. Metribuzin may be classified as high to very high mobile in soil ($K_{oc}$ = 24.3 – 106.0 mL / g). Desamino-diketo-metribuzin is high mobile in soil ($K_{oc}$ = 60.3 – 116.8 mL / g). The meeting of MS experts agreed that the experimentally derived $K_{oc}$ for metabolite diketo-metribuzin was necessary to finalise the ground water assessment.

Metribuzin is stable to hydrolysis in buffer solutions (pH 5, 6, 7 and 9) at 25 ºC. Photolysis may strongly contribute to the dissipation of metribuzin in water with half lives shorter than one day. Main photolysis metabolite is desamino-metribuzin (max. 83.8 % AR after 6 h).

Metribuzin is proposed not to be ready biodegradable for classification purposes.

In water / sediment systems metribuzin was adsorbed to the sediment up to 13.6 –26 % AR after one or two weeks. It dissipated from water phases with half lives of 31.1 to 52.6 and degrades in the whole systems with half lives of 47 – 50 d. Desamino-metribuzin was a major metabolite both in water (14.5 – 28. 7 % AR) and sediment (12.1 – 22.1 %). In one study a half life of 93 d in the whole system was proposed for this metabolite. In another study, half lives were estimated as 135.4 -284.1 d in the water and 87.6 – 90.6 d in the sediment. Mineralization was very low and non extractable radioactivity increased up to 38 % AR after 100 d.

The rapporteur Member State calculated $PEC_{SW}$ for metribuzin and desamino-metribuzin based on spray drift loadings only with worst case assumptions with respect to application rate (1050 g / ha) and half lives. Run off and drain flow may need to be considered for the risk assessment, since from the calculations presented by one of the applicants (based on a non standard approach) these routes of entry to surface water may be as relevant or more than spray drift. For $PEC_{SED}$, the rapporteur Member State accepted the approach presented by one of the applicants based on standard spray drift loadings and non standard estimation of run off and drainflow. This calculation does not cover the worst case application rate of 1050 g / ha but $PEC_{SED}$ are actually not needed to finalize the aquatic risk assessment (driven by toxicity to Lemna and $PEC_{SW}$)

The rapporteur Member State considered that FOCUS GW assessments presented by the applicants do not corresponds to the first tier approach used for the EU risk assessment and produced new calculations for metribuzin, diketo-metribuzin and desamino-diketo-metribuzin. Median half lives were used for metribuzin ($DT_{50}$ = 9.6 d) and diketo-metribuzin ($DT_{50}$ = 42.3 d) and geometric mean for desamino-diketo-metribuzin ($DT_{50}$ = 14.3 d) (the calculations of the rapporteur Member State make use of all available data form both notifiers). For diketo-metribuzin a $K_{oc}$ = 98.6 L / kg was assumed, based on a PcKocWin v. 1.66 estimation. In this calculation diketo-metribuzin exceeds the trigger 0.1 µg / L in one scenario and desamino-diketo-metribuzin in three scenarios of the nine FOCUS GW scenarios simulated. The meeting of MS experts identified a new data gap with respect to metabolite diketo-metribuzin for the necessary information (including experimentally derived Koc) to produce revised FOCUS GW assessment. Major soil photolysis metabolite desamino-metribuzin needs also to be addressed. Relevance assessment for metabolite desamino-diketo-metribuzin and diketo-metribuzin may be then necessary.

One of the applicants (Bayer) submitted a lysimeter study where leaching was investigated after application of 5-$^{13}C$/$^{14}C$-metribuzin (applied at 500 g a.s / ha as WG 70 formulation). Product was applied to potatoes on the first experimental season. Metribuzin and diketo-metribuzin were below 0.01 µg / L. However, desamino-diketo-metribuzin amounted for 0.14 – 0.23 µg / L the first year and 0.09- 0.14 µg / L the second year. Two other metabolites were found in the leachate: 4-methyl-desamino-diketo-metribuzin (M17, at levels of 0.05 – 0.06 µg / L the first year and 0.06 – 0.07 µg / L the second year) and desmethylthio-metribuzin (U1, at levels of 0.05 µg / L and 0.09 – 0.1 µg / L). The relevance of the lysimeter study with respect to the EU risk assessment was discussed by the meeting of MS experts. The meeting identified a new data gap for the necessary information on metabolites 4-methyl-desamino-diketo-metribuzin and desmethylthio-metribuzin to undertake the FOCUS GW assessment (pre-emergence application of 1.05 kg a.s. / ha should be modelled) and for the relevance assessment of metabolite desamino-diketo-metribuzin.

Due to its properties, long range transport of metribuzin in the atmosphere is not expected.

A first tier high acute risk was identified for insectivorous and herbivorous birds and a high long-term risk to insectivorous birds and herbivorous mammals. The risk assessment for birds was refined by choosing the yellow hammer (*Emberiza citronella*) as representative of insectivorous birds and the grey partridge (*Perdix perdix*) as representative of herbivorous birds. Based on these refinements the risk to birds was considered to be low. It is noted by the EFSA that also the acute risk assessment was refined. For other active substances where a use in potato fields has been proposed the yellow wagtail (M*ontacilla flava*) has often been proposed as a focal species for insectivorous birds. In the PPR Panel Opinion on metamidophos[23] it was concluded that yellow wagtails nest in potato fields and that some individuals may obtain close to 100 % of their food within the treated field. It is therefore proposed by the EFSA that for a full assessment of the acute risk to birds also other bird species that might be relevant are considered at Member State level. The assessment of long-term risk to mammals was refined based on estimated $DT_{50}$ in green plant material and the risk was concluded to be low.

Metribuzin is very toxic to green algae and aquatic plants. For the most sensitive species, *Lemna gibba,* risk mitigation measures comparable to buffer zones of 15 m are required to meet the Annex VI trigger of 10. The risk to bees is low. An in-field risk to other non-target arthropods was identified. However, considering that the species of concern are leaf dwellers, that residues of metribuzin can be expected to disappear within a week and that the off-field risk is low, it was concluded that there is a potential for recovery within an ecologically relevant time period. The risk to earthworms, other soil macro-organism, soil micro-organisms and biological methods of sewage treatment is considered low. Risk mitigation comparable to a 5 m buffer zone is required to protect non-target plants outside the treated field.

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

- Risk mitigation measures comparable to a 15 m buffer zone are required to protect algae and aquatic plants.
- Risk mitigation measures comparable to a 5 m buffer zone are required to protect non-target plants outside the treated field.

## Critical areas of concern

- The operator, worker and bystander risk assessment has to be considered as inconclusive.

[23] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from the Commission related to the evaluation of methamidophos in ecotoxicology in the context of Council Directive 91/414/EEC. The EFSA Journal (2004) 144, 1-50.
http://www.efsa.europa.eu/science/ppr/ppr_opinions/769_en.html

- The increased pup mortality in the multigeneration study was considered to be flagged to ISPRA for possible classification as R62/63, together with the alterations in ureter and kidney in rats, which could be potentially considered malformations.
- Potential groundwater contamination by metabolites diketo-metribuzin, desamino-diketo-metribuzin and desmethylthio-metribuzin under vulnerable situations. Further assessment needed for diketo-metribuzin, desamino-metribuzin and 4-methyl-desamino-diketo-metribuzin.
- Metribuzin is very toxic to green algae and aquatic plants. Risk mitigation measures comparable to a 15 m buffer zone are required.
- Risk mitigation measures comparable to 5 m buffer zones are required to protect non-target plants outside the treated field.

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

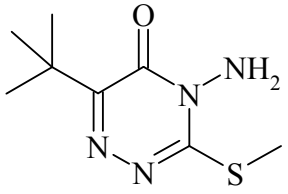
(Abbreviations used in this list are explained in appendix 2)

## Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

| | |
|---|---|
| Active substance (ISO Common Name) ‡ | Metribuzin |
| Function (e.g. fungicide) | Herbicide |

| | |
|---|---|
| Rapporteur Member State | Germany |
| Co-rapporteur Member State | -- |

### Identity (Annex IIA, point 1)

| | | |
|---|---|---|
| Chemical name (IUPAC) ‡ | 4-amino-6-tert-butyl-3-methylthio-1,2,4-triazin-5(4H)-one | |
| Chemical name (CA) ‡ | 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one | |
| CIPAC No ‡ | 283 | |
| CAS No ‡ | 21087-64-9 | |
| EEC No (EINECS or ELINCS) ‡ | 244-209-7 | |
| FAO Specification ‡ (including year of publication) | 930 g/kg ± 20 g/kg [283/TC/S/F (1991)]<br>water: max. 10 g/kg<br>insoluble in acetone: max. 10 g/kg | |
| Minimum purity of the active substance as manufactured ‡ (g/kg) | 930 (Bayer CropScience) | 930 (Feinchemie) |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg) | None | |
| Molecular formula ‡ | $C_8H_{14}N_4OS$ | |
| Molecular mass ‡ | 214.3 g/mol | |
| Structural formula ‡ |  | |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | | |
|---|---|---|
| Melting point (state purity) ‡ | Bayer CropScience | Feinchemie |
| | 125 °C (98.7 %) | 125.3 °C (98.3 %) |
| Boiling point (state purity) ‡ | No data submitted | 366 °C (calculated) |
| Temperature of decomposition | > melting point<br>*(open point)* | no sign of decomposition observed (*open point*) |
| Appearance (state purity) ‡ | Colourless crystals<br>(99.3 %) | Colourless crystals<br>(99.0 %) |
| Relative density (state purity) ‡ | 1.26 (99.8 %) | 1.26 (94.5 %) |
| Surface tension | 63.0 mN/m at 20 °C<br>(99.8 %) | 63.2 mN/m at 20 °C,<br>90 % saturated solution<br>(93 %) |
| Vapour pressure (in Pa, state temperature) ‡ | Data not acceptable | $1.21 \times 10^{-4}$ (20 °C) |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) ‡ | Data not acceptable | $2.0 \times 10^{-5}$ |
| Solubility in water ‡ (g/L or mg/L, state temperature) | 1.05 g/L at 20 °C (unbuffered water)<br>same for pH values 4 – 9 | 1.28 g/L at 25 °C (unbuffered water)<br>1.21 g/L at 23 °C (pH 5)<br>1.23 g/L at 23 °C (pH 9) |
| Solubility in organic solvents ‡ (in g/L or mg/L, state temperature) | *n*-Heptane 0.84<br>1-Octanol 54<br>Xylene 60<br>Dichlormethane > 250<br>2-Propanol > 250<br>Ethyl acetate > 250<br>PEG > 250<br>Acetone > 250<br>Acetonitrile > 250<br>DMSO >250<br>(g/L, all 20 °C) | *n*-Heptane 0.8<br>Toluene 117.3<br>Methanol 259.9<br>Ethyl acetate 336.0<br>1,2-Dichlorethane 426.9<br>Acetone 449.4<br>(g/L, all 22 °C) |
| Partition co-efficient (log POW) ‡ (state pH and temperature) | 1.6 at 20 °C (unbuffered) same for pH values 4 – 9<br>Metabolites:<br>DA: 2.51 (calculated)<br>DK: 0.90 at 21°C<br>DADK: 1.49 at 21°C<br>(pH-dependence of water solubility of DADK was not taken into account) | 1.7 at 25 °C (unbuffered) |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | | |
|---|---|---|
| Hydrolytic stability ($DT_{50}$) ‡ (state pH and temperature) | [5-$^{14}$C]metribuzine: Hydrolytically stable at 25 °C in the pH range 5-9. | Hydrolytically stable at 20-25 °C in the pH range 4-9. |
| Dissociation constant ‡ | No dissociation occurs in water | |
| UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength) | 294 nm (ε 8796) | 294 nm (ε 7553) |
| Photostability ($DT_{50}$) ‡ (aqueous, sunlight, state pH) | $DT_{50}$: 4.34 h<br>major degradation product: desamino-metribuzin 55 % (6 h) | $DT_{50}$: 1.5 h (cal. for May)<br>major degradation product: desamino-metribuzin 50 % (9 h) |
| Quantum yield of direct phototransformation in water at λ> 290 nm ‡ | 0.00899 | 0.0159 |
| Flammability ‡ | Not highly flammable | |
| Explosive properties ‡ | No thermal or mechanical sensitivity with respect to shock or friction was observed. | |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## 1) Summary of representative uses evaluated* (Bayer CropScience)

| 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 | | | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Type (d-f) | Conc. of a.s. (i) | method kind (f-h) | growth stage & season (j) | number min max (k) | PHI*** (l) | % product min max (n) | water l/ha min max | kg a.s./ha min max | ( m) |
| Potato | Northern Europe | Sencor, Sencoral, Sencorex, Senkor | F | Weeds | WG | 700 g/kg | Spraying | Pre/Post-em.** | 1-3 | 60 | 0.04 - 0.75 | 200 - 700 | 0.21-1.05 | max 1.05 kg a.s./ha/season Post-em. max 0.35 kg a.s./ha [1] |
| Potato | Southern Europe | Sencor, Sencoral, Sencorex, Senkor | F | Weeds | WG | 700 g/kg | Spraying | Pre/Post-em.** | 1-3 | 60 | 0.04 - 0.75 | 200 - 700 | 0.21-1.05 | max 1.05 kg a.s./ha/season Post-em. max 0.35 kg a.s./ha [1] |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

**2) Summary of representative uses evaluated∗ (Feinchemie Schwebda)**

| 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) | kg a.s./hL min max | water L/ha min max | kg a.s./ha min max | | |
| Potato | Belgium | Mistral | F | Annual dicotyledonous weeds and some annual grass weeds | WG | 700 g/kg | spraying | 1) pre-emergence<br>2) post-emergence | 1 | not relevant | 1) 0.13 - 0.26<br>2) 0.09 - 0.18 | 200 - 400 | 1) 0.525<br>2) 0.35 | not stated | [1] |
| Potato | Germany | Mistral | F | Annual dicotyledonous weeds and some annual grass weeds | WG | 700 g/kg | spraying | 1) pre-emergence (before cracking)<br>2) post-emergence (plant height max. 5 cm) | 1 | not relevant | 1) 0.13 - 0.26<br>2) 0.09 - 0.18 | 200 - 400 | 1) 0.525<br>2) 0.35 | 1) F<br>2) 42 | [1] |
| Potato | Greece | Mistral 70 WG | F | Annual dicotyledonous weeds and some annual grass weeds | WG | 700 g/kg | spraying | 1) pre-emergence<br>2) post-emergence | 1 | not relevant | 1) 0.09 - 0.26<br>2) 0.09 - 0.18 | 200 - 400 | 1) 0.35-0.525<br>2) 0.35 | not stated | [1] |

[1] The operator risk assessment is inconclusive

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | | | | | |
|---|---|---|---|---|---|
| Remarks: | * | Uses for which risk assessment could not been concluded are marked grey | | (i) | g/kg or g/L |
| | (a) | For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure) | | (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 **Post-emergence recommendations vary |
| | (b) | Outdoor or field use (F), glasshouse application (G) or indoor application (I) | | | |
| | (c) | *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds | | (k) | The minimum and maximum number of applications possible under practical conditions of use must be provided |
| | (d) | waterdispersible granule | | | |
| | (e) | GCPF Codes - GIFAP Technical Monograph No 2, 1989 | | (l) | PHI - minimum pre-harvest interval in days, ***only relevant when applied postemergence |
| | (f) | All abbreviations used must be explained | | | |
| | (g) | Method, spray application | | (m) | Remarks may include: Extent of use/economic importance/restrictions |
| | (h) | Kind: overall spraying - type of equipment used: standard field sprayer | | (n) | product concentration of spray liquid |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## Appendix 1.2: Methods of Analysis

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

| | |
|---|---|
| Technical as (principle of method) | HPLC-UV<br>GC-FID (CIPAC 283/TC/(M), 1984) |
| Impurities in technical as (principle of method) | HPLC-UV<br>GC-FID |
| Plant protection product (principle of method) | HPLC-UV<br>GC-FID |

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

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | GC-MS 0.02 mg/kg (apple) DFG S 19<br>0.04 mg/kg (potato)<br>0.05 mg/kg (tomato) |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | Not required since no MRLs are proposed. |
| Soil (principle of method and LOQ) | GC-PND 0.05 mg/kg<br>HPLC-DAD 0.05mg/kg<br>*Depending on the final residue definition, additional methodology may be required.* |
| Water (principle of method and LOQ) | HPLC-UV 0.05 µg/L (surface water)<br>HPLC-DAD 0.1 µg/L (drinking water, surface water)<br>*Depending on the final residue definition for ground water, additional methodology may be required.* |
| Air (principle of method and LOQ) | HPLC-UV 1.5 µg/m$^3$<br>GC-MS 0.1 µg/m$^3$ |
| Body fluids and tissues (principle of method and LOQ) | Not relevant because metribuzin is not classified as toxic or highly toxic. No methods submitted for body fluids. |

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

| | |
|---|---|
| with regard to physical/chemical data | None |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## Appendix 1.3: Impact on Human and Animal Health

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

| | |
|---|---|
| Rate and extent of absorption ‡ | Rapid and nearly complete within 36 h, based on excretion via urine (40,4 %) and faeces (51,8 %) after oral and i.v. application. |
| Distribution ‡ | Widely distributed with highest concentrations in liver and kidney (elimination half lives in all tissues ranged between 18.4 and 33.6 h) |
| Potential for accumulation ‡ | No evidence for accumulation after single and repeat oral administration. |
| Rate and extent of excretion ‡ | Rapid, mostly within 24 h via urine (38 %) and faeces (52 %) following either intravenous or oral dosing. |
| Metabolism in animals ‡ | Extensively metabolised (> 97 %); main metabolites Desaminometribuzin (DA), 6-tert-butyl-4,5-dihydro-1,2,4-triazin-5-one-3-mercapturic acid and t-buOH-DA |
| Toxicologically significant compounds ‡ (animals, plants and environment) | Metribuzin and DK, DADK, U1 and M17 |

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

| | |
|---|---|
| Rat $LD_{50}$ oral ‡ | 322 mg/kg bw (R22) |
| Rat $LD_{50}$ dermal ‡ | > 5000 mg/kg bw |
| Rat $LC_{50}$ inhalation ‡ | 2.045 mg/L (dust) |
| Skin irritation ‡ | Not irritating |
| Eye irritation ‡ | Not irritating |
| Skin sensitization ‡ (test method used and result) | Not sensitising (Buehler and M&K test) |

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

| | |
|---|---|
| Target / critical effect ‡ | Liver, kidney (chronic inflammation) (rats, rabbits and dogs), thyroid gland (changes in hormone levels), erythrocytes (dogs) |
| Lowest relevant oral NOAEL / NOEL ‡ | Overall NOAEL (rat, rabbit, dog): 2 mg/kg bw/d (R48/22?) |
| Lowest relevant dermal NOAEL / NOEL ‡ | 21-d, rabbit (15 applications): 40 mg/kg bw/d |
| Lowest relevant inhalation NOAEL / NOEL ‡ | 21-d, rat (15 applications): 0.031 mg/L air |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| ……. | No genotoxic potential. |

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

| | |
|---|---|
| Target/critical effect ‡ | Liver, thyroid gland, kidney |
| Lowest relevant NOAEL / NOEL ‡ | 2-yr rat: 1.3 mg/kg bw/d |
| Carcinogenicity ‡ | No carcinogenic potential |

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

| | |
|---|---|
| Reproduction target / critical effect ‡ | Parental: Reduced body weight (gain) and food/water consumption, behaviour (hypoactivity, ptosis, ataxia), liver<br>Reproductive/fertility: no effect on the reproductive performance.<br>Offspring: increased pup mortality and reduced bodyweight gain **(R62?)** |
| Lowest relevant reproductive NOAEL/NOEL ‡ | NOAEL (parental): 2.2 mg/kg bw/d<br>NOAEL (reproductive/fertility): > 67 mg/kg bw/d<br>NOAEL (offspring): 2.2 mg/kg bw/d |
| Developmental target / critical effect ‡ | Maternal: reduced bodyweight and food consumption<br>Developmental: skeletal retardation (rats, rabbits)<br>Alterations in ureter and kidney in rats (dose) **(R63?)** |
| Lowest relevant developmental NOAEL / NOEL ‡ | NOAEL (maternal): < 25 mg/kg bw/d (rats, lowest dose tested), 30 mg/kg bw (rabbits)<br>NOAEL (developmental): < 10 mg/kg bw/d (rabbits, lowest dose tested) |

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

| | |
|---|---|
| Acute neurotoxicity study, rat: | NOAEL neurotoxicity: 100 mg/kg bw<br>NOAEL general toxicity: 2 mg/kg bw<br>No evidence of neurotoxicity |
| Subchronic neurotoxicity study, rat | NOAEL neurotoxicity: 70 mg/kg bw/d<br>NOAEL general toxicity: 2.19 mg/kg bw/d<br>No evidence of neurotoxicity |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| with metabolites | t-BuOH-DADK-Metribuzin: $LD_{50}$ > 2000 mg/kg bw<br>DADK-Metribuzin**:** $LD_{50}$ 700 mg/kg bw,<br>28-d oral, rat: NOAEL: 5 mg/kg bw/d (no direct toxic effects on the thyroid gland), no genotoxic potential in vitro (Ames-Test, L5178Y mouse lymphoma cells<br>(hprt locus), chromosomal aberration assay with human peripheral blood lymphocytes)<br>DK-Metribuzin: $LD_{50}$ 266 mg/kg bw<br>DA-Metribuzin: $LD_{50}$ 468 mg/kg bw |

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

| | |
|---|---|
| …….. | No detrimental effects on health in manufacturing personnel |

| **Summary** (Annex IIA, point 5.10) | Value | Study | Safety factor |
|---|---|---|---|
| ADI ‡ | 0.013 mg/kg bw | Rat, 2-yr study | 100 |
| AOEL systemic ‡ | 0.02 mg/kg bw/d | Overall short-term NOAEL | 100 |
| ARfD ‡ (acute reference dose) | 0.02 mg/kg bw | Rat, acute neurotoxicity study | 100 |

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

| | |
|---|---|
| …….. | 70% for dilution and 50% for concentrate, based on rat in vivo and rat/human in vitro (Sencor)<br>100% default value (Mistral) |

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

| | |
|---|---|
| Operator | The operator risk assessment should be considered as inconclusive due to the lack of transparency and since the calculations were not made available for peer review. |
| Workers | The risk assessment should be considered as inconclusive due to the lack of transparency and since the calculations were not made available for peer review. |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| Bystanders | The risk assessment should be considered as inconclusive due to the lack of transparency and since the calculations were not made available for peer review. |

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

| | |
|---|---|
| with regard to toxicological data | Dir. 67/548/EEC, 29th ATP: Xn, R 22 |
| | EPCO expert's meeting<br>Xn, Harmfull<br>R48/22 Harmful: danger of serious damage to health by prolonged exposure through inhalation<br>R62/63? Possible risk to impaired fertility/ possible risk to unborn child |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## Appendix 1.4: Residues

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

| | |
|---|---|
| Plant groups covered | Root vegetables (Potato)<br>Although metabolism studies were provided for Cereals (wheat) and Oil Seeds (soybean) the residue definitions proposed do not cover these crop groups |
| Rotational crops | Not applicable |
| Plant residue definition for monitoring | Potatoes only: metribuzin<br>Other plant matrices: no proposal – the data from the covered plant groups suggests that ratio's metribuzin to metabolites differ from crop to crop. A residue definition for other crops should be dealt with on member state level. |
| Plant residue definition for risk assessment | Potatoes only: sum of metribuzin, metabolite M01, metabolite M02 and metabolite M03, expressed as metribuzin<br>Other plant matrices: no proposal – The data from the covered plant groups suggests that the ratio's metribuzin to metabolites differ from crop to crop. A Residue definition for other crops should be dealt with on member state level. |
| Conversion factor (monitoring to risk assessment) | Potatoes only: 2 |

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

| | |
|---|---|
| Animals covered | Not required but a goat metabolism study was provided |
| Animal residue definition for monitoring | Not proposed |
| Animal residue definition for risk assessment | Not proposed |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | Yes |
| Fat soluble residue: (yes/no) | No |

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

| | |
|---|---|
| ……. | Not applicable |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| …… | Metribuzin, metabolites DA-metribuzin, DK-metribuzin and DADK-metribuzin at -5 °C stable for 24 months. |

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

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: no | Poultry: no | Pig: no |
|---|---|---|---|
| Muscle<br>Liver<br>Kidney<br>Fat<br>Milk<br>Eggs | No study conducted / required. | | |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| Crop | Northern or Mediterranean Region | Trials results relevant to the critical GAP (a) | Recommendation/comments | MRL | STMR (b) |
|---|---|---|---|---|---|
| Potato | Northern | < 0.04 (5), <0.05 (5) | Analysed for metribuzin only | 0.05* | 0.05 |
| | | <0.05 (5) | Analysed for risk assessment definition | 0.05* | 0.05 |
| Potato | Southern | <0.05 (2) | Analysed for metribuzin only | 0.05* | 0.05 |
| | | - | Analysed for risk assessment definition | 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 critical GAP

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| ADI | 0.013 mg/kg bw/d |
| TMDI (European Diet) (% ADI) | 4.5 |
| TMDI (German Diet) (% ADI) | 1.97 |
| ARfD | 0.02 mg/kg bw |
| Acute exposure (UK, large portions) (% ARfD) | 76.9 (infants) |
| Acute exposure (DE, large portions) (% ARfD) | 24 (16 kg bw child) |

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

| Crop/processed crop | Number of studies | Transfer factor | % Transference * |
|---|---|---|---|
| No study conducted / required. | | | |

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

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

| | |
|---|---|
| Potatoes | 0.05* mg/kg |

* Indicates that the MRL is set at the level of the LOQ (Limit Of Quantification) of the method of analysis.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## Appendix 1.5: Fate and Behaviour in the Environment

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

| | |
|---|---|
| Mineralization after 100 days ‡ | range: 15 – 38.9 %<br>Hein 2000a:<br>29.7 %; 33.1 %; 36.3 %; 38.9 % (after 126 days)<br>Blech 1996:<br>15 % (after 100 days) |
| Non-extractable residues after 100 days ‡ | range: 36.6 – 51.8 %<br>Hein 2000a:<br>9.7% (day 14,21); 9.7% (day 7); 8.2% (day 14); 6.4% (day 21)<br>Blech 1996:<br>36.6 % (after 100 days) |
| Relevant metabolites - name and/or code, % of applied ‡ (range and maximum) | Diketo-metribuzin (DK; M02):<br>range: 5.4 – 9.7 %<br>Hein 2000a:<br>9.7 % (day 21); 6.8 % (day 21); 8.1 % (day 14); 6.4 % (day 21)<br>Blech 1996:<br>6.3 % (day 16)<br>Schneider 1996:<br>5.4 % (day 28)<br>Desamino-diketo-metribuzin (DADK; M03):<br>range: 8.1 - 16.7 %<br>Hein 2000a:<br>16.7 % (day 21); 13.2 % (day 21); 8.1 % (day 14); 14.5 % (day 21)<br>Blech 1996:<br>8.4 % (day 31)<br>Schneider 1996:<br>8.8 % (day 65) |

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

| | |
|---|---|
| Anaerobic degradation ‡ | - Mineralisation:<br>< 1 % at the end of the study<br>- Non-extractable residues:<br>6.6 % at the end of the study |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| | - Metabolites:<br>Desamino-metribuzin (DA; M01): max. 7.5 % (day 31)<br>Desamino-diketo-metribuzin (DADK; M 03): max. 9.4 % (day 60) |
| Soil photolysis ‡ | After 13 d: Desamino-metribuzin (DA) 21.0 % (major photolysis metabolite, also found < 5 % AR in aerobic studies) no other metabolites > 10 %. |

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

| | |
|---|---|
| **Method of calculation** | 1st order kinetics acc. to ModelMaker[a)] or Timme et al.[b)] |
| Laboratory studies ‡ (range or median, with n value, with $r^2$ value) | Metribuzin (n = 9)<br>$DT_{50lab}$ (20 °C, aerobic): 5.3 – 17.7 days,<br>$DT_{50lab}$ (moisture corrected): 5.2. – 17.3 days<br>mean 12.3 d (moisture corrected 11.5 d)<br>median 11.0 (moisture corrected 9.6 d) |

| soil type | $DT_{50}$ | $DT_{50}$ moisture corrected |
|---|---|---|
| sand loam | 9.2 | 8.7[b)] |
| silt loam | 5.3 | 5.2[b)] |
| silt | 8.3 | 8.3[b)] |
| loamy sand | 10.2 | 9.6[b)] |
| sand | 15.4 | 15.04[a)] |
| loamy sand | 17.3 | 17.3[a)] |
| sandy loam | 11.0 | 9.2[a)] |
| silt loam | 17.7 | 11.2[a)] |
| loamy sand | 16.7 | 16.7[a)] |

DADK (n = 3)
$DT_{50lab}$ (20 °C, aerobic): 9.1 – 22.1 days,
$DT_{50lab}$ (moisture corrected): 9.1. – 19.1 days
mean 16.4 d (moisture corrected 15.0 d)

| soil type | $DT_{50}$ | $DT_{50}$ moisture corrected |
|---|---|---|
| loamy sand | 18.1 | 16.7[b)] |
| clay loam | 22.1 | 19.1[b)] |
| sandy loam | 9.1 | 9.1[b)] |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| | DK (n = 5 )<br>$DT_{50lab}$ (20 °C, aerobic): 29.9 – 48.6 days[1],<br>$DT_{50lab}$ (moisture corrected): 29.3. – 48.6 days<br>mean 41.3 d (moisture corrected 40.3 d)<br><br>soil type / $DT_{50}$ / $DT_{50}$ moisture corrected<br>sandy loam 44.83 42.3 b)<br>silt loam 29.9 29.3 b)<br>silt 36.24 36.2 b)<br>loam 46.79 45.2 b)<br>loamy sand 48.62 48.6 b) |
| | Metribuzin:<br>$DT_{90lab}$ (20 °C, aerobic): 17.6 - 91.8 days, n = 9<br>mean 49.0 d, median 50.4 d<br>soil type / $DT_{50}$<br>sandy loam 30.6 b)<br>silt loam 17.6 b)<br>silt 27.6 b)<br>loamy sand 33.9 b)<br>sand 50.4 a)<br>loamy sand 91.8 a)<br>sandy loam 58.8 a)<br>silt loam 74.3 a)<br>loamy sand 55.67 a) |
| | $DT_{50lab}$ (10 °C, aerobic): no data |
| | $DT_{50lab}$ (20 °C, anaerobic): 109 d and 439 d |
| | Degradation in the saturated zone: no data |
| Field studies ‡ (state location, range or median with n value) | $DT_{50f}$: test not required<br><br>$DT_{90f}$: |
| Soil accumulation and plateau concentration ‡ | not expected due to degradation in soil |

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

| | |
|---|---|
| $K_f$ /$K_{oc}$ ‡<br>$K_d$ ‡ | Metribuzin (n = 7):<br>$K_f$: 0.018 - 1.9<br>1/n: 0.89 - 1.52 |

[1] Degradation parameters for diketo-metribuzin (DK), obtained from laboratory degradation in soil studies performed with the parent compound should be taken with caution since fitting procedures, kinetic employed and goodness of fitting are not reported and assessed in the DAR.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| | Koc: 3.14 - 81.5 (mean 37.9)<br><br>oc % $K_f$ 1/n Koc<br>sandy loam 1.35 0.50 0.91 37.1<br>Sand 0.58 0.240 1.08 46.70<br>Sandy loam 0.64 0.018 1.52 3.14<br>Silt loam 1.69 0.221 1.16 14.50<br>clay loam 1.28 0.196 1.05 17.00<br>sandy loam 1.65 1.32 0.92 81.5<br>silt loam 2.94 1.90 0.89 65.5<br>(strongest correlation between $K_f$ and oc content)<br><br>DADK (n = 4):<br>$K_f$: 0.13 - 0.51<br>1/n: 0.86 - 1.04<br>Koc: 26.6 - 37.4 (mean 32.6)<br>oc % Kf 1/n Koc<br>sand 0.35 0.13 0.862 37.4<br>clay 0.53 0.19 1.040 36.4<br>sandy loam 1.59 0.47 0.937 30.0<br>silt loam 1.94 0.51 0.926 26.6<br><br>DK:<br>Koc: 98.6 (PCKOCWIN v.1.66)<br><br>Experimental derived data needed to finalize ground water assessment<br><br>4-methyl-desamino-diketo-metribuzin (Lysimeter metabolite M17):<br><br>Experimental derived data needed to finalize ground water assessment<br><br>Desmethylthio-metribuzin (Lysimeter metabolite U1):<br><br>Experimental derived data needed to finalize ground water assessment |
| pH dependence (yes / no)<br>(if yes type of dependence) | No dependence observed |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| Column leaching ‡ | No data |
| Aged residues leaching ‡ | No data |
| Lysimeter/ field leaching studies ‡ | 2 lysimeters<br>location: Monheim, Germany<br>application: 500 g a.s./ha<br>annual rainfall including irrigation (mm): 796 (1st year), 847 (2nd year)<br><br>annual average conc. (highest conc. during the study) [µg/L]: |

| | lys 21 | lys 22 |
|---|---|---|
| Metribuzin | < 0.01 | < 0.01 |
| M01 (DA) | < 0.01 | < 0.01 |
| M02 (DK) | < 0.01 | < 0.01 |
| M03 (DADK) | 0.23 | 0.14 |
| M17 | 0.07 | 0.06 |
| U1 | 0.10 | 0.09 |

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

**Parent**

| | |
|---|---|
| Method of calculation | First Order kinetics using the 90th percentile of standardised lab. values:<br>$DT_{50}$ (Metribuzin): 16.8 d<br><br>Soil depths: 5 cm, bulk density: 1.5 kg/L |
| Application rate | 1 x 1050 g a.s./ha (no interception) |

| **$PEC_{(s)}$** (mg/kg) | PECactual Metribuzin | PECtwa Metribuzin |
|---|---|---|
| Initial | 1.400 | 1.400 |
| Short term | | |
| 24h | 1.343 | 1.372 |
| 2d | 1.289 | 1.344 |
| 4d | 1.187 | 1.291 |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| **PEC**$_{(s)}$ (mg/kg) | PECactual Metribuzin | PECtwa Metribuzin |
|---|---|---|
| Long term | | |
| 7d | 1.049 | 1.216 |
| 28d | 0.441 | 0.830 |
| 50d | 0.178 | 0.592 |
| 100d | 0.023 | 0.334 |

**Metabolites**

| | |
|---|---|
| Method of calculation | First Order kinetics using the 90$^{th}$ percentile of standardised lab. values:<br>$DT_{50}$ (DK): 47.2 d<br>$DT_{50}$ (DADK): 18.6 d<br><br>Max. amounts of metabolites formed:<br>DK: 9.7 %<br>DADK: 16.7 %<br><br>Soil depths: 5 cm, bulk density: 1.5 kg/L |
| Application rate | 1 x 1050 g a.s./ha (no interception) |

| **PEC**$_{(s)}$ (mg/kg) | $PEC_{actual}$ DK | $PEC_{twa}$ DK | $PEC_{actual}$ DADK | $PEC_{twa}$ DADK |
|---|---|---|---|---|
| Initial | 0.117 | 0.117 | 0.185 | 0.185 |
| Short term | | | | |
| 24h | 0.115 | 0.116 | 0.178 | 0.181 |
| 2d | 0.113 | 0.115 | 0.171 | 0.178 |
| 4d | 0.110 | 0.113 | 0.159 | 0.171 |
| Long term | | | | |
| 7d | 0.105 | 0.111 | 0.142 | 0.162 |
| 28d | 0.077 | 0.096 | 0.065 | 0.115 |
| 50d | 0.056 | 0.083 | 0.029 | 0.084 |
| 100d | 0.027 | 0.061 | 0.004 | 0.048 |

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

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) ‡<br>(state pH and temperature) | pH 4: stable over 34 days at 25 °C (applicant A)<br>stable over 28 days at 50 °C (applicant B) |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| | pH 7: stable over 34 days at 25 °C (applicant A)<br>stable over 28 days at 50 °C (applicant B) |
| | pH 9: stable over 34 days at 25 °C (applicant A)<br>hydrolysis (50 %) at 50 °C; major product DK;<br>$DT_{50}$ = 1317 d (20 °C), 635 d (25 °C) (applicant B) |
| Photolytic degradation of active substance and relevant metabolites ‡ | quartz cell; sterile water; sunlight exposure for 6 h<br>$DT_{50}$ = 4.34 h<br>Metabolite: 55 % of DA after 6 h<br>other metabolites: < 10 %<br>(applicant A)<br>quartz cell; artificial light (Xe); river Rhine water<br>continuous radiation for 8 h<br>$DT_{50}$ = 0.63 h<br>Metabolite: 83.8 % of DA after 6 h<br>other metabolites: < 10 %<br>(applicant A) |
| Readily biodegradable (yes/no) | Test not conducted, considered to be not readily biodegradable. |
| Degradation in water/sediment<br>- $DT_{50}$ water ‡ | Blech 1996:<br>41 d/41 d<br>Spiteller, 1993:<br>52.6 d/31.1 d |
| - $DT_{90}$ water ‡ | Blech 1996:<br>136 d/166 days |
| - $DT_{50}$ whole system ‡ | Blech 1996:<br>50 d/47 d |
| - $DT_{90}$ whole system ‡ | Blech 1996:<br>166 d/156 d |
| Mineralization | Blech 1996:<br>1.8 %/0.2 % at day 201/202<br>Spiteller, 1993:<br>3.5 %/2.1 % at day 100 |
| Non-extractable residues | Blech 1996:<br>27.8 %/22.9 % at day 201/202<br>Spiteller, 1993:<br>21.9 %/38 % at day 100 |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| Distribution in water / sediment systems (active substance) ‡ | > 10 % AR in sediment:<br>Blech 1996:<br>day 2 - 98 max. 26.3 % / day 7 - 59 max. 17.1 %<br>Spiteller, 1993:<br>day 60 - 100 max. 12.1 % / day 29 - 100 max.21.2 % |
| Distribution in water / sediment systems (metabolites) ‡ | Desaminometribuzin (DA; M01)<br>Blech 1996:<br>whole system max. 36.6 %/37.3 % at day 201/202<br>> 10 % AR in sediment:<br>day 61 - 201 max. 22.1 % / day 105 - 202 max. 17.5 %<br>Spiteller, 1993:<br>whole system max. 40.8 and 43 % at day 100<br>> 10 % AR in sediment:<br>day 60 - 100 max. 12.1 % / day 29 - 100 max. 21.2 % |

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

**Parent**

| | |
|---|---|
| Method of calculation | Entry via spray drift in a standing water body of 1 $m^2$ area and 0.3 m depth in1 m dist. to treated area/ run-off spray drift, 1m: 2.77% (1 application, 90th percentile drift value according to Rautmann, 2001)<br>direct run-off: rain event 3 days after application, run-off water 100,000 l in total, 0.5% of applied amount on soil<br>$DT_{50}$ (metribuzin): 52.6 d (max. for all four water/sediment systems) |
| Application rate | 1 x 1050 g a.s./ha |
| Main routes of entry | Spray drift Note: run off and drainage values have not been used for the risk assessment in ecotoxicology and are not standard calculations. |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| **PEC**$_{(sw)}$ [µg/L] | $PEC_{actual}$ Metribuzin spray-drift / run-off / drainage | $PEC_{twa}$ Metribuzin spray-drift / run-off / drainage |
|---|---|---|
| Initial | 9.7 / 9.1/ 1.48 | 9.7 / 9.1 / 1.48 |
| Short term | | |
| 24 h | 9.57 / 8.95 / 1.45 | 9.63 / 9.03 / 1.47 |
| 2 d | 9.44 / 8.8 / 1.43 | 9.57 / 8.95 / 1.46 |
| 4 d | 9.2 / 8.51 / 1.38 | 9.44 / 8.8 / 1.43 |
| Long term | | |
| 7 d | 8.84 / 8.08 / 1.31 | 9.26 / 8.59 / 1.4 |
| 14 d | 8.06 / 7.18 / 1.17 | 8.85 / 8.11 / 1.32 |
| 21 d | 7.35 / 6.38 / 1.04 | 8.447 / 7.66 / 1.24 |
| 28 d | 6.7 / 5.67 / 0.92 | 8.11 / 7.25 / 1.18 |
| 42 d | 5.57 / 4.48 / 0.73 | 7.45 / 6.52 / 1.06 |

**Metabolite**

| | |
|---|---|
| Method of calculation | Entry via spray drift, 1 m dist. to treated area/ run-off<br>$DT_{50}$ (DA): 284.1 d (max. for all four water/sediment systems)<br>Metabolism factor:100 % |
| Application rate | 1 x 1050 g a.s./ha |
| Main routes of entry | Spray drift Note: run off and drainage values have not been used for the risk assessment in ecotoxicology and are not standard calculations. |

| **PEC**$_{(sw)}$ [µg/L] | $PEC_{actual}$ DA spray-drift / run-off / drainage | $PEC_{twa}$ DA spray-drift / run-off / drainage |
|---|---|---|
| Initial | 9.02 / 0.1 / 0.02 | 9.02 / 8.45 / 1.37 |
| Short term | | |
| 24 h | 8.99 / 0.13 / 0.02 | 9.01 / 8.42 / 1.37 |
| 2 d | 8.97 / 0.11 / 0.02 | 8.99 / 8.39 / 1.36 |
| 4 d | 8.93 / 0.12 / 0.02 | 8.97 / 8.33 / 1.35 |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| **PEC**$_{(sw)}$ [µg/L] | $PEC_{actual}$ DA spray-drift / run-off / drainage | $PEC_{twa}$ DA spray-drift / run-off / drainage |
|---|---|---|
| Long term | | |
| 7 d | 8.86 / 0.15 / 0.02 | 8.94 / 8.24 / 1.34 |
| 14 d | 8.71 / 0.24 / 0.04 | 8.86 / 8.03 / 1.3 |
| 21 d | 8.57 / 0.38 / 0.06 | 8.79 / 7.83 / 1.27 |
| 28 d | 8.42 / 0.47 / 0.08 | 8.72 / 7.63 / 1.24 |
| 42 d | 8.14 / 0.5 / 0.08 | 8,57 / 7.26 / 1.18 |

**PEC (sediment)**

Calculation for application rate of 1050 g / ha is missing. However, PECsed data are not required for the risk assessment. This is driven by the toxicity to *Lemna* and based on PECsw values.

**Parent**

| | |
|---|---|
| Method of calculation | Proportions (in % as in sediment at day t) compared to initial concentration of metribuzin from water/sediment study<br>standard sediment body; area 1 $m^2$, depth of sediment layer 2 cm<br>PECsed(t) = [PECini.sw * Vsw * Psed(t)] / [Vsed * bdsed * 100] [µg/g]<br>PECini.sw - initial PEC in surface water [µg/L] for entry via drift/ run-off<br>Vsw - water volume [300 L],<br>Psed(t) - portion of active substance (or the metabolite) in sediment at time t [%]<br>Vsed - volume of sediment (20.0000 $cm^3$)<br>bulk density of wet sediment 1.3 g/$cm^3$results for spray-drift / run-off |
| Application rate | 1 x 525 g a.s./ha |

| **PEC**$_{(sed)}$ (µg / kg) | PECactual Metribuzin [µg/g] spray-drift / run-off | PECtwa Metribuzin [µg/g] spray-drift / run-off |
|---|---|---|
| Initial | 1.566 / 2.941 | not calc. |
| Short term | | |
| 24 h | 4.195 / 7.878 | not calc. |
| 2 d | 6.013 / 11.292 | not calc. |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| **PEC**$_{(sed)}$ (µg / kg) | PECactual Metribuzin [µg/g] spray-drift / run-off | PECtwa Metribuzin [µg/g] spray-drift / run-off |
|---|---|---|
| Long term | | |
| 7 d | 9.286 / 17.438 | not calc. |
| 14 d | 12.139 / 22.795 | not calc. |
| 30 d | 10.796 / 20.274 | not calc. |
| 60 d | 9.090 / 17.070 | not calc. |
| 120 d | 6.013 / 11.292 | not calc. |
| 202 d | 1.231 / 2.311 | not calc. |

**Metabolite**

| | |
|---|---|
| Method of calculation | Proportions (in % as in sediment at day t) compared to initial concentration of metribuzin from water/sediment study<br>Standard sediment body; area 1 m$^2$, depth of sediment layer 2 cm<br><br>Metabolite DA: correction of PEC$_{ini.sw}$ by molecular weight (correction factor: 0,929)<br>PECini.sw(metabolite)·= PECini.sw(parent) * MWmetabolite/MWparent<br>results for spray-drift / run-off |
| Application rate | 1 x 525 g a.s./ha |

| **PEC**$_{(sed)}$ (µg / kg) | PECactual DA [µg/g] spray-drift / run-off | PECtwa DA [µg/g] spray-drift / run-off |
|---|---|---|
| Initial | 0.052 / 0.098 | not calc. |
| Short term | | |
| 24 h | 0.130 / 0.244 | not calc. |
| 2 d | 0.182 / 0.341 | not calc. |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| **PEC**$_{(sed)}$ (µg / kg) | PECactual DA [µg/g] spray-drift / run-off | PECtwa DA [µg/g] spray-drift / run-off |
|---|---|---|
| Long term | | |
| 7 d | 0.753 / 1.414 | not calc. |
| 14 d | 2.000 / 3.756 | not calc. |
| 30 d | 4.233 / 7.950 | not calc. |
| 60 d | 5.324 / 9.999 | not calc. |
| 120 d | 9.921 / 18.631 | not calc. |
| 202 d | 9.636 / 18.095 | not calc. |

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

Preliminary values. Experimentally derived Koc for metabolite diketo-metribuzin (DK) needed.

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter ) | Modelling with FOCUS-PELMO 3.3.2<br>crop: potatoes; single application: 7 d before emergence; no interception<br><br>$K_{oc}$ / 1/n / $DT_{50}$<br>Metribuzin: 37 / 0.910 / 9.6<br>DK[24]: 98.6 / 0.9 / 42.3<br>DADK: 32.2 / 0.968 / 14.3 |
| Application rate | Scenario 1: 1 x 1050 g a.s./ha (applicant A: max. rate)<br>Scenario 2:1 x 525 g a.s./kg (applicant B: max. rate) |

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

| | |
|---|---|
| Maximum concentration | Not available, not required. |
| Average annual concentration<br>(Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance) | concentration in the percolate at 1 m soil depth (80th percentiles) [µg/L]<br><br>Scenario 1 (1050 g a.s./ha)[24]<br>scenario / Metribuzin / DK / DADK<br>Chateaudun / < 0.001 / 0.002 / 0.038<br>Hamburg / 0.001 / 0.015 / 0.247<br>Jokioinen / < 0.001 / < 0.001 / 0.040<br>Kremsmünster / < 0.001 / 0.002 / 0.046<br>Okehampton / 0.001 / 0.007 / 0.128 |

[24] Preliminary values. Experimentally derived Koc for metabolite diketo-metribuzin (DK) still needed

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | | | |
|---|---|---|---|
| Piacenza | 0.013 | 0.149 | 0.355 |
| Porto | < 0.001 | < 0.001 | 0.001 |
| Sevilla | < 0.001 | < 0.001 | 0.001 |
| Thiva | < 0.001 | < 0.001 | 0.001 |

Scenario 2 (525 g a.s./ha)[24]

| scenario | Metribuzin | DK[24] | DADK |
|---|---|---|---|
| Chateaudun | < 0.001 | 0.001 | 0.016 |
| Hamburg | < 0.001 | 0.005 | 0.107 |
| Jokioinen | < 0.001 | < 0.001 | 0.017 |
| Kremsmünster | < 0.001 | 0.001 | 0.020 |
| Okehampton | < 0.001 | 0.002 | 0.056 |
| Piacenza | 0.005 | 0.059 | 0.162 |
| Porto | 0.001 | < 0.001 | 0.001 |
| Sevilla | < 0.001 | < 0.001 | < 0.001 |
| Thiva | < 0.001 | < 0.001 | < 0.001 |

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

| | |
|---|---|
| Direct photolysis in air ‡ | Not available, not required. |
| Quantum yield of direct phototransformation | Not available, not required. |
| Photochemical oxidative degradation in air ‡ | According to Atkinson model (AOPWIN 1.91)<br>Applicant A: $DT_{50}$ = 7.03 h<br>($1.5 \times 10^6$ OH radicals/cm³)<br>Applicant B: $DT_{50}$ = 21 h<br>($5 \times 10^5$ OH radicals/cm³) |
| Volatilization ‡ | From plant surfaces: no data<br>from soil: no data |

**PEC (air)**

| | |
|---|---|
| Method of calculation | Not calculated |

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

| | |
|---|---|
| Maximum concentration | Not calculated |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| Relevant to the environment | Soil<br>Definitions for risk assessment: metribuzin, diketo-metribuzin, desamino-diketometribuzin and desamino-metribuzin (major photolysis metabolite).<br>Definitions for monitoring: metribuzin, desamino-metribuzin (pending to be addressed and assessed)<br><br>Water<br><br>Ground water<br>Definitions for exposure assessment: metribuzin, diketo-metribuzin, desamino-diketo-metribuzin, desmethyl-thio-metribuzin (U1), 4-methyl-desamino-diketo-metribuzin (M17) and desamino-metribuzin (major photolysis metabolite).<br>Definitions for monitoring: metribuzin, diketo-metribuzin (pending assessment), desamino-diketo-metribuzin (pending assessment), desmethyl-thio-metribuzin (U1) (pending assessment), 4-methyl-desamino-diketo-metribuzin (M17) (pending assessment) and desamino-metribuzin (major photolysis metabolite, pending assessement).<br><br>Surface water<br>Definitions for risk assessment: metribuzin, desamino-metribuzin<br>Definitions for monitoring: metribuzin<br><br>Air<br>Definitions for risk assessment: metribuzin<br>Definitions for monitoring: metribuzin |

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

| | |
|---|---|
| Soil (indicate location and type of study) | No data |
| Surface water (indicate location and type of study) | No data |
| Ground water (indicate location and type of study) | No data |
| Air (indicate location and type of study) | No data |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| with regard to fate and behaviour data | Candidate for<br>R53 May cause long-term adverse effect to the aquatic environment |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

## Appendix 1.6: Effects on non-target Species

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

| | |
|---|---|
| Acute toxicity to mammals ‡ | 322 mg a.s./kg bw |
| Reproductive toxicity to mammals | 2.2 mg a.s./kg bw/d |
| Acute toxicity to birds ‡ | 164 mg a.s./kg bw |
| Dietary toxicity to birds ‡ | >359 mg a.s./kg bw/d |
| Reproductive toxicity to birds ‡ | 28.3 mg a.s./kg bw/d |

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

| Application rate (kg a.s./ha) | Crop | Category (e.g. insectivorous bird) | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|---|
| Tier I assessment | | | | | |
| 0.35 | potato | medium herbivorous bird | acute | 7.1 | 10 |
| | | | short-term | > 33.9 | 10 |
| | | | long-term | 5.1 | 5 |
| 1.05 | potato | insectivorous bird | acute | 2.9 | 10 |
| | | | short-term | > 11.3 | 10 |
| | | | long-term | 0.9 | 5 |
| 0.35 | potato | medium herbivorous mammal | acute | 37.7 | 10 |
| | | | long-term | 1.1 | 5 |
| Refined risk assessment | | | | | |
| 0.35 | potato | medium herbivorous bird (grey partridge) | acute | 22.6 | 10 |
| 1.05 | potato | insectivorous bird (Yellowhammer) | acute | 22.6 | 10 |
| | | | long-term | 9.0 | 5 |
| 0.35 | potato | medium herbivorous mammal | long-term | 7.2 | 5 |

An additional acute and long-term risk assessment based on yellow wagtail (*Motacilla flava*) is available in addendum 6 of May 2006 but has not been peer reviewed.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| Group | Test substance | Time-scale | Endpoint | Toxicity (mg/L) |
|---|---|---|---|---|
| Laboratory tests ‡ | | | | |
| **Metribuzin** | | | | |
| *O. mykiss* | metribuzin | acute (96 h, static) | mortality, $LC_{50}$ | 74.6 |
| | | long-term (21 d semi-static) | growth, NOEC | 5.6 |
| | | long-term (ELS, 95 d, flow-through) | growth, NOEC | 4.4 |
| *D. magna* | metribuzin | acute (48 h) | immobilisation, $EC_{50}$ | 49.0 |
| | | chronic (21 d, semi-static) | reproduction, NOEC | 0.32 |
| *S. subspicatus* | metribuzin | chronic (72 h) | growth rate, $EC_{50}$ | 0.02 |
| *L. gibba* | metribuzin | long-term (14 d, semi-static) | fronds, $EC_{50}$ | 0.0079 |
| aquatic microflora | metribuzin | short term (3 h) | $EC_{50}$ | 761 |
| Microcosm or mesocosm tests | | | | |
| Outdoor microcosms with sediment, middle Europe: Renkum, Netherlands, under GLP conditions. Test substance: Metribuzin WG 70, single application, treatment levels: 0 µg/L, 1.8 µg/L, 5.6 µg/L, 18 µg/L, 56 µg/L, 180 µg/L active substance, NOEAEC: 18 µg a.s./L | | | | |

| Group | Test substance | Time-scale | Endpoint | Toxicity (mg/L) |
|---|---|---|---|---|
| Laboratory tests ‡ | | | | |
| **DADK** (Desaminodiketo-metribuzin) | | | | |
| *Oncorhynchus mykiss* | DADK | acute (96 h) | $LC_{50}$ | > 100. |
| | | long-term (21 d) | NOEC | 31.6 |
| *Daphnia magna* | DADK | 2 d | $EC_{50}$ | > 18.0 |
| | | 21 d | NOEC | 3.2 |
| *Scenedesmus subspicatus* | DADK | 3 d | $ErC_{50}$ | > 18.0 |
| *Lemna gibba* | DADK | 7 d | $EC_{50}$ | > 100.0 |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| Group | Test substance | Time-scale | Endpoint | Toxicity (mg/L) |
|---|---|---|---|---|
| **DK** (Diketo-metribuzin) | | | | |
| *Pseudokirchneriella subcapitata* | DK | 3 d | $ErC_{50}$ | > 100.0 |
| *Lemna gibba* | DK | 7 d | $EC_{50}$ | > 100.0 |
| *Chironomus riparius* | DK | 28 d | NOEC | > 99.0 |
| Formulated products | | | | |
| *Oncorhynchus mykiss* | Mistral | 4 d | $LC_{50}$ | 134.2 |
| | Metribuzin WG 70 | 21 d | NOEC | 10.01 |
| *Daphnia magna* | Mistral | 2 d | $EC_{50}$ | 58.0 |
| | Sencor WG 70 | 21 d | NOEC | 5.6 |
| *Scenedesmus subspicatus* | Mistral | 3 d | $ErC_{50}$ | 0.040 |

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

| Application rate (kg a.s./ha) | Crop | Organism | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|
| 1.05 | potato | *Lemna gibba* | 7-days | 1~~1~~ | 0.8 | 10 |
| 1.05 | potato | *Lemna gibba* | 7-days | 15 | 11 | 10 |

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) ‡ | A study on bioconcentration in fish is not required for metribuzin and its metabolites DA-metribuzin, DADK-metribuzin and DK-metribuzin, because log Pow <3 |
| Annex VI Trigger:for the bioconcentration factor | - |
| Clearance time ($CT_{50}$) ($CT_{90}$) | - |
| Level of residues (%) in organisms after the 14 day depuration phase | - |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

| | |
|---|---|
| Acute oral toxicity ‡ | $LD_{50}$: 166 µg technical Metribuzin/bee<br>$LD_{50}$: 53 µg Metribuzin 70 WG/bee (37.1 µg a.s./bee)<br>$LD_{50}$: 192 µg Mistral/bee (134 µg a.s./bee) |
| Acute contact toxicity ‡ | $LD_{50}$: 200 µg technical Metribuzin/bee<br>$LD_{50}$: 283 µg Metribuzin 70 WG /bee (200µg a.s./bee)<br>$LD_{50}$: 1000 µg Mistral /bee (700 µg a.s./bee) |

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

| Application rate (kg a.s./ha) | Crop | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|---|
| Laboratory tests | | | | |
| 1.05 | potatoes | oral | 6.3 | 50 |
| 1.05 | potatoes | contact | 5.3 | 50 |
| Application rate (kg product/ha) | | | | |
| Laboratory tests: formulation | | | | |
| 1.50 | potatoes | oral | 28.6 | 50 |
| 1.50 | potatoes | contact | 5.3 | 50 |
| 1.50 | potatoes | oral | 7.8 | 50 |
| 1.50 | potatoes | contact | 1. 5 | 50 |

| Field or semi-field tests |
|---|
| 2 semifield tests with GLP certificate following EPPO-Guideline 170 and BBA-Guideline VI, 23-1 have been performed with more than the highest recommended dose of application (Wilhelmy, 1999 with 2.26 kg/ha Mistral and Mühlen (1999) with 2 kg/ha Mistral). In these studies no negative effects on honey bees were observed compared to the water treated control regarding mortality, flight activity and behaviour of the bees as well as strength of colonies and state of brood. |

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

| Species | Stage | Test Substance | Dose (kg a.s./ha) | Endpoint | Effect | Annex VI Trigger |
|---|---|---|---|---|---|---|
| Laboratory tests | | | | | | |
| *Typhlodromus pyri* | proto-nymph | Metribuzin WG 70 | 0.010 – 0.404 kg a.s./ha | Mortality | $LR_{50}$: 72.9 g a.s./ha | |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| Species | Stage | Test Substance | Dose (kg a.s./ha) | Endpoint | Effect | Annex VI Trigger |
|---|---|---|---|---|---|---|
| *Aphidius rhopalosiphi* | adult | Metribuzin WG 70 | 0.008 – 0.300 kg a.s./ha | Mortality | $LR_{50}$: 65.9 g a.s./ha | |
| *Chrysoperla carnea* | larvae | Metribuzin WG 70 | 1.050 kg a.s./ha | Mortality<br>Reproduction | 2.1 %<br>< 30 % | 30 % |
| *Coccinella septempunctata* | larvae | Metribuzin WG 70 | 0.100 – 1.050 kg a.s./ha | Mortality | $LR_{50}$: 385.4 g a.s./ha | |
| *Poecilus cupreus* | adult | FSG 01094 H | 0.700 kg a.s./ha | Mortality<br>Feeding rate | 0 %<br>11.1 % | 30 % |
| *Pardosa sp.* | adult | Metribuzin WG 70 | 1.050 kg a.s./ha | Mortality<br>Feeding rate | 0 %<br>7.5 % | 30 % |
| Extended laboratory tests | | | | | | ESCORT II Trigger |
| *Typhlodromus pyri* | proto-nymph | Metribuzin WG 70 | 0.014 – 0.525 kg a.s./ha on potato leaves | Mortality | $LR_{50}$: 84.0 g a.s./ha | |
| *Aphidius rhopalosiphi* | adult | Metribuzin WG 70 | 2.100 kg a.s./ha on barley seedlings | Mortality<br>Reproduction | 0 %<br>8 % | 50 % |
| *Aphidius rhopalosiphi* | adult | Metribuzin WG 70 | 1.050 kg a.s./ha on potato leaves | Mortality<br>Reproduction | 17 %<br>64 % | 50 % |
| *Coccinella septempunctata* | larvae | Mistral | 0.350 kg a.s./ha on potato leaves | Mortality<br>Reproduction | 51.0 %<br>not assessed | 50 % |
| Aged residue tests | | | | | | |
| *Typhlodromus pyri* | proto-nymph | Metribuzin WG 70 | 0.350 kg a.s./ha aged on potato leaves | Mortality<br>Reproduction | 25.5 % (14 d)<br>7.8 % (28 d)<br>45 % (14 d)<br>0 % (28 d) | 50 % |

| Field or semi-field tests |
|---|
| not submitted |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

**Toxicity/exposure ratio for other arthropods** (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

| First tier risk assessment (HQ approach according to ESCORT 2) | | | | | | |
|---|---|---|---|---|---|---|
| Species | Application rate (g a.s./ha) | $LR_{50}$ (g a.s./ha) | In-field HQ | Off-field HQ 1m | Off-field 5m | Trigger* |
| *Aphidius rhopalosiphi* | 1050 | 65,9 | 15.93 | 0.44 | 0.09 | 2 |
| *Typhlodromus pyri* | 1050 | 72,9 | 14.40 | 0.40 | 0.08 | 2 |

*: according to SANCO/10329/2002

| Second tier risk assessment (TER approach) | | | | | |
|---|---|---|---|---|---|
| Distance from treated area (m) | Drift (%) | Amount of drift - PEC (g a.s./ha) [1] | TER (A. rhopalosiphi, $LR_{50}$: 65.9 g a.s./ha) | TER (T. pyri, $LR_{50}$: 84 g a.s./ha)* | Trigger[2] |
| 1 | 2.77 | 5.9 | 11.2 | 14.2 | 5 |
| 5 | 0.57 | 1.3 | 50.7 | 64.6 | 5 |

*: extended study.
[1]: considering a vegetation distribution factor of 5 instead of 10 – according to experimental data the ESCORT 2 value of 10 is deemed unreliable for a realistic worst-case exposure assessment
[2]: used by the German Federal Environmental Agency (Schulte et al., 1999: UWSF 11(5) 261-266)

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

| | |
|---|---|
| Acute toxicity metribuzin | $LC_{50}$: 427 mg a.s./kg (14 d) |
| Acute toxicity Metabolite DADK-metribuzin | $LC_{50}$: > 1000 mg a.s./kg (14 d) |
| Acute toxicity Metabolite DK-metribuzin | $LC_{50}$: > 1000 mg a.s./kg (14 d) |
| Acute toxicity ”FSG 01094 H” | $LC_{50}$: 529 mg a.s./kg (14 d) |
| Reproductive toxicity ”-metribuzin 70 WG” | NOEC: > 5.25 kg a.s./ha (56 d) |

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

| Application rate (kg a.s./ha) | Crop | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|
| 1.05 (a.s.) | potato | short-term | 305 | 10 |
| 1.05 (DADK) | potato | short-term | > 4450 | 5 |
| 1.05 (DK) | potato | short-term | > 7000 | 5 |
| 1.05 (70 WG) | potato | long-term | 5 | 5 |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

**Effects on other soil macro-organisms** (Annex IIA, point 8.4 Annex IIIA, point 10.6)

| | |
|---|---|
| Effects on soil arthropods (DADK-Metribuzin) | *F. candida*, $LC_{50}$: 645 mg a.s./kg, NOEC: 125 mg a.s./kg |
| Effects on soil arthropods (DK-Metribuzin) | *F. candida*, $LC_{50}$: 945 mg a.s./kg, NOEC: 316 mg a.s./kg |

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

| | |
|---|---|
| Nitrogen mineralization ‡ | Metribuzin, DADK, DK:<br>deviation from control < 25 % at day 28 |
| Carbon mineralization ‡ | Metribuzin, DADK:<br>deviation from control < 25 % day 28<br>DK:<br>no study presented, metabolite formed in sufficient amounts in the study with metribuzin |

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

| | |
|---|---|
| Seedling emergence test (metribuzin) | *Brassica napus* (most sensitive species):<br>$EC_{50}$: 15.7 g a.s./ha |
| Seedling emergence test (combined dataset: metribuzin, 70 WG) | Species sensitivity distribution (10 species)<br>$HC_5$: 16.17 g a.s./ha |
| Vegetative vigour test (metribuzin) | *Brassica napus* (most sensitive species):<br>$EC_{50}$ : 12.3 g a.s./ha |
| Vegetative vigour test (combined dataset: metribuzin, 70 WG) | Species sensitivity distribution (13 species)<br>$HC_5$: 10.87 g a.s./ha |
| Vegetative vigour test (70 WG) | *Beta vulgaris* (most sensitive species):<br>$EC_{50}$ : 9.0 g /ha (6.3 g a.s./ha) |
| Seedling emergence test (DADK) | 3 species tested (2 dicots, 1 monocot):<br>NOEC: ≥1000 mg pm/kg d.wt.s |
| Growth test (DADK) | *Brassica rapa* (most sensitive species):<br>$LC_{50}$: 14.6 mg pm/kg d.wt.s. (11 kg pm/ha)<br>NOEC: 1 mg pm/kg d.wt.s.(0.75 kg pm/ha) |
| Screening test (U1=KTS9450) | Pre-emergence test (5 monocots, 5 dicots)<br>No significant effects up to 500 g a.s./ha (highest conc.)<br>Post-emergence test (5 monocots, 5 dicots):<br>No significant effects up to 125 g a.s./ha (highest conc.) except *Beta vulgaris* with effects <30% at 125 g a.s./ha |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

**Toxicity/exposure ratio for terrestrial plants** (Annex IIIA, point 10.8)

| Distance from treated area (m) | Drift (%) | Amount of drift - PEC (g a.s./ha) | TER (Brassica napus, $EC_{50}$ 12.3 g a.s./ha) | TER (Beta vulgaris, $EC_{50}$ 6.3 g a.s./ha) | TER (SSD veg. vigour, HC5 10.87 g a.s./ha) |
|---|---|---|---|---|---|
| 1 | 2.77 | 30 | 0.4 | 0.2 | 0.36 |
| 5 | 0.57 | 6.0 | 2.1 | 1.1 | 1.81 |

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

with regard to ecotoxicological data

| | |
|---|---|
| N; | Harmful to the environment |
| R50/R53 | Very toxic to aquatic organisms, may cause long term-adverse effects in the aquatic environment |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

# APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

| | |
|---|---|
| ADI | acceptable daily intake |
| AOEL | acceptable operator exposure level |
| ARfD | acute reference dose |
| a.s. | active substance |
| bw | body weight |
| CA | Chemical Abstract |
| CAS | Chemical Abstract Service |
| CIPAC | Collaborative International Pesticide Analytical Council Limited |
| d | day |
| 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) |
| ε | decadic molar extinction coefficient |
| $EC_{50}$ | effective concentration |
| 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 |
| FAO | Food and Agriculture Organisation of the United Nations |
| FOCUS | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| GAP | good agricultural practice |
| GCPF | Global Crop Protection Federation (formerly known as GIFAP) |
| GS | growth stage |
| h | hour(s) |
| ha | hectare |
| hL | hectolitre |
| HPLC | high pressure liquid chromatography<br>or high performance liquid chromatography |
| IEDI | international estimated daily intake |
| ISO | International Organisation for Standardisation |
| IUPAC | International Union of Pure and Applied Chemistry |
| $K_{oc}$ | organic carbon adsorption coefficient |
| L | litre |
| LC | liquid chromatography |
| LC-MS | liquid chromatography-mass spectrometry |
| LC-MS-MS | liquid chromatography with tandem mass spectrometry |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

| | |
|---|---|
| $LC_{50}$ | lethal concentration, median |
| $LD_{50}$ | lethal dose, median; dosis letalis media |
| LOAEL | lowest observable adverse effect level |
| LOD | limit of detection |
| LOQ | limit of quantification (determination) |
| µg | microgram |
| mN | milli-Newton |
| MRL | maximum residue limit or level |
| MS | mass spectrometry |
| NESTI | national estimated short term intake |
| NIR | near-infrared-(spectroscopy) |
| nm | nanometer |
| NOAEL | no observed adverse effect level |
| NOEC | no observed effect concentration |
| NOEL | no observed effect level |
| PEC | predicted environmental concentration |
| $PEC_A$ | predicted environmental concentration in air |
| $PEC_S$ | predicted environmental concentration in soil |
| $PEC_{SW}$ | predicted environmental concentration in surface water |
| $PEC_{GW}$ | predicted environmental concentration in ground water |
| PHI | pre-harvest interval |
| $pK_a$ | negative logarithm (to the base 10) of the dissociation constant |
| PPE | personal protective equipment |
| ppm | parts per million ($10^{-6}$) |
| ppp | plant protection product |
| $r^2$ | coefficient of determination |
| RPE | respiratory protective equipment |
| STMR | supervised trials median residue |
| TER | toxicity exposure ratio |
| TMDI | theoretical maximum daily intake |
| UV | ultraviolet |
| WHO | World Health Organisation |
| WG | water dispersible granule |
| yr | year |

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles