European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance penoxsulam[1]

(Question No EFSA-Q-2009-312)

Issued on 31 August 2009

SUMMARY

Penoxsulam is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[2] Italy received an application from Dow AgroScience for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2004/131/EC [3].

Following the agreement between the EU-Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State Italy made the report of its initial evaluation of the dossier on penoxsulam, hereafter referred to as the draft assessment report (DAR), available on 10 February 2005.

The peer review was initiated on 16 February 2005 by dispatching the DAR for consultation of the Member States and the applicant. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed by EFSA. Remaining issues as well as further data made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in September 2006 and January 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with Member States in April 2009 leading to the conclusions as laid down in this report.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance penoxsulam *EFSA Scientific Report* (2009) 343, 1-90

[2] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19

[3] OJ No L 37, 10.2.2004

The conclusion was reached on the basis of the evaluation of the representative uses as a herbicide on rice for the control of *Echinochloa crus-galli*, sedges and broad leaf weeds as proposed by the applicant. Full details of the GAP can be found in the attached end points.
The representative formulated product for the evaluation was 'penoxsulam DE-638' (GF-657), an oil dispersion (OD) containing 20.4 g/l of penoxsulam.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Adequate methods are available to monitor all compounds given in the respective residue definitions for monitoring for food/feed of plant origin and for environmental matrices.

In the mammalian metabolism studies, penoxsulam was rapidly and almost completely absorbed upon oral administration. There was no evidence of bioaccumulation. Excretion was rapid, but dose and sex dependent as excretion was primarily observed via faeces in males and primarily excreted in urine in females. Penoxsulam was bio-transformed to a large number of metabolites; however the majority of the radioactivity was eliminated as unchanged parent compound. Plant and environmental metabolites BST[4] and BSTCA[5] were not identified in the rat metabolism studies. Toxicological information was lacking on the metabolite BSTCA to conclude on its relevance as a plant metabolite, moreover, it cannot be ruled out that BSTCA is also relevant according to the guidance document on the relevance of metabolites in groundwater[6].
The acute toxicity of penoxsulam was low by the oral, dermal and inhalation route; slight skin and eye irritation were observed, but no potential for skin sensitisation. The dog was found to be the most sensitive species with the kidneys as the main target organ; the overall short-term NOAEL in dogs was 18 mg/kg bw/day. Long-term toxicity reflected the same target organ observed in the short-term studies: the liver in mice and the kidneys in rats. The relevant long-term NOAEL was the dose level of 5 mg/kg bw/day from the 2-year rat study. No potential for genotoxicity, carcinogenicity or neurotoxicity was observed. No effect was seen on the reproductive performance and parameters; no developmental effect was observed either in rats. In rabbits, a slight increase in resorption rate parameters was associated with maternal toxicity, evidenced by gastro-intestinal upset and decreased body weight gain during the middle gestation.
The Acceptable Daily Intake (ADI) of penoxsulam was 0.05 mg/kg bw/day based on the NOAEL from the 2-year rat study and applying a safety factor of 100; the Acceptable Operator Exposure Level (AOEL) was 0.18 mg/kg bw/day based on the short-term dog studies and a safety factor of 100, no correction factor was needed to account for enteral resorption; no Acute Reference Dose (ARfD) was allocated. Dermal absorption was 10% for both the concentrate and in-use spray dilution of the representative formulation. The level of operator exposure for a maximum application rate of 0.04 kg penoxsulam/ha in rice was below the AOEL even without the use of personal protective equipment

[4] BST: 2-(2,2-difluoroethoxy)-*N*-(1*H*-1,2,4-triazol-3-yl)-6-(trifluoromethyl)benzenesulfonamide
[5] BSTCA: 3-({[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1*H*-1,2,4-triazole-5-carboxylic acid
[6] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

(PPE) according to both the German[7] and the UK POEM[8] models. Worker and bystander exposure were considered negligible.

A metabolism study in rice demonstrated that following foliar application of penoxsulam the total residues decreased rapidly to insignificant levels present at harvest of the crop. Therefore, the residue definition in rice grain was proposed as penoxsulam by default.
In supervised residue trials penoxsulam was found to be always below the Limit of Quantification of 0.01 mg/kg in rice grain, while in rice straw residues ranged up to 0.08 mg/kg. Consequently, an MRL for grain was proposed at 0.01 mg/kg, which is the lowest validated level of the analytical method. For straw an MRL is not required.
Rice may be grown in monoculture but also in rotation with other crops. A submitted confined crop rotation study showed that after a plant back interval of 90 days low residues could still be found in some crops. Other plant back intervals were not investigated. Moreover, a metabolite BSTCA, identified at significant levels in rotated crops, was neither found in primary crop metabolism nor in rat metabolism. The toxicological relevance of this metabolite for consumer risk assessment could not be addressed. As rotation practices in Member States seem to differ and the submitted data on rotational crops were limited, a final conclusion on the relevance of residues in rotated crops other than cereals could not be reached. Hence the experts agreed that further elaboration on the issue is required. A data requirement for further rotational crop data is proposed.
If only the scenarios of rice grown in monoculture and of rice rotated with other cereals are considered it can be concluded that exposure to livestock is not expected to be significant. Under these conditions, on the basis of the submitted animal metabolism studies, residues in food of animal origin are expected to occur at extremely low levels that would not be appropriate for monitoring. The experts therefore agreed that, for the time being, it would not be necessary to propose a residue definition and MRLs for food of animal origin. However, it should be noted that the assessment is not finalised with regard to potential livestock exposure to residues in rotational crops other than cereals.
Consumer exposure to residues of penoxsulam in rice grain is insignificant and thus in a chronic risk assessment intakes were well below to ADI. No acute assessment was conducted as an ARfD was not allocated. However, the consumer risk assessment cannot be finalised with regard to residues of metabolite BSTCA since a lack of sufficient occurrence data and toxicological data was identified. As BSTCA may also occur in drinking water derived from ground water at a level >0.1 µg/L, total consumer exposure to BSTCA has to be assessed in order to conclude on the consumer risk assessment.

Based on the available environmental fate and behaviour studies in soil and 2 field studies in rice paddies, penoxsulam and the breakdown products 5-OH-penoxsulam[9] (max 40.5% applied

[7] Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protections); Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirschaft, Berlin-Dahlem, n° 277, 1992
[8] Scientific Subcommittee on Pesticides and British Agrochemicals Joint Medical Panel, Estimation of Exposure and Absorption of Pesticides by Spray Operators (UK MAFF, 1986) and the Predictive Operator Exposure Model (POEM) (UK MAFF, 1992), version of 2003

radioactivity (AR) in soil) and BSTCA (max 53% AR in soil), were concluded as requiring environmental exposure assessments. In a sterilised laboratory aqueous photolysis study TPSA[10], 2-amino-TP[11] and 5-OH-2-amino-TP[12] were major metabolites but it was concluded that these did not need to be assessed, as though sought, they were not detected in relevant field studies in rice paddies. Penoxsulam and 5-OH-penoxsulam were characterised as exhibiting moderate persistence in soil with BSTCA exhibiting medium to high persistence. Additionally in aerobic natural sediment water systems the metabolites PCA-5-OH[13] and OH-BSTCA[14] were formed at up to 16%AR (sum of both compounds) in sediment, so exposure assessments were necessary for these metabolites and are available.

In the aerobic laboratory incubations mineralisation of both the phenyl and the 2-triazolopyrimidine rings to carbon dioxide was low accounting for only 0.3-2.4 % AR after 99 to 120 days. The formation of unextractable residues was a sink, accounting for 10-16 % AR in aerobic soil (same radiolabels) after 120 days and 21-58 % AR in aerobic natural sediment water studies after 99 days. Penoxsulam was characterised as exhibiting high to medium mobility, 5-OH-penoxsulam high mobility and BSTCA very high to medium mobility. Further details are necessary regarding a refined higher tier surface water exposure assessment that included definitions of novel scenarios, not prescribed by EU MED-Rice (2003) guidance[15]. It can be concluded that the potential for penoxsulam or its metabolite 5-OH-penoxsulam to contaminate vulnerable groundwater above the parametric drinking water limit of 0.1µg/L from the applied for intended uses is low. For the metabolite BSTCA the potential to contaminate vulnerable groundwater above the parametric drinking water limit of 0.1µg/L is low in situations represented by the MED-Rice clay scenario. However in situations represented by the MED-Rice sand scenario, BSTCA may be present in vulnerable groundwater at > 0. 1µg/L (calculations indicate concentrations up to 0.23µg/L). Therefore a non-relevance assessment for BSTCA was triggered.

In the risk assessment for birds, species representing insectivorous birds (wren), omnivorous birds eating large aquatic insects (mallard), omnivorous birds eating aquatic plants (mallard), large herbivorous birds (geese) and piscivorous birds (heron) were considered. All TER values were well above the relevant Annex VI trigger indicating a low risk to birds from the use of penoxsulam in rice paddies. Water vole (small herbivorous mammal), water shrew (eating aquatic invertebrates) and otter (eating fish and amphibians) were selected as focal species for the "in-field" risk assessment for mammals. The lowest TER obtained was 25 for the long-term risk to water vole. Since this was above

[9] 5-OH-penoxsulam: 2-(2,2-difluoroethoxy)-N-(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
[10] TPSA: (5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid
[11] 2-amino-TP: 5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-amine
[12] 5-OH-2-amino-TP: 2-amino-8-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-5-ol
[13] PCA-5-OH: 3-(2,2-difluoroethoxy)-2-[(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)sulfamoyl]benzoic acid
[14] OH-BSTCA: 3-({[2-(2,2-difluoroethoxy)-?-hydroxy-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-1,2,4-triazole-5-carboxylic acid
[15] Sanco/1090/2000-rev.1 June 2003 Guidance document for environmental risk assessments of active substances used on rice in the EU for annex 1 inclusion. Document prepared by Working Group on MED-Rice.

the relevant Annex VI trigger a low risk was concluded. For both birds and mammals the exposure from intake of contaminated paddy water was included in the estimation of the daily dose by simply adding the drinking water dose to the dietary dose. The log P_{ow} for penoxsulam is <3 and also the surface water metabolites were considered to have a log P_{ow}<3, hence the potential for bioaccumulation and secondary poisoning was considered as low.

Penoxsulam was classified as very toxic to aquatic organisms. The first tier risk assessment for algae and aquatic plants, based on PEC_{sw} in the "off-field" area, gave TERs of 46 and 2.9, respectively. An assessment was provided for fish and aquatic invertebrates in paddy water. No assessment was provided for algae or higher plants in paddy water, considering the herbicidal activity of penoxsulam. The lowest acute TER value was 202, which was obtained for *Daphnia* using the EC_{50} for the formulation. The lowest long-term TER was 83. It was concluded that the first tier risk to aquatic plants in the "off-field" area was high. Refinements based on a higher tier study with *Lemna* were not accepted in the peer review, and the risk to aquatic plants remains to be addressed. The risk to aquatic organisms from metabolites was addressed, as was the risk from bioaccumulation (log P_{ow}<3).

The risk to bees, non-target arthropods, earthworms, soil micro-organisms and non-target plants was assessed as low.

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

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC[16] Italy received an application from Dow AgroScience for inclusion of the active substance penoxsulam in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision 2004/131/EC[17].

Following the agreement between the EU-Commission and EFSA for EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the designated rapporteur Member State Italy submitted the report of its initial evaluation of the dossier on penoxsulam hereafter referred to as the draft assessment report (DAR) (Italy, 2005), to the EFSA on 10 February 2005. This DAR was distributed for consultation to the Member States and the applicant on 16 February 2005.

Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for data requirements to be addressed by the applicant as well as issues for further detailed discussion at expert level was agreed by EFSA.

Taking into account the information received from the applicant addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in September 2006 and January 2007. 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 in a written procedure with Member States in April 2009 leading to the conclusions as laid down in this report.

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

Following the agreement between the EU-Commission and EFSA regarding the peer review of new active substances, 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. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A.

The documentation developed during the peer review was compiled as a **peer review report** (EFSA, 2009) comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's DAR:

- the comments received,
- the resulting reporting table (rev. 1-1, 16 May 2006)

[16] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19
[17] OJ No L 37, 10.2.2004

as well as the documents summarising the follow-up of the issues identified as not finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (rev. 2-1, 11 June 2009).

Given the importance of the draft assessment report including its addendum (compiled version of January 2009) 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

Penoxsulam is the ISO common name for 3-(2,2-difluoroethoxy)-*N*-(5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide (IUPAC).

Penoxsulam belongs to the class of sulfonamide herbicides and triazolopyrimidine herbicides. Penoxsulam acts through inhibition of the enzyme acetolactate synthase (ALS) involved in the synthesis of branched-chain amino acids, leading to the cessation of cell division and subsequent growth processes in plants. Penoxsulam is absorbed via leaves, shoots and roots and is translocated in plants to meristematic tissues. Penoxsulam is a herbicide for controlling a wide range of weeds in rice crops.

The representative formulated product for the evaluation was 'penoxsulam DE-638' (VIPER, GF-657), an oil dispersion (OD) containing 20.4 g/l of penoxsulam. It should be noted however that some of the data were generated using other formulations: 'GF-237' (25.2 g/l OD) and 'GF-239' (200.1g/l OD).

The representative uses evaluated comprise post-emergence applications with conventional tractor-mounted spraying devices or self-propelled hydraulic sprayers to control *Echinochloa crus-galli*, sedges and broad leaf weeds in rice, from growth stage of BBCH 11 up to growth stage of BBCH 31, in Southern Europe, at a single application at a maximum application rate of 40 g a.s./ha.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of penoxsulam is 980 g/kg. No FAO specifications exist.

The experts at PRAPeR meeting 01 (September, 2006) considered that the proposed specification based on the pilot plant production was unreliable, the proposed values for the impurities were not acceptable.

The applicant was requested to provide a new technical specification based on the large scale five batch data, or a justification for the levels proposed. The applicant submitted the large scale five batch

data, which were evaluated in an addendum to the DAR volume 4 (Italy, 2009) but were not peer reviewed. The proposed specification was not changed except for the level of the relevant impurity. As a consequence there is no agreed specification for the impurities in the technical material. The specified maximum value of the relevant impurity Bis-CHYMP[18] was changed to max. 0.1 g/kg. The experts at PRAPeR meeting 01 (September, 2006) identified a data requirement for the validation data for the analytical method used for the determination of the relevant impurity.
Three of the industrial scale batches were found to contain new impurities at levels < 0.1%, identified by electrospray liquid chromatography-mass spectrometry (ESI/LC/MS) in the positive ion and negative ion modes. The data were evaluated in the addendum to vol. 4 but were not peer reviewed.

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 penoxsulam or the respective formulations. The main data regarding the identity of penoxsulam and its physical and chemical properties are given in Appendix A.

Adequate analytical methods based on HPLC-UV (285 nm) are available for the determination of penoxsulam in the technical material and in the representative formulations as well as for the determination of the respective impurities in the technical material (HPLC-UV).

Sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant origin and environmental matrices. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed.
An LC-MS/MS analytical method is available to monitor residues of penoxsulam in rice and rice processed products, with a LOQ of 0.01 mg/kg. The multi-residue enforcement method DFG S19 is considered not applicable as a residue enforcement method for the active substance penoxsulam.
Adequate LC-MS/MS method is available to monitor residues of penoxsulam and its metabolites in soil with LOQs of 0.003 mg/kg for each analyte.
An LC-MS/MS method is available to monitor penoxsulam residues in water (drinking water, surface water, ground water) with a LOQ of 0.05 µg/L. It should be noted that an LC-MS/MS method also exists for the monitoring of penoxsulam and its metabolites in surface water and drinking water with LOQs of 0.003 mg/L for each analyte.
Residues of penoxsulam in air can be determined with LC/MS with a LOQ of 1.5 µg/m³.
Analytical methods for the determination of residues in body fluids and tissues are not required as penoxsulam is not classified as toxic or highly toxic, however, an LC-MS/MS method is available to monitor its residues in body fluids and tissues with a LOQ of 0.01 µg/ml.

[18] Bis-CHYMP: 2-chloro-4-[2-(2-chloro-5-methoxy-4-pyrimidinyl)hydrazino]-5-methoxypyrimidine

2. Mammalian toxicology

Penoxsulam was discussed at the PRAPeR expert's meetings on mammalian toxicology, PRAPeR 04 in September 2006 and PRAPeR 14 in January 2007.

Information is available on the composition of the batches used in the toxicological studies, and is assessed in the addendum to the DAR volume 4. This information was not peer reviewed and therefore a formal data requirement was set to conclude on the comparability of the batches used in the toxicological studies with the proposed specification.

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

Oral absorption of penoxsulam was rapid and almost complete, with 81 % and 88 % of the dose being absorbed in males and females respectively, based on the radioactivity recovered in urine, tissues (excluding the gastro-intestinal tract), carcass, cage wash and bile 24 h after dosing. Radioactivity was primarily associated with blood, gastro-intestinal tract, liver and kidneys; there was no evidence of bioaccumulation independently of the administered dose or repeated dosing. Excretion was rapid, but dose and sex dependent: at low dose, excretion in males was primarily via faeces (36 % in urine, 56 % in faeces), while in females, excretion was primarily via urine (69 % in urine, 20 % in faeces). Biliary excretion accounted for the majority of the administered dose found in faeces in males (56 %) and females (14 %). At high dose, the majority of the radioactivity was excreted in faeces, very likely reflecting a lower oral absorption.

Penoxsulam was biotransformed into 36 different metabolites, although the majority of radioactivity was eliminated as unchanged parent compound. Metabolism occurred primarily through demethylation and ring hydroxylation, with subsequent conjugation with glucuronic acid or glutathione; minor sulfonamide bridge cleavage was also detected. Attempts to identify the metabolites were found to be inconclusive, except for the 2-hydroxyphenyl-penoxsulam[19] metabolite, however a metabolic pathway was proposed.

2.2. Acute toxicity

Penoxsulam presented low acute toxicity by the oral, dermal and inhalation route; slight skin and eye irritation was observed, not triggering classification. No skin sensitisation was observed in a Maximization test in guinea pig.

2.3. Short term toxicity

The oral short-term effects of penoxsulam were investigated in 28-day and 90-day dietary studies in rats, mice and dogs, and in a one-year feeding study in dogs that were all considered as acceptable. Other routes were tested in a 28-day dermal study in rats.

The target organ of penoxsulam in mice was limited to the liver, with increased liver weight and hepatocellular hypertrophy seen at 100 mg/kg bw/day; the NOAEL was the dose level of 10 mg/kg bw/day. In rats both the liver and kidneys were affected with increased organ weight associated with

[19] 2-hydroxyphenyl-penoxsulam: *N*-(5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-2-hydroxy-6-(trifluoromethyl)benzenesulfonamide

histopathological changes; the NOAEL was 50 mg/kg bw/day. Dogs were found to be the most sensitive species; the kidneys were identified as the main target organ characterised by hyperplasia of the transitional epithelium of the renal pelvis and crystals in the renal pelvis and collecting ducts observed at 45 mg/kg bw/day dose level. The overall NOAEL in dogs was set at 18 mg/kg bw/day.
Percutaneous application of penoxsulam to rats for 28 days did not exhibit dermal irritation or systemic toxicity, thus the NOAEL was the highest dose tested of 1000 mg/kg bw/day.

2.4. GENOTOXICITY

Penoxsulam was tested *in vitro* for reverse mutation in *Salmonella typhimurium* and *Escherichia coli*, forward mutation at the hypoxanthine-guanine phosphoribosyl transferase locus of Chinese hamster ovary cells (CHO/HGPRT) and chromosome aberration using rat lymphocytes; *in vivo* genotoxicity was performed in a mouse bone marrow micronucleus test. All tests gave negative results; no genotoxic potential was attributed to penoxsulam.

2.5. LONG TERM TOXICITY

Long-term toxicity was examined in a 2-year study in rat and an 18-month study in mouse.
In rats, the kidneys were confirmed as target organs, the NOAEL was the dose level of 5 mg/kg bw/day based on a dose-related increase in the severity of chronic progressive glomerulonephropathy at 50 and 250 mg/kg bw/day. The only neoplasm that had statistically identified increase was large granular lymphocytic (LGL) leukaemia in male rats. Considering the high spontaneous incidence of LGL leukaemia unique to this specific strain of rat (Fisher 344) and the lack of a dose-response in both incidence and severity, the experts agreed with the RMS conclusion that no tumourigenic or carcinogenic potential was related to penoxsulam ingestion.
In mice, the NOAEL was the dose level of 10 mg/kg bw/day based on increased liver weight with hepatocellular hypertrophy in males at the dose of 100 mg/kg bw/day; there was no increase in the incidence of neoplasm in any tissue that was attributed to penoxsulam administration.

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity of penoxsulam was tested in a two-generation reproduction toxicity study in rat, and a developmental toxicity study in rat and in rabbit.

Reproduction toxicity

No effect on the reproductive performance and parameters was found up to the highest dose tested of 300 mg/kg bw/day. In both generations, offspring body weights at 300 mg/kg bw/day dose level were lower than controls throughout lactation following the same pattern as the maternal feed consumption and body weight. Parental toxicity consisted also in increased organ weight associated with histopathological changes in the liver and kidneys. The NOAEL for reproductive effects was the highest dose of 300 mg/kg bw/day, the NOAEL for offspring toxicity was 100 mg/kg bw/day, while the NOAEL for parental toxicity was 30 mg/kg bw/day dose level.

Developmental toxicity

In the developmental toxicity study in rat, no developmental effect was observed, therefore the developmental NOAEL was the highest dose tested of 1000 mg/kg bw/day. The maternal NOAEL was 500 mg/kg bw/day based on decreased body weight gain and increased kidney weight at 1000 mg/kg bw/day.

In rabbits, maternal toxicity was evidenced by clinical sign of gastro-intestinal upset manifested by abnormal/decreased/absent faeces, containing mucoid matter and decreased body weight gain during the middle gestation at the high dose level of 75 mg/kg bw/day. These effects were associated with a slight increase in resorption rate parameters (post-implantation loss, number of resorptions per litter, implantations resorbed and number of resorptions per litter with resorptions). The maternal and developmental NOAELs were the 25 mg/kg bw/day dose level.

2.7. NEUROTOXICITY

Acute neurotoxicity

In an acute neurotoxicity study in rats, no treatment-related neurotoxic effects were noted; the NOAEL for neurotoxicity was 2000 mg/kg bw (the highest dose tested).

Chronic neurotoxicity

A chronic (1-year) neurotoxicity study in rats was conducted as part of a two-year chronic/ carcinogenicity study. The only treatment-related effect noted was the presence of perineal urine soiling in the mid- and high-dose levels. Given the lack of any treatment-related effect on any other parameters and the absence of neuropathological findings in either the central or peripheral nervous system, perineal soiling was not considered the result or expression of neurotoxicity. The NOAEL for neurotoxicity following one year dietary exposure was 250 mg/kg bw/day, the highest dose tested.

2.8. FURTHER STUDIES

Metabolites

Supplementary studies were conducted on three metabolites of penoxsulam, 5-OH-penoxsulam[20], BSTCA[21] and BST[22]. From these metabolites, only the 5-OH-penoxsulam was found as well in rat and goat metabolism studies.

BSTCA may appear in groundwater at levels above 0.1 µg/L according to fate and behaviour environmental models (please refer to point 4.2.2).

The three metabolites 5-OH-penoxsulam, BSTCA and BST were tested *in vitro*, in an Ames test (reverse mutation test in *Salmonella typhimurium* and *Escherichia coli)*, a CHO/HGPRT forward mutation assay and a chromosomal aberration assay using rat lymphocytes. All tests gave negative results; there was no evidence of genotoxic potential for these three penoxsulam metabolites.

[20] 5-OH-penoxsulam: 2-(2,2-difluoroethoxy)-N-(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide

[21] BSTCA: 3-({[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-1,2,4-triazole-5-carboxylic acid

[22] BST: 2-(2,2-difluoroethoxy)-N-(1H-1,2,4-triazol-3-yl)-6-(trifluoromethyl)benzenesulfonamide

The experts agreed that 5-OH-penoxsulam and BST were not relevant in terms of groundwater hazard assessment[23] based on the toxicological properties of the parent compound.
The metabolite BSTCA may appear also at significant levels in rotational crops (please refer to point 3.1.2); however it was not identified as a rat metabolite. Except for the genotoxicity studies referred to above, no information is available on its toxicity. Consequently no conclusion could be drawn by the experts on its relevance as a plant metabolite, and moreover, it cannot be ruled out that BSTCA is also relevant according to the guidance document on the relevance of metabolites in groundwater.

2.9. MEDICAL DATA

Limited information is available as penoxsulam is a new active substance. At the time of the dossier submission, it had been produced only in laboratory quantities and no manufacturing personnel exposure had occurred. There have been no reports on alleged human health effects associated with penoxsulam reported to the US EPA by the applicant; searches of the open literature produced no reports of adverse effects in humans related to this active substance.

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

ADI

As proposed by the rapporteur Member State in the DAR, **the ADI for penoxsulam was set at 0.05 mg/kg bw/day** based on the long term rat study presenting a NOAEL of 5 mg/kg bw/day and a safety factor of 100.

AOEL

The proposal made by the RMS in the DAR and clarified in the addendum to the DAR volume 3, B.6 dated December 2006 (Italy, 2009) was agreed by the experts. **The AOEL was set at 0.18 mg/kg bw/day** base on the short term dog studies with a NOAEL of 18 mg/kg bw/day and a safety factor of 100; no correction for enteral resorption was needed.

ARfD

As the compound was of low acute toxicity, and no neurotoxicity or reproductive toxicity was observed, the establishment of an acute reference dose was not deemed necessary. **No ARfD was allocated.**

2.11. DERMAL ABSORPTION

Dermal absorption was investigated in an *in vivo* study in rat using a formulation (OD formulation containing 25 g penoxsulam/L) similar to the representative formulation (OD formulation containing 20.4 g penoxsulam/L) and its in-use spray dilution (0.03 g penoxsulam/L). The approach initially proposed by the RMS was not agreed by the experts, as the skin depot was not included as a potentially absorbable amount and a default value of 10 % was set.

[23] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

EFSA note: This conclusion is supported by the data of the study where all animals were treated for 24 hours. At the 72 h time-point analysis, the same value of about 10 % dermal absorption was obtained adding the radioactivity found in urine, rinse, faeces, carcass, tissues (including application-site skin) and final cage wash for both the concentrate and diluted formulations.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product 'penoxsulam DE-638' (GF-657) is an oil dispersion (OD) formulation containing 20.4 g penoxsulam/L. It is a post-emergence herbicide used in direct seeded rice. The product should be applied once per growing season at a maximum application rate of 40 g penoxsulam/ha (2 L product/ha) in a spray volume of 150 to 500 L/ha.

Operator exposure

The operator exposure estimates were calculated using both the German[24] and the UK POEM[25] models. According to the German model assumptions, the body weight of operators is 70 kg and the work rate is 20 ha/day. According to the UK POEM, body weight of operators is 60 kg and work rate is 50 ha/day; container size is 1 L. Dermal absorption is 10 % for both the formulation and the in-use spray dilution.

Estimated operator exposure presented as % of AOEL (0.18 mg/kg bw/day) with tractor mounted equipment in rice, application rate of 0.04 kg penoxsulam/ha

Tractor-mounted (field crop)	Work rate (ha/day)	Spray volume (L/ha)	% of AOEL No PPE
UK POEM	50	150	14.39
German model	20	-	2.89

PPE: personal protective equipment

The estimated operator exposure was below the AOEL according to both models even when no personal protective equipment (PPE) was considered.

Worker exposure

According to normal rice agricultural practices, re-entry to the crop prior to harvest is not necessary. Residues of penoxsulam would then be negligible at harvest and would lead to insignificant worker exposure; therefore the experts agreed that no further risk assessment was necessary.

[24] Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protections); Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirschaft, Berlin-Dahlem, n° 277, 1992

[25] Scientific Subcommittee on Pesticides and British Agrochemicals Joint Medical Panel, Estimation of Exposure and Absorption of Pesticides by Spray Operators (UK MAFF, 1986) and the Predictive Operator Exposure Model (POEM) (UK MAFF, 1992), version of 2003

Bystander exposure

Bystander exposure was estimated using drift data from Ganzelmeier *et al.* 1995[26], for a bystander located at the boundary of the field at a distance of five meters from the spray equipment (0.6 % drift) and considering inhalation exposure as negligible. Assuming a 100 % dermal absorption for an average body weight of 60 kg, the systemic exposure would then be 0.0004 mg/kg bw/day corresponding to 0.2 % of the AOEL (of 0.18 mg/kg bw/day).

3. Residues

Penoxsulam was discussed in the meeting of experts in residues PRAPeR 05 in September 2006 on the basis of the DAR and the addendum to the DAR volume 3, B.7 (Italy, 2009).

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

A metabolism study in rice demonstrated that the total radioactive residue (TRR) upon application of ^{14}C labelled penoxsulam decreased rapidly following foliar application. This was likely due to a combination of metabolic activity and biological growth dilution. There was very little translocation of radioactivity into the grain. Residues in both grain and straw contained penoxsulam, the 5-OH analogue of penoxsulam and two unidentified metabolites. One of these two unknown metabolites was very polar in nature and thus may represent a conjugate of the 5-OH analogue of penoxsulam or of other metabolites. However, due to their low concentrations, no attempts were made to identify these unknown compounds.

In the plant metabolism study penoxsulam was applied at a rate 2.5 times greater than the maximum proposed field application rate. Total residues in the mature plants were approximately 0.022 mg penoxsulam equivalents per kg in straw and 0.003 mg penoxsulam equivalents per kg in the grain. Hence, under field conditions total residues (sum of penoxsulam and metabolites) in the crop at harvest would be expected to occur at levels below 0.01 mg/kg.

It was noted that the application to the rice plants in the study happened earlier than defined by the latest time of application in the GAP. However, the conditions chosen in the rice metabolism study provided the possibility for a maximum of identification of all potentially significant components of the residue on the crop. It was presumed by the experts that a later application time according to GAP criteria would not have lead to a significantly different qualitative or quantitative result in the metabolism study.

In view of the very low levels of total residues, the residue definition for rice grain was proposed as penoxsulam by default. A residue definition for rice straw is not necessary since it is not consumed by livestock or humans.

Supervised residue trials to determine residues of penoxsulam in grain at harvest following an application to rice were conducted according to conditions that met the critical GAP. In total, eleven

[26] Studies on the Spray Drift of Plant Protection Products (Federal Biological Research Centre for Agriculture and Forestry; Berlin; No. 305; 1995)

trials were conducted in typical rice growing areas of Italy, Spain, and Greece over two growing seasons. In residue decline studies residue levels of penoxsulam decreased rapidly after application. In all trials residues in rice grain were below the Limit of Detection (<0.002 mg/kg). Penoxsulam residues in rice straw ranged between 'not detected' (<0.002 mg/kg) and 0.08 mg/kg, but were merely below the Limit of Quantification (LOQ) of 0.01 mg/kg.

According to the RMS adequate stability of penoxsulam residues in samples of grain, straw and whole plants under frozen storage was demonstrated for the full period the samples were stored for, however these data were not presented in the DAR. As agreed in the meeting PRAPeR 05, an evaluation was submitted by the RMS in the addendum to the DAR volume 3, B.7. The data are not peer reviewed, but according to EFSA seem to be acceptable to confirm the validity of the results obtained in the supervised residue trials.

The available residue trials are considered sufficient to propose an MRL for penoxsulam in rice grain at LOQ level. No MRL is proposed for rice straw.

Due to the very low residue levels in rice grain, studies on the effects of industrial processing are not necessary.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Rice may be grown in monoculture, but it seems also to be practice in European countries with rice cultivation that rice can be succeeded by other crops (e.g. Soya, maize, tomato).

Thus, the potential uptake of residues from soil by succeeding crops was assessed. In a confined rotational crop study wheat, kale and potatoes were planted in soil 90 days after application of radio-labelled penoxsulam at a rate corresponding to the notified maximum seasonal rate (1N rate) and at approx. 2 fold the notified rate (2N rate), respectively.

From the data it appeared that after a plant back interval of 90 days low residues could be found in some crops (e.g. 0.024 mg equ./kg in wheat straw, 0.5 mg/kg in potato foliage at 1N rate). Data on plant back intervals other than 90 days were not available to the experts; and it could not be excluded that residues could occur at a longer plant back interval. Moreover, from the residue trials in the primary crop it appeared that also a shorter period than 90 days might theoretically be possible between the application to rice and a potential replanting. The experts therefore requested the RMS to evaluate in an addendum data on plant back intervals other than 90 days, if available, as well as any additional information with regard to residues in succeeding crops not yet reported in the DAR.

Since no follow-up on this issue has been provided by the RMS in an addendum, it is assumed by EFSA that no additional data or information than already presented in the DAR are available to the RMS. To properly address the concern raised by the experts in the meeting, and to be consistent within the assessment of pesticide compounds under directive 91/414 in terms of necessary data, EFSA proposes a new data requirement to fully address residues in succeeding crops, preferably according to OECD guidelines. In the commenting period on the conclusion the RMS indicated their disagreement with this conclusion. The RMS believes there is no need for additional investigation on succeeding crops but refers to Annex III applications for any further investigation.

In the context of the following crops assessment it is also noted that a metabolite BSTCA was identified in plant material in the succeeding crop study. Metabolite BSTCA represented 25% of the TRR in potato foliage, but was not found in the primary crop study on rice. Metabolite BSTCA was also found in soil metabolism studies and might thus have been taken up from the soil. Moreover metabolite BST was detected in soil. Considering metabolite structure and common metabolic pathways the experts in the PRAPeR 05 meeting expected BSTCA to be further metabolised to BST also in plants, though it was not actually identified in the available study. It is noted that identification of residues in crops other than potato was limited by low total residue levels.
Concerning information on the toxicological properties and/or relative toxicity of the two metabolites BSTCA and BST, the experts in the PRAPeR 05 meeting decided to consult the experts on toxicology. According to the experts' meeting of toxicology the metabolites BST and BSTCA were not detected in the rat metabolism. Only very limited toxicological data are available, and the information was considered insufficient to conclude on their relevance for consumer risk assessment. Hence the applicant may provide sufficient data and information on the toxicological profile of BSTCA in order to assess its relevance as a plant metabolite. If the required data on succeeding crops also confirm the presence of BST, its toxicological profile will have to be addressed accordingly.

Based on the data available, the meeting concluded that, if only cereals were grown as succeeding crops no residue levels significant for consumer and livestock exposure would probably be present. However, it was pointed out that with the data available it is not possible to exclude that significant residues can occur in other succeeding crops. With regard to the findings in potato foliage, considering potato is only a model crop in the confined crop rotation study, a similar residue situation in leaves or tops of other crops has to be assumed. Depending of the following crop this might be of relevance to human and/or livestock exposure.
The experts in the PRAPeR 05 meeting proposed that particular consideration of the aspect should be given in Member States if practices deviate from the practice that could be assessed by the meeting with the data available, i.e. cereals as a following crop.
As a matter of fact, the issue on residues in succeeding crops could not be concluded for following crops other than cereals. EFSA notes that, if the experts agreed the data available are insufficient to assess an unrestricted use, a data requirement should have been identified in the peer review procedure for penoxsulam. Therefore, as already mentioned above, EFSA has made a respective proposal after the PRAPeR 05 expert meeting for additional data to address residues in succeeding crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The use of penoxsulam in rice does not lead to significant residues (>0.1 mg/kg) in potential livestock feed neither does penoxsulam tend to accumulate in the tissue. Thus, livestock metabolism and feeding studies are not required.
Nevertheless, livestock metabolism studies with penoxsulam were conducted in lactating goats and laying hens and evaluated in the DAR. Upon repeated dosing of an exaggerated rate (*ca* 1000 times greater than the theoretical maximum exposure in the livestock diet from rice grain) more than 92% of the total radioactivity recovered was found in goat and hen excreta.

The only tissues or edible products found to have levels of radioactivity of 0.01 mg penoxsulam equivalents per kg or greater were goat liver and kidney, and hen liver. Goat liver and kidney contained a maximum of 0.0712 and 0.0512 mg/kg total radioactive residue, respectively, while the maximum residue in hen liver was 0.017 mg/kg.

The major identifiable residue in all tissues was penoxsulam. Levels of the metabolites were low and were not characterised further. Additionally, results of the studies indicated that cleavage of the sulfonamide bridge did not occur to any significant extent as a result of animal metabolism.

The RMS provided a livestock dietary exposure assessment in the DAR. In terms of residues of penoxsulam in rice grain, the dose level in these studies was about 1000 times greater than the theoretical maximum exposure of livestock in the diet. Therefore, actual residues in edible tissues after consumption of rice grain by the animals will be considerably less than 0.01 mg/kg, and livestock feeding studies are not necessary.
However, potential residues in rotated crops that could also be fed to livestock were not considered in this assessment, as the issue of rotational crop residues needs to be addressed further (see 3.1.2 above). Based on the available data on solely primary and rotated cereals, residues might not lead to a significant livestock dietary burden, however, further rotational crop data for all relevant crop categories and plant back intervals should be submitted and assessed to conclude the issue.

The experts agreed that in terms of the use scenario as assessed by the RMS (only rice grain) a residue definition for animal products would not be necessary. Metabolism studies have indicated that residues in edible tissues, including milk and eggs, if present, are expected to occur at extremely low levels that would not be appropriate for monitoring. Therefore, the experts agreed that an MRL for food of animal origin is currently not necessary.

3.3. CONSUMER RISK ASSESSMENT

A chronic dietary intake and risk assessment for consumers (TMDI) on the basis of the MRL of 0.01 mg/kg proposed for rice grain showed that exposure to penoxsulam residues in rice is well below (0.02%) the ADI of 0.05 mg/kg bw/day. Taking into account that residues were not detected in rice grain in residue field trials (i.e. were below <0.002 mg/kg), human dietary exposure to penoxsulam residues on rice is even lower than estimated with the TMDI and can therefore be regarded as negligible.
However, the issue of residues in rotational crops could not be concluded for following crops other than cereals. Residues in cereal crops planted after rice are expected to be very low and thus insignificant for consumer and livestock exposure. However, depending on crop rotation practices applied in Member States metabolite BSTCA, and potentially BST, is expected to be present at significant levels in rotational crops other than cereals. There are currently insufficient occurrence data in rotational crops and insufficient toxicological data available with regard to metabolites. Hence BSTCA could not be considered in the livestock and consumer intake estimates and in the risk assessment, and as such these cannot be finalised.

Though dietary exposure of consumers and livestock with regard to residues in the primary crop rice is negligible, it appeared that there may be also consumer exposure to metabolite BSTCA via drinking water derived from ground water. In order to apply the threshold-of-concern-approach for BSTCA residues, the draft guidance document on assessment of relevance of groundwater metabolites[27] requires the consideration of potential consumer exposure from all sources, to ensure the total exposure of consumers to the metabolite will not exceed the threshold-of-concern of 0.02µg/kg bw/day. With the currently available data there is an indication the threshold might be exceeded, however, a sound prediction is not possible.

3.4. PROPOSED MRLS

The residue definition in rice is penoxsulam. Since residue was not detected in rice grain in any trials at the critical GAP, the MRL for grain is proposed at 0.01 mg/kg, which is the lowest validated level of the analytical method.

Residue levels in food commodities from livestock are predicted to be very low and not present at levels that would be appropriate for monitoring. Therefore, MRLs for food commodities from livestock (i.e. meat, poultry, dairy products and eggs) are not considered necessary.

4. Environmental fate and behaviour

Penoxsulam was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 02 in September 2006.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Soil experiments (4 different soils) were carried out under aerobic conditions in the laboratory (20°C 40% maximum water holding capacity (MWHC)) in the dark. Mineralisation to carbon dioxide of the applied phenyl ring-^{14}C-radiolabel accounted for only 0.5-1.4 % of the applied radiolabel (AR) after 120 days. The value for the 2-triazolopyrimidine ring-^{14}C-radiolabel was also comparably low. The formation of residues not extracted by calcium chloride followed by acidified acetonitrile and acetone were a sink for these applied radiolabels (accounting for 10.2-15.6% AR after 120 days). The major (>10%AR) extractable breakdown products present were: 5-OH-penoxsulam (max. 15.3 to 40.5 %AR at 14 to 58 days days), and BSTCA (max. 29.4 to 53 %AR at 14-120 days).

As the applied for intended use of penoxsulam is for rice, the relevant EU MED-Rice (2003) guidance[28] requires that aerobic laboratory flooded soil degradation studies are provided on at least 2 soils. Such experiments were not included in the applicant's dossier. However additional information was available that when all considered together, resulted in it being considered that these studies did not need to be requested in this case. This information was:

[27] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

[28] Sanco/1090/2000-rev.1 June 2003 Guidance document for environmental risk assessments of active substances used on rice in the EU for annex 1 inclusion. Document prepared by Working Group on MED-Rice.

An anaerobic flooded 20°C soil study was available on a single silty clay loam soil. This experiment indicated that penoxsulam degrades at a comparable rate as it did under aerobic (not flooded) conditions though it dissipated slightly faster producing more not extracted residues. It formed the same major breakdown products as under aerobic not flooded conditions: 5-OH-penoxsulam (max. 33 %AR at 14 days), and BSTCA (max. 19.1 %AR at 120 days).
A laboratory soil photolysis study on soil at 75% 1/3 bar water holding capacity, where the major breakdown product BSTCA (max. 11.3 %AR at 30 days, also formed in the dark), as well as the novel breakdown product 2-amino-TP[29] (max. 10.4 %AR at 37 days) were identified.
Flooded not radiolabelled field studies at 2 sites (described below in section 4.1.2), where analyses were carried out for the appropriate expected (including aqueous photolytic) breakdown products.
Using all of this information, it was concluded that the substances that required exposure assessments in the soil compartment and consideration for groundwater exposure were penoxsulam, 5-OH-penoxsulam and BSTCA.

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

The rate of degradation of penoxsulam, 5-OH-penoxsulam and BSTCA were estimated from the results of the studies described in 4.1.1 above. Single first order DT_{50} from soils used to characterise the route of degradation were for penoxsulam: 22, 24, 25 and 58 days (20°C, not flooded aerobic conditions), 6.6 days (20°C, flooded anaerobic conditions whole system, 8.8 days estimated for just the soil) and 19 days (25°C not flooded moist photolysis conditions 40°N summer sunlight) all estimated using linear regression. For 5-OH-penoxsulam single first order DT_{50} were 19, 23, 24 and 37 days (20°C, not flooded aerobic conditions) and 5.1 days (20°C, flooded anaerobic conditions). For BSTCA single first order DT_{50} were 70, 61, 67 and 118 days (20°C, not flooded aerobic conditions). All these metabolite DT_{50} were estimated from experiments where penoxsulam was dosed, using non-linear regression and a compartment model implemented in ModelMaker.

Field paddy dissipation studies (no crop present) were provided from a site in northern Italy and a site in southern Spain where an application was made in May to soil in drained paddies. The paddies had been flooded just before application (of 100g penoxsulam/ha, 2.5N) and were reflooded 16 to 24 hours after the application. Water depth was maintained at 10 to 14 cm. Water did not flow out the paddy through a surface water outlet. The water that was added just replenished evaporation or leaching down the soil profile. Soil samples (cores) taken were analysed for penoxsulam, 5-OH-penoxsulam, BSTCA, BSA[30], sulfonamide[31] and 2-amino-TP with a limit of quantification of 3 µg/kg. Water samples were analysed for penoxsulam, 5-OH-penoxsulam, BSTCA, BSA, sulfonamide, 2-amino-TP, 5-OH-2-amino-TP[32] and TPSA[33] with a limit of quantification of 3 µg/L.

[29] 2-amino-TP: 5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-amine
[30] BSA: 2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid
[31] Sulfonamide: 2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonamide
[32] 5-OH-2-amino-TP: 2-amino-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-5-ol
[33] TPSA: (5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid

The only residues detected were penoxsulam, BSTCA and BSA, although BSA was only detected in one soil and one water sample.
For penoxsulam paddy water single first order DT_{50} were 5.6 to 6.1 days. For soil these values were < 1 day (values estimated by linear regression). DT values for BSTCA were not calculated.

The experts agreed to use the flooded anaerobic laboratory penoxsulam soil single first order DT_{50} of 8.8 days (noting in the field studies the soil DT_{50} was less than 1 day) and an arithmetic mean $K_d$oc of 94mL/g (see section 4.1.3) for use in step 1 MED-Rice (2003) PEC soil calculations. For the breakdown products 5-OH-penoxsulam, BSTCA the observed formation fractions of 0.33 (flooded laboratory anaerobic soil study) and 0.53 (aerobic soil study) were agreed for use when calculating a PEC utilising the initial penoxsulam PEC calculated. These input parameters and the resulting PEC can be found in Appendix A of this conclusion.

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

The adsorption / desorption of penoxsulam was investigated in 17 soils in satisfactory guideline batch adsorption experiments. Calculated adsorption $K_d$oc values varied from 12 to 305 mL/g, with there being evidence of a correlation of adsorption with pH (lower adsorption at higher pH). The experts agreed it would be appropriate to use an arithmetic mean value of the 4 European soils (94mL/g) in exposure calculations, noting that this gave a similar arithmetic mean value to that calculated using all the available data (73mL/g).

The adsorption / desorption of 5-OH-penoxsulam was investigated in 8 soils in satisfactory guideline batch adsorption experiments. Calculated adsorption $K_d$oc values varied from 17 to 144 mL/g. There was no evidence of a correlation of adsorption with pH. The experts agreed it would be appropriate to use an arithmetic mean value of the 4 European soils (59mL/g) in exposure calculations, noting that this gave a similar arithmetic mean value to that calculated using all the available data (45mL/g).

The adsorption / desorption of BSTCA was investigated in 6 soils in satisfactory guideline batch adsorption experiments. Calculated adsorption $K_d$oc values varied from 5 to 444 mL/g. There was no evidence of a correlation of adsorption with pH. The experts agreed it would be appropriate to use an arithmetic mean value of the 4 European soils (174mL/g) in exposure calculations, noting that this gave a fairly similar arithmetic mean value to that calculated using all the available data (125mL/g).

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Penoxsulam was stable under sterile hydrolysis conditions at 50°C at pH 4, 7 and 9.

In a laboratory study where direct aqueous photolysis of penoxsulam was investigated under sterile pH 7 buffer and sterile natural water (25°C) penoxsulam degraded with a single first order DT_{50} of 2 days equated summer sunlight at 40°N to the major metabolites TPSA (max 56%AR at 1 day) 2-amino-TP (max 18%AR at 1 day), 5-OH-2-amino-TP (max 23%AR at 14 days) and BSA (max

36%AR at 1.5 days). Using the ModelMaker program and a compartment model for these metabolites single first order DT_{50} were estimated to be 2-4.7 days, 0.6 days, not calculated and 0.7-0.9 days respectively. It should be noted that of these aqueous photolysis metabolites identified in these laboratory experiments only BSA and then only at one sampling time was detected at > 3 µg/L in the two available field experiments in rice paddies, (all metabolites were analysed for and the study was overdosed (2.4N compared to the use applied for), see section 4.1.2).

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

In dark water-sediment studies (2 systems studied at 20°C in the laboratory, sediment pH 7.3 and 5.3,) penoxsulam degraded with single first order whole system DT_{50} 11 and 34 days, (dissipating from the water phase with single first order DT_{50} of 10 and 20 days). The major metabolites were 5-OH-penoxsulam (max. 30 % AR at 35 days relatively equally distributed between water and sediment) and BSTCA (max. 24 % AR at 66 days primarily in water). In the sediment of one system PCA-5-OH[34] and OH-BSTCA[35] were identified as being potentially major metabolites. A single first order whole system DT_{50} of 24 and 75 days were estimated for 5-OH-penoxsulam. The terminal metabolite, CO_2, accounted for only 0.8 to 2.4 %AR of the phenyl ring-^{14}C and 2-triazolopyrimidine ring-^{14}C radiolabels by 99 days. Residues not extracted from sediment by acidified acetonitrile were a significant sink representing 21 and 58 % AR for the two systems investigated.

With regard to the MED-Rice (2003) step 1 surface water and sediment PEC calculations, the experts accepted the available calculations. The resulting PEC surface water and sediment can be found in Appendix A.

After the meeting of experts the RMS presented higher tier surface water exposure modelling they had received from the applicant, to refine the risk characterisation to higher aquatic plants (see the final addendum section B.8.5.2 pages 210 to 217 (Italy, 2009)). These simulations therefore have not been peer reviewed. The Member State experts only discussed and agreed substance property input parameters that were appropriate for use with MED-Rice (2003) step 1 surface water and sediment PEC calculations. Consequently this conclusion indicates that further information is required, in the 'list of studies available but not peer reviewed' section. The level of detail included in the addendum prepared by the RMS in relation to these simulations was insufficient to allow any view on the approach (particularly scenario definitions) that was used in these simulations. EFSA noted (when consulting the applicant's original report of these model simulations), that though the approach used and scenario definitions selected are well described, the applicability of the scenario definitions selected and parameterisation chosen with its associated assumptions is not a straight forward task. Such an assessment would need very careful consideration by experts with knowledge of rice

[34] PCA-5-OH: 3-(2,2-difluoroethoxy)-2-[(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamoyl]benzoic acid

[35] OH-BSTCA: 3-({[2-(2,2-difluoroethoxy)-?-hydroxy-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-1,2,4-triazole-5-carboxylic acid

production systems in Europe. EFSA also noted that some substance properties selected for input in the simulations that the models require to be degradation rates, were in fact dissipation rates estimated from the field studies or laboratory sediment water experiments. This should not be accepted without a clear justification why this could be appropriate in this case. Such a clear justification was not included in the applicant's documentation.

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

As a worst case, pre-emergence applications to rice (i.e. no crop interception) was assumed in calculations for application to 10cm deep paddy water using the MED-Rice (2003) step 1 method. The substance property input parameters used were: penoxsulam single first order DT_{50} 5.3 days, K_{doc} 94 L/kg; 5-OH-penoxsulam formation fraction from penoxsulam 0.33 single first order DT_{50} 5.1 days, K_{doc} 59 L/kg; and BSTCA formation fraction from penoxsulam 0.50 single first order DT_{50} 100 days, K_{doc} 174 L/kg. The peer review accepted these PEC calculations with these substance input parameters

Penoxsulam was calculated to be present in leachate leaving the upper soil layer at an annual average concentration of <0.0013µg/L for both the step 1 defined clay and sand soil scenarios. These values for 5-OH-penoxsulam were 0. 0001µg/L. For BSTCA and the clay scenario the concentration was calculated to be <0.0001µg/L, but for the sand scenario the concentration calculated was 0.234µg/L. On the basis of these calculations it cannot be excluded that the metabolite BSTCA could be present in groundwater above the parametric drinking water limit of 0.1µg/L for the applied for intended use in situations represented by the MED-Rice sand scenario. Therefore a non-relevance assessment is triggered for the metabolite BSTCA.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of penoxsulam (2.49×10^{-14} Pa at 20°C) means that penoxsulam would not be expected to volatilise from plant surfaces, water or soil water. Calculations using the method of Atkinson for indirect photo-oxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at 2.1 hours (assuming an atmospheric hydroxyl radical concentration of 1.5×10^{6} radicals cm^{-3}). This Atkinson half-life indicates that any small proportion of applied penoxsulam that did reach the upper atmosphere (for example as aerosols formed at the time of spraying) would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Penoxsulam was discussed at the PRAPeR experts' meeting for ecotoxicology PRAPeR 03 in September 2006 on the basis of the DAR and an addendum to the DAR volume 3, B.9 dated August 2008 (Italy, 2009).

Penoxsulam (code: DE-638) is the active substance in the formulated product GF-657 (oil-dispersion) with the trade name VIPER (20.4 g/L). Some formulation studies were generated using another formulation GF-237 OD (25 g a.s./L), considered to be similar. The representative field uses were as a herbicide in rice paddies (BBCH 11-31) at application rates up to 1 x 40 g a.s./ha.

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

5.1. RISK TO TERRESTRIAL VERTEBRATES

In the risk assessment for birds, species representing insectivorous birds (wren), omnivorous birds eating large aquatic insects (mallard), omnivorous birds eating aquatic plants (mallard), large herbivorous birds (geese) and piscivorous birds (heron) were considered. Residue values given in SANCO/4145/2000 for large insects and short grass were used for aquatic insects and aquatic plants, respectively. Since penoxsulam is not systemic or has no potential to bio-accumulate (log P_{ow} <3) this could be considered as a worst case. Data on body weight and food ingestion rate for the non-standard species were taken from Crocker et al. 2002[36]. The concentration of penoxsulam in fish and amphibian diet for herons was calculated using PEC_{sw} and the determined BCF. All TER values were well above the relevant Annex VI trigger indicating a low risk to birds from the use of penoxsulam in rice paddies.

In the DAR the long-term risk assessment for mammals used a NOEL of 100 mg/kg bw/day for pup body weight. The assessment was revised due to a comment from one MS and a NOEL of 25 mg/kg bw/day for maternal body weight and development from a rabbit development study was chosen. Updated TER values are provided in Appendix A. Water vole (small herbivorous mammal), water shrew (eating aquatic invertebrates) and otter (eating fish and amphibians) were selected as focal species for the "in-field" risk assessment for mammals. For the "off-field" assessment vole, hare, shrew and otter were selected. As for birds, data on body weight and food ingestion rate for the non-standard species were taken from Crocker et al. 2002, and the concentration of penoxsulam in fish and amphibian diet for herons was calculated using PEC_{sw} and the determined BCF. The lowest TER obtained was 25 for the long-term risk to a water vole. Since this was above the relevant Annex VI trigger a low risk was concluded.

For both birds and mammals the exposure from intake of contaminated paddy water was included in the estimation of the daily dose by simply adding the drinking water dose to the dietary dose.

[36] Crocker, D., Hart, A., Gurney, J. and McCoy, C. 2002. Project PN0908: Methods for estimating daily food intake of wild birds and mammals: Final Report. Central Science Laboratory, Department for Environment, Food and Rural Affairs, Sand Hutton, United Kingdom.

The log P_{ow} for penoxsulam is <3 and also the surface water metabolites were considered to have a log P_{ow}<3, hence the potential for bioaccumulation and secondary poisoning was considered as low.

No separate toxicity studies with the metabolites detected in rice plants or in surface water were available for birds and mammals. The metabolite 5-OH-penoxsulam was identified as a metabolite in mammals and it was considered likely that it would also be a metabolite in the avian system. Hence no separate testing was warranted. The risk assessment for metabolites was conducted based on the assumption of same toxicity as for penoxsulam, measured residues in rice plants, and calculated daily dose from intake of paddy water. It was concluded that even if the metabolites would be 10 times more toxic than penoxsulam, the risk from exposure to penoxsulam metabolites would be considered as low.

5.2. RISK TO AQUATIC ORGANISMS

Penoxsulam was classified as very toxic to aquatic organisms, based on an E_rC_{50} of 0.0864 mg a.s./L for *Pseudokirchneriella subcapitata* and an E_rC_{50} of 0.00329 mg a.s./L for *Lemna gibba*. Toxicity to fish and aquatic invertebrates were low. The formulation GF-237 (representative of GF-657) exhibited some acute toxicity to *Daphnia magna.* Therefore, short-term TER values for the formulated product GF-657 (based on toxicity data for GF-237) were calculated.

The most important routes of entry to surface water during boom-sprayer application was considered to be via spray drift at the time of application and via outflow when paddy water was discharged to drainage channels some time after application. Surface water includes irrigation and drainage channels immediately adjacent to the treated paddy as well as static and flowing water bodies further downstream. Similarly, the term "sediment" refers to the solid layer below surface water but not the soil in the flooded rice paddy. The term "paddy water" refers to the water inside the rice paddy. For the calculation of PEC in paddy water, surface water and sediment see section 4.2.1.

The first tier risk assessment for algae and aquatic plants, based on PEC_{sw} in the "off-field" area, gave TERs of 46 and 2.9, respectively. An assessment was provided for fish and aquatic invertebrates in paddy water. No assessment was provided for algae or higher plants in paddy water, considering the herbicidal activity of penoxsulam. The lowest acute TER value was 202, which was obtained for *Daphnia* using the EC_{50} for the formulation. The lowest long-term TER was 83. It was concluded that the first tier risk to aquatic plants in the "off-field" area was high. The risk to algae in the "off-field" area was considered to be low and the risk to fish and aquatic invertebrates was low in the "off-field" area as well as in the paddy water itself.

Results from a higher tier study with *Lemna gibba* were used to refine the assessment for aquatic plants in the DAR. The outdoor formulation study (including sediment) indicated some level of recovery after 28 days. The study was discussed by Member State experts. Compared with effects from the tier 1 *Lemna* study the toxicity was quite comparable after 14 days. Except for the potential of re-colonisation the second study did not provide results being so different. It was concluded that the studies were comparable and the lowest value of E_rC_{50} = 3.29 µg/L at 14 days from the standard

Lemna study should be used as the valid endpoint. A TER of 2.9 was calculated based on this end point. Experts considered that the effects of recovery observed for one species did not necessarily indicate a recovery for other species. Therefore further refinement of recovery potential and variability of sensitivity between species should be explored to address the "off-field" risk to higher aquatic plants. EFSA notes that refinements, which were not peer reviewed, were provided in an addendum to the DAR volume 3, B.5.8.2, pages 210 to 217 of the final addendum (Italy, 2009). The refinements were based on revised exposure estimates, however the detail of the refined exposure calculations as reported in the addendum was considered insufficient (see section 4.2.1).

TER values for the major metabolites 5-OH-penoxsulam and BSTCA indicate a low risk. TER values were also provided for the minor metabolites BSA, TPSA, 2-amino-TP and 5-OH-2-amino-TP, all indicate a low risk.

A worst case risk assessment for sediment-dwelling organisms was conducted for penoxsulam and the metabolites 5-OH-penoxsulam, BSTCA, OH-BSTCA and PCA-5-OH using the worst case PEC_{soil} for clay soil for penoxsulam and the NOEC from the long term study with *Chironomus riparius*. The toxicity of the metabolites was assumed to be equal to that for penoxsulam. The TER for organisms in paddy soil was calculated to 27180, indicating a negligible risk for penoxsulam and the metabolites.

The log P_{ow} for penoxsulam is <3 and hence the potential for bioaccumulation and secondary poisoning is considered as low. Log P_{ow} for the metabolites were estimated using the quantitative structure-activity program, KOWWIN v.1.66. The calculated log P_{ow} values were all well below 3, indicating a low potential for bioaccumulation.

5.3. RISK TO BEES

The oral and contact toxicity to bees was tested with penoxsulam technical and the formulation GF-657. The oral and contact HQ quotients based on an application rate of 40 g a.s/ha were below the Annex VI trigger of 50 and the risk was therefore considered as low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Tests with terrestrial arthropods were conducted with the formulation GF-657. Hazard quotients (HQ) for "in-field" were calculated based on LR_{50} values for *Aphidius rhopalosiphi* and *Typhlodromus pyri*, obtained in glass plate tests. A HQ value of 5.4 was calculated for *T. pyri* while the HQ for *A. rhopalosiphi* was <1. Extended laboratory studies with the same species did not reveal effects >50% on survival or reproduction at 40 g a.s./ha. No effects on survival or fecundity were observed in the green lacewing, *Crysoperla carnea* at 40 g a.s./ha in a glass plate study. Based on these data the risk to non-target arthropods was considered to be low.

5.5. RISK TO EARTHWORMS

Flooded conditions in rice paddies were not considered to provide a suitable habitat for earthworms. Therefore in this case as penoxsulam is only moderately persistent (no carry-over of soil residues was

expected in potential non-flooded following crop cultivations), the exposure assessment for earthworms was limited to the "off-field" scenario. Therefore the most relevant exposure was considered to be spray drift to adjacent not flooded fields. As a worst case direct overspray leading to a PEC_{soil} of 1.97 mg/kg dw soil for the formulated product and 0.0533 mg/kg dw soil for penoxsulam were used, based on standard mixing in 5 cm of soil with a density of 1.5 g/cm^3. EFSA noted that this PEC_{soil} value was not provided in the fate section of the DAR and it could be considered as a more conservative exposure than the PEC_{soil} value calculated in accordance with the MED-RICE guidance document for direct over-spraying (as provided in the fate section). Acute TER values were >18760 and >5076 based on EC_{50} values obtained in studies with the active substance and the formulated product, respectively. Thus the acute risk to earthworms was considered as low.

No studies with earthworms are available for the soil metabolites. The risk assessment in the DAR was performed by assuming the same toxicity as for penoxsulam. PEC_{soil} for the metabolites were calculated as penoxsulam equivalents, using the maximum percent applied radioactivity observed in any of the aerobic, anaerobic or soil photolysis studies. The lowest TER obtained was >35399. Even assuming ten times higher toxicity for the metabolites compared to penoxsulam, TER values indicating a low risk would be the result.

No long-term studies with earthworms were required since the acute toxicity is low, the $DT90_{field}$ in soil for parent and metabolites were less than 100 days and only one application per season was proposed.

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

Studies with other soil non-target macro-organisms were not required since the acute toxicity was low, the $DT90_{field}$ in soil for parent and metabolites was less than 100 days and only one application per season was proposed.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Effects on soil respiration and nitrogen transformation were tested with penoxsulam technical. No deviations >25% compared to the control were observed after 28 days at 12.5 times the field application rate. The risk assessment on penoxsulam was considered also to cover soil metabolites.

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

Tier I screening tests on 19 different plant species indicate no herbicical activity from the two soil metabolites BSTCA and 5-OH-penoxsulam. Tier II seedling emergence and vegetative vigour studies with penoxsulam using 4 monocotyledonous species (*Zea mays*, *Allium cepa*, *Lolium perenne*, *Triticum aestivum*) and 6 dicotyledonous species (*Gossypium hirsutum*, *Cucumis sativus*, *Brassica oleracea acephala*, *Glycine max*, *Beta vulgaris altissima* and *Lycopersicon esculentum*) were available. Based on EC_{50} values, the greatest sensitivity in the emergence study was with sugarbeet shoot weight, which had an EC_{50} of 6.2 g a.s./ha. In the vegetative vigour study, the lowest EC_{50} value was also 6.2 g a.s./ha, which was based on soybean shoot weight.

The potential exposure to terrestrial non-target plants was based on 2.77% spray drift of the proposed application rate of 40 g a.s./ha at a distance of 1 m from the treated area. The TERs for both seedling emergence (pre-emergence exposure) and vegetative vigour (post-emergence exposure) were 5.6 which is greater than the Annex VI trigger of 5 indicating a low risk.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The 30 minute EC_{50} obtained in a microbial respiratory inhibition test with sludge inoculum is >1000 mg a.s./L (nominal) indicating that the risk to biological methods of sewage treatment is low.

6. Residue definitions

Soil

Definition for risk assessment: penoxsulam, 5-OH-penoxsulam[37], BSTCA[38]

Definition for monitoring: penoxsulam

Water

Ground water

Definition for exposure assessment: penoxsulam, 5-OH-penoxsulam, BSTCA

Definition for monitoring: penoxsulam

Surface water

Definition for risk assessment:

in surface water:	penoxsulam, 5-OH-penoxsulam, BSTCA.
in sediment:	penoxsulam, 5-OH-penoxsulam, PCA-5-OH[39], OH-BSTCA[40]
Definition for monitoring:	penoxsulam

Air

Definition for risk assessment: penoxsulam

Definition for monitoring: penoxsulam

Food of plant origin

Definition for risk assessment: penoxsulam by default (only applicable to assessed use)

Definition for monitoring: penoxsulam by default (only applicable to assessed use)

[37] 5-OH-penoxsulam: 2-(2,2-difluoroethoxy)-N-(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide

[38] BSTCA: 3-({[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-1,2,4-triazole-5-carboxylic acid

[39] PCA-5-OH: 3-(2,2-difluoroethoxy)-2-[(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamoyl]benzoic acid

[40] OH-BSTCA: 3-({[2-(2,2-difluoroethoxy)-?-hydroxy-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1H-1,2,4-triazole-5-carboxylic acid

Food of animal origin

Definition for risk assessment: not necessary (only applicable to assessed use scenario)

Definition for monitoring: not proposed

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
penoxsulam	moderate persistence Single first order DT_{50} 22-58 days (20°C, 40%MWHC soil moisture)	The risk was assessed as low for non-target arthropods, earthworms and soil non-target micro-organisms.
5-OH-penoxsulam	moderate persistence Single first order DT_{50} 19-37 days (20°C, 40%MWHC soil moisture)	The risk was assessed as low for non-target arthropods, earthworms and soil micro-organisms.
BSTCA	medium to high persistence Single first order DT_{50} 61-118 days (20°C, 40%MWHC soil moisture)	The risk was assessed as low for non-target arthropods, earthworms and soil micro-organisms.

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one MedRice scenario)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
penoxsulam	High to medium mobility K_{doc} 12-253[41] mL/g	No	Yes	Yes	Yes
5-OH-penoxsulam	High mobility K_{doc} 17-144 mL/g	No	No	No	No
BSTCA	Very high to medium mobility K_{doc} 5-444 mL/g	Yes in one of the 2 scenarios. In the sandy scenario the concentration was 0.23µg/L. There is also the potential for consumer exposure from residues in crops planted following rice.	No	Data gap	No

[41] Range excludes a volcanic soil and an aquatic sediment.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
penoxsulam	Penoxsulam is very toxic to aquatic organisms, based on the data available. The "off-field" risk to higher aquatic plants was not addressed. For the remaining aquatic organism the risk was assessed as low.
5-OH-penoxsulam	The risk was assessed as low for aquatic organisms.
BSTCA (water only)	The risk was assessed as low for aquatic organisms.
PCA-5-OH (sediment only)	The risk was assessed as low for aquatic organisms.
OH-BSTCA (sediment only)	The risk was assessed as low for aquatic organisms.

Air

Compound (name and/or code)	Toxicology
penoxsulam	Rat LC_{50} inhalation > 3.50 mg/L air/4 h, nose only (the highest technically achievable concentration), no classification proposed

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

- Industrial scale five batch data (relevant for all representative uses evaluated, data requirement identified by PRAPeR 1 meeting, (September, 2006), data submitted and evaluated in an addendum to the DAR volume 4 (Italy, 2009), however not peer reviewed, refer to chapter 1).
- A revised technical specification based on industrial production (relevant for all representative uses evaluated, data gap identified by PRAPeR 1 meeting, (September, 2006), date of submission unknown, refer to chapter 1)
- Validation data for the analytical method used for the determination of the relevant impurity (relevant for all representative uses evaluated, data requirement identified by PRAPeR 1 meeting, (September, 2006), submitted in June 2007, evaluated in an addendum to the DAR volume 4, however not peer reviewed, refer to chapter 1)
- Detailed composition of the batches used in the toxicological studies in order to assess the relevance of the impurities and check on the comparability of these batches with the proposed technical specification (relevant for all representative uses evaluated; submitted in June 2007, evaluated in an addendum to the DAR volume 4, however not peer reviewed, refer to chapter 2)
- Toxicological information on the metabolite BSTCA to assess its relevance as a plant metabolite (relevant for all representative uses evaluated; submission date unknown; refer to point 2.8)
- Further data to address residues in succeeding crops at all relevant plant back intervals is required, in particular in view of levels of non-rat metabolite BSTCA present in succeeding crops and its potential degradate BST (relevant for all representative uses evaluated; data requirement per se identified by PRAPeR 05 and proposed accordingly by EFSA; submission date unknown; refer to point 3.1.2)
- An audited corrigendum to the original report Yoder, R.N. (2000) Dow report number 990058, to correct the K_F, 1/n and K_{Foc} values for the Amagon soil in line with the clarification that was already provided by the applicant (relevant for all representative uses evaluated; submission date unknown; refer to section 4 of the evaluation table, rev. 2-1, 11 June 2009).
- A refined risk assessment for higher aquatic plants (relevant for all representative uses evaluated; note information has been provided which refined the exposure estimate, an evaluation by the RMS was included in an addendum to the DAR volume 3, B.8.5.2 (Italy, 2009), however the detail of the refined exposure calculations as reported in the addendum is limited; refer to point 4.2.1 and 5.2)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprise post-emergence applications with conventional tractor-mounted spraying devices or self-propelled hydraulic sprayers to control *Echinochloa crus-galli*, sedges and broad leaf weeds in rice, from growth stage of BBCH 11 up to growth stage of BBCH 31, in Southern Europe, at a single application at a maximum application rate of 40 g a.s./ha.

The representative formulated product for the evaluation was 'penoxsulam DE-638' (VIPER, GF-657), an oil dispersion (OD) containing 20.4 g/l of penoxsulam, however some of the data were generated using other formulations: 'GF-237' (25.2 g/l OD) and 'GF-239' (200.1g/l OD).

At the moment there is no agreed specification for the impurities in the technical material.

Adequate analytical methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant origin and environmental matrices.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

In the mammalian metabolism studies, penoxsulam was rapidly and almost completely absorbed upon oral administration. There was no evidence of bioaccumulation. Excretion was rapid, but dose and sex dependent as excretion was primarily observed via faeces in males and primarily excreted in urine in females. Penoxsulam was biotransformed to a large number of metabolites; however the majority of the radioactivity was eliminated as unchanged parent compound. Plant and environmental metabolites BST and BSTCA were not identified in the rat metabolism studies. Toxicological information was lacking on the metabolite BSTCA to conclude on its relevance as a plant metabolite, moreover, it cannot be ruled out that BSTCA is also relevant according to the guidance document on the relevance of metabolites in groundwater.

The acute toxicity of penoxsulam was low by the oral, dermal and inhalation route; slight skin and eye irritation were observed, but no potential for skin sensitisation. The dog was found to be the most sensitive species with the kidneys as the main target organ; the overall short-term NOAEL in dogs was 18 mg/kg bw/day. Long term toxicity reflected the same target organ observed in the short term studies: the liver in mice and the liver and kidneys in rats. The relevant long term NOAEL was the dose level of 5 mg/kg bw/day from the 2-year rat study. No potential for genotoxicity, carcinogenicity or neurotoxicity was observed. No effect was seen on the reproductive performance and parameters; no developmental effect was observed in rats. In rabbits, a slight increase in resorption rate parameters was associated with maternal toxicity, evidenced by gastro-intestinal upset and decreased body weight gain during the middle gestation.

The Acceptable Daily Intake (ADI) of penoxsulam was 0.05 mg/kg bw/day; the Acceptable Operator Exposure Level (AOEL) was 0.18 mg/kg bw/day; no Acute Reference Dose (ARfD) was allocated. The level of operator exposure was below the AOEL even without the use of personal protective equipment (PPE) according to both the German and the UK POEM models. Worker and bystander exposure were considered negligible.

A metabolism study in rice demonstrated that following foliar application of penoxsulam the total residues decreased rapidly to insignificant levels present at harvest of the crop. Therefore, the residue definition in rice grain was proposed as penoxsulam by default.
In supervised residue trials penoxsulam was found to be always below the Limit of Quantification of 0.01 mg/kg in rice grain, while in rice straw residues ranged up to 0.08 mg/kg. Consequently, an MRL for grain was proposed at 0.01 mg/kg, which is the lowest validated level of the analytical method. For straw an MRL is not required.
Rice may be grown in monoculture but also in rotation with other crops. A submitted confined crop rotation study showed that after a plant back interval of 90 days low residues could still be found in some crops. Other plant back intervals were not investigated. Moreover, a metabolite BSTCA, identified at significant levels in rotated crops was neither found in primary crop metabolism nor in rat metabolism. The toxicological relevance of this metabolite for consumer risk assessment could not be addressed. As rotation practices in member States seem to differ and the submitted data on rotational crops were limited, a final conclusion on the relevance of residues in rotated crops other than cereals could not be reached. Hence the experts agreed that further elaboration on the issue is required. A data requirement for further rotational crop data is proposed.
If only the scenarios of rice grown in monoculture and of rice rotated with other cereals are considered it can be concluded that exposure to livestock is not expected to be significant. Under these conditions, on the basis of the submitted animal metabolism studies, residues in food of animal origin are expected to occur at extremely low levels that would not be appropriate for monitoring. The experts therefore agreed that, for the time being, it would not be necessary to propose a residue definition and MRLs for food of animal origin. However, it should be noted that the assessment is not finalised with regard to potential livestock exposure to residues in rotational crops other than cereals.
Consumer exposure to residues of penoxsulam in rice grain is insignificant and thus in a chronic risk assessment intakes were well below to ADI. No acute assessment was conducted as an ARfD was not allocated. However, the consumer risk assessment cannot be finalised with regard to residues of metabolite BSTCA since a lack of sufficient occurrence data and toxicological data was identified. As BSTCA may also occur in drinking water derived from groundwater at a level >0.1 µg/L, total consumer exposure to BSTCA has to be assessed in order to conclude on the consumer risk assessment.

The peer reviewed information available was sufficient to enable a satisfactory environmental exposure assessment to be completed at EU level, with the notable exception of the not peer reviewed refined higher tier surface water exposure assessment. The details available in the RMS evaluation of this refined higher tier surface water exposure assessment were insufficient to conclude on the appropriateness of the approach followed, that included the definition of novel scenarios. It can be concluded that the potential for penoxsulam or its metabolite 5-OH-penoxsulam to contaminate vulnerable groundwater above the parametric drinking water limit of 0.1µg/L from the applied for intended uses is low. For the metabolite BSTCA the potential to contaminate vulnerable groundwater above the parametric drinking water limit of 0.1µg/L is low in situations represented by the MED-Rice clay scenario. However in situations represented by the MED-Rice sand scenario, BSTCA may

be present in vulnerable groundwater at > 0. 1µg/L (calculations indicate concentrations up to 0.23µg/L). Therefore a non-relevance assessment for the metabolite BSTCA was triggered.

In the risk assessment for birds, species representing insectivorous birds (wren), omnivorous birds eating large aquatic insects (mallard), omnivorous birds eating aquatic plants (mallard), large herbivorous birds (geese) and piscivorous birds (heron) were considered. All TER values were well above the relevant Annex VI trigger indicating a low risk to birds from the use of penoxsulam in rice paddies. Water vole (small herbivorous mammal), water shrew (eating aquatic invertebrates) and otter (eating fish and amphibians) were selected as focal species for the "in-field" risk assessment for mammals. The lowest TER obtained was 25 for the long-term risk to water vole. Since this was above the relevant Annex VI trigger a low risk was concluded. For both birds and mammals the exposure from intake of contaminated paddy water was included in the estimation of the daily dose by simply adding the drinking water dose to the dietary dose. The log P_{ow} for penoxsulam is <3 and also the surface water metabolites were considered to have a log P_{ow} <3, hence the potential for bioaccumulation and secondary poisoning was considered as low.
Penoxsulam was classified as very toxic to aquatic organisms. The first tier risk assessment for algae and aquatic plants, based on PEC_{sw} in the "off-field" area, gave TERs of 46 and 2.9, respectively. An assessment was provided for fish and aquatic invertebrates in paddy water. No assessment was provided for algae or higher plants in paddy water, considering the herbicidal activity of penoxsulam. The lowest acute TER value was 202, which was obtained for *Daphnia* using the EC_{50} for the formulation. The lowest long-term TER was 83. It was concluded that the first tier risk to aquatic plants in the "off-field" area was high. Refinements based on a higher tier study with *Lemna* were not accepted in the peer review, and the risk to aquatic plants remains to be addressed. The risk to aquatic organisms from metabolites was addressed, as was the risk from bioaccumulation (log P_{ow}<3).
The risk to bees, non-target arthropods, earthworms, soil micro-organisms and non-target plants was assessed as low.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Limitation of succeeding crops to the cereal crop group has been proposed.

ISSUES THAT COULD NOT BE FINALISED

- Consumer exposure assessment not finalised. The lack of toxicological information on metabolite BSTCA does not allow a conclusion to be reached on its relevance as a ground water metabolite. Since BSTCA is both a plant metabolite in succeeding crops and a ground water metabolite, the guidance document on assessment of relevance of groundwater metabolites[42] requires ensuring the total exposure of consumers to the metabolite will not exceed the threshold-of-concern of 0.02 µg/kg bw/day. There is an indication the threshold

[42] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

might be exceeded, however, a sound prediction is not possible with the data that are currently available.

- The risk assessment to higher aquatic plants from exposure to the active substance penoxsulam is not finalised.

CRITICAL AREAS OF CONCERN

- The risk to higher aquatic plants from exposure to the active substance penoxsulam could not be addressed based on the data available.

REFERENCES

Italy, 2005. Draft Assessment Report (DAR) on the active substance penoxsulam prepared by the rapporteur Member State Italy in the framework of Directive 91/414/EEC, January 2005.

Italy, 2009. Final Addendum to the Draft Assessment Report on penoxsulam, compiled by EFSA (European Food Safety Authority), January 2009.

EFSA, 2009. Peer Review Report on penoxsulam, August 2009.

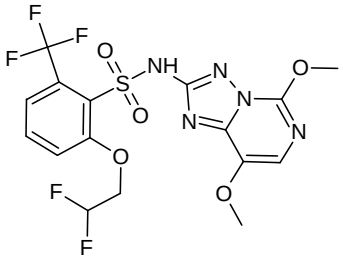
APPENDICES

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

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

Active substance (ISO Common Name)	Penoxsulam
Function (*e.g.* fungicide)	Herbicide
Rapporteur Member State	Italy

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	3-(2,2-difluoroethoxy)-*N*-(5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-α,α,α-trifluorotoluene-2-sulfonamide
Chemical name (CA)	Benzenesulfonamide: 2-(2,2-difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-c] pyrimidin-2-yl)-6-(trifluoromethyl)-
CIPAC No	758
CAS No	219714-96-2
EEC No (EINECS or ELINCS)	Not available
FAO Specification (including year of publication)	Not available
Minimum purity of the active substance as manufactured (g/kg)	980 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Bis-CHYMP 2-chloro-4-[2-(2-chloro-5-methoxy-4-pyrimidinyl)hydrazino]-5-methoxypyrimidine Max content: 0.1 g/kg
Molecular formula	$C_{16}H_{14}F_5N_5O_5S$
Molecular mass	483.37
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	212°C purity: 98.8%
Boiling point (state purity)	Not applicable, decomposes before melting.
Temperature of decomposition	214°C purity: 98.8%
Appearance (state purity)	Pale pink solid at 23°C Purity: 98.8% Slight musty Purity: 98.8%
Surface tension	67.5 mN/m (90% saturated solution in water) Purity: 97.7%
Vapour pressure (in Pa, state temperature)	9.55 x 10^{-14} Pa at 25°C; 2.49 x 10^{-14} Pa at 20°C Purity: 99.1%
Henry's law constant (Pa m^3 mol^{-1})	Unbuffered water: 2.44 x 10^{-12} Pa m^3/mol at 20°C pH 5: 2.13 x 10^{-12} Pa m^3/mol at 20°C pH 7: 2.95 x 10^{-14} Pa m^3/mol at 20°C pH 9: 8.25 x 10^{-15} Pa m^3/mol at 20°C
Solubility in water (g/l or mg/l, state temperature)	pH 5: 5.66 mg/L at 19°C
	pH 7: 408 mg/L at 20°C
	pH 9: 1460 mg/L at 20°C
	Unbuffered: 4.91 ± 0.07 mg/L at 19°C; pH = 5.05 ± 0.04 at 19°C
Solubility in organic solvents (in g/l or mg/l, state temperature)	n-heptane: < 1 µg/ml at 19°C
	xylene: 0.017 g/L at 19°C
	1,2-dichloroethane: 1.99 g/L at 19°C
	Methanol: 1.48 g/L at 19°C
	Acetone: 20.3 g/L at 19C
	Ethyl acetate: 3.23 g/L at 19°C
	n-octanol: 0.035 g/L at 19°C
	N,*N*-dimethylformamide: 39.8 g/L at 19°C
	N-methyl pyrrolidinone: 40.3 g/L at 19°C
	dimethylsulfoxide: 78.4 g/L at 19°C
	acetonitrile: 15.3 g/L at 19°C
Partition co-efficient (log P_{OW}) (state pH and temperature)	pH 5: 1.137 at 19°C Purity: 99.1%
	pH 7: -0.602 at 19°C Purity: 99.1%
	pH 9: -1.418 at 19°C Purity: 99.1%
	Unbuffered: -0.354 at 19°C Purity: 99.1%

Dissociation constant	pKa=5.1 Purity: 98.8%
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Neutral: λ_{max} = 284 nm, ε = 9530 L/(mol*cm) Acid: λ_{max} = 251 nm, ε = 7450 L/(mol*cm); λ_{max} = 284 nm, ε = 9520 L/(mol*cm) Basic: λ_{max} = 228 nm, ε = 44300 L/(mol*cm); λ_{max} = 284 nm, ε = 9380 L/(mol*cm) A λ = 290 nm; ε = 8846 L/(mol*cm)
Flammability	Not highly flammable Purity: 97.7%
Explosive properties	Not explosive Purity: 97.7%
Oxidising properties	Not oxidizing (theoretical justification)

Summary of intended uses (active substance)

Crop and/or situation	Member State or Country	Product Name	F G or	Pests or Group of pests controlled	Formulation	Application	Application rate per treatment	PHI (days)	Remarks
(a)			I (b)	(c)	Type (d-f)	Conc. of a.s. (i)	Method Kind (f-h)	Growth stage & season (j)	Number min max (k)	kg a.s./ha min max	water (L/ha) min max	kg a.s./hL min max	(l)	(m)
Rice	Italy	penoxsulam DE-638 (GF-657)	F	Echinochloa crus-galli, sedges and broad leaf weeds.	OD	20.4 g/L	Broadcast spray**	BBCH 11-31 May-June	1	0.03-0.04	200-400	0.0075-0.02	N.N*	[1]
Rice	Spain	penoxsulam DE-638 (GF-657)	F	Echinochloa crus-galli, sedges and broad leaf weeds.	OD	20.4 g/L	Broadcast spray**	BBCH 11-31 May-June	1	0.03-0.04	150-400	0.0075-0.027	N.N	[1]
Rice	Portugal	penoxsulam DE-638 (GF-657)	F	Echinochloa crus-galli, sedges and broad leaf weeds.	OD	20.4 g/L	Broadcast spray**	BBCH 11-31 May-June	1	0.03-0.04	150-400	0.0075-0.027	N.N	[1]
Rice	Greece	penoxsulam DE-638 (GF-657)	F	Echinochloa crus-galli, sedges and broad leaf weeds.	OD	20.4 g/L	Broadcast spray**	BBCH 11-31 May-June	1	0.03-0.04	300-500	0.006-0.013	N.N	[1]
Rice	France	penoxsulam DE-638 (GF-657)	F	Echinochloa crus-galli, sedges and broad leaf weeds.	OD	20.4 g/L	Broadcast spray**	BBCH 11-31 May-June	1	0.03-0.04	150-300	0.01-0.027	N.N	[1]

[1] The risk to aquatic plants has not been addressed
** The assessment covers only tractor application technology

Methods of Analysis

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

Technical as (principle of method)	**Moreland, J., Fonquerne, C. (2002) Validation of Analytical Method DAS-AM-02-003 for the Analysis of penoxsulam in Technical Grade penoxsulam** A reversed phase liquid chromatographic method, o-toluic acid internal standard and UV detection at 285 nm. Samples are dissolved in internal standard solution and diluted with eluent prior to analysis.
Impurities in technical as (principle of method)	Moreland, J., Fonquerne, C. (2002) Validation of Analytical Method DAS-AM-01-051 for the Determination of Impurities in Technical Grade penoxsulam For impurities 1-11 and 13, - reversed phase liquid chromatography using a C8 column, o-toluic acid internal standard and UV detection at 285 nm. Samples are dissolved in internal standard solution and diluted with eluent prior to analysis. Impurity 12 - reversed phase liquid chromatography using a C18 column, phthalimide internal standard and UV detection at 265 nm. Samples are dissolved in internal standard solution and diluted with acetonitrile prior to analysis. Bis-CHYMP – reversed phase liquid chromatography using a C18 column, external standard calibration and UV detection at 360 nm. Samples are dissolved in acetonitrile and mobile phase. The LOQ for Bis-CHYMP is 86 ppm.
Plant protection product (principle of method)	Nelson, R. (2002) Analytical Method and Validation for the Determination of penoxsulam in GF-237 and GF-657 Formulations A liquid chromatographic method with UV detection. External and internal standard calibration (o-toluic acid internal standard). Detection at 285 nm Samples are dissolved in internal standard solution and diluted with mobile phase prior to analysis.

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) on rice	Hastings, M.J., Schelle, G.E. (2002): Determination of Residues of penoxsulam in Rice and Rice Processed Products by Liquid Chromatography with Tandem Mass Spectrometry Extraction: acetonitrile: water (80:20 v/v). Clean up: Solid phase extraction (SPE) plate; elution with acetonitrile:formic acid (100:0.1). Liquid chromatography with positive ion electrospray tandem mass spectrometry (LC/MS/MS). Ion: Q1 484.0 m/z; Q3 = 195.0 m/z. LOQ = 0.01 mg/kg Chickering, C.D., (2002): Independent Laboratory Validation of Dow AgroSciences LLC Method GRM01.25 – Determination of Residues of penoxsulam in Rice and Rice Processed Products by Liquid Chromatography with Tandem Mass Spectrometry Detection. Extraction: acetonitrile:water (80:20 v/v). Clean up: Solid phase extraction (SPE) plate; elution with acetonitrile:formic acid (100:0.1). Liquid chromatography with positive ion electrospray tandem mass spectrometry (LC/MS/MS). Ion: Q1 484.0 m/z; Q3 = 195.0 m/z LOQ = 0.01 mg/kg
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	No methods have been developed for determination residues in meat, milk or eggs because no residues of penoxsulam occur in crops that are components of animal feed.
Soil (principle of method and LOQ)	**Hastings, M. J., Schelle G.E. (2002): Determination of Residues of penoxsulam and Metabolites in Soil and Sediment by Liquid Chromatography with Tandem Mass Spectrometry** Penoxsulam and its metabolite are analysed. Extraction: acetonitrile:1.0 N hydrochloric acid solution (90:10 v/v). Clean up: HLB solid-phase extraction plate (SPE); elution with an acetonitrile:methanol (80:20 v/v). The final solution is analysed by LC/MS/MS. Ion: Q1 484.0 m/z; Q3 = 195.0 m/z. LOQ = 0.003 mg/kg for each analyte.

Water (principle of method and LOQ)	**Hastings, M. J. (2002): Determination of Residues of penoxsulam and Metabolites in Water by Liquid Chromatography with Tandem Mass Spectrometry**. Penoxsulam and its metabolite are analysed in surface water and drinking water. An aliquot of the water sample is filtered if necessary and transferred to an autosampler vial. Liquid chromatography with tandem mass spectrometry (LC/MS/MS). Ion: Q1 484.0 m/z; Q3 = 195.0 m/z. LOQ = 0.003 mg/L for each analyte. It was calculated as the lowest level of fortification for recovery samples **Hastings, M. J. (2002): Determination of Residues of penoxsulam in Water by Liquid Chromatography with Tandem Mass Spectrometry** Penoxsulam is analysed in ground water, surface water and drinking water. Extraction: polymeric-anion exchange solid phase extraction cartridge (SPE); elution with acetonitrile:formic acid solution (100:0.1). Liquid chromatography with positive-ion electrospray tandem mass spectrometry (LC/MS/MS). Ion: Q1 484.0 m/z; Q3 = 195.0 m/z. LOQ = 0.05 µg/L.
Air (principle of method and LOQ)	Wais, A. (2002): Validation of the Residue Analytical Method for penoxsulam in Air by LC/MS Sampling: 360 L of air. Sampling time: 6 hours Temperature and humidity conditions: about 35°C and min. 80% rH The rH of min 80% was achieved by bubbling the air through distilled water prior to passing the air through the Tenax adsorption tubes. Extraction - acetonitrile by ultrasonic bath for about 5 min. and then diluted with water. 1 ml of this solution is diluted with 30% acetonitrile/70% water and filtered through a 0.45-µm PTFE filter for analysis by LC/MS. Ion: 484

	m/z LOQ = 1.5 µg/m^3
Body fluids and tissues (principle of method and LOQ)	Chickering, C.D. (2002): Determination of Residues of penoxsulam in Whole Blood and Urine by Liquid Chromatography with Tandem Mass Spectrometry Detection As penoxsulam is not classified as a toxic or highly toxic compound no method for the determination of residues is relevant. However, a method for body fluids and tissues does exist. Urine. Sample is diluted with water and then transferred to an autosampler vial for analysis by LC/MS/MS. Whole human blood samples. An aliquot of the sample is diluted with water and extracted with acetonitrile. After centrifugation, the extract is diluted with water and then transferred to an autosampler vial for analysis by LC/MS/MS. LOQ = 0.01 µg/ml..

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data on penoxsulam	none

Classification and proposed labelling

with regard to physical/chemical data on penoxsulam DE-638 (GF-657)	none

IMPACT ON HUMAN AND ANIMAL HEALTH

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

Rate and extent of oral absorption ‡	Rapid and extensive (> 80 %, based on urinary and biliary excretion, tissues, carcass and cage wash within 24 h) at low doses (single and repeated). Saturation at high dosage.
Distribution ‡	Primarily blood, liver and kidneys
Potential for accumulation ‡	None
Rate and extent of excretion ‡	Rapid and extensive. Sex and dose dependent. At low doses, excretion in males is primarily in faeces (56 %), while in females primarily in urine (69 %). At high doses, faecal excretion predominant in both sexes, very likely due to unabsorbed material.
Metabolism in animals ‡	36 metabolites identified, due to hydroxylation, demethylation, minor sulphonamide bridge cleavage, and conjugation reactions. However, most of the excreted radioactivity (> 55 %) was associated with the parent compound.
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolite BSTCA
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 5000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 3.5 mg/L air/4 h – highest attainable air concentration, zero deaths in 10 animals tested (nose-only)	
Skin irritation ‡	Non irritant	
Eye irritation ‡	Non irritant	
Skin sensitisation ‡	Non sensitizer (Maximization test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat: Liver and Kidney; Mouse: Liver; Dog: Kidney: (renal pelvic epithelial hyperplasia)	
Relevant oral NOAEL ‡	90-day dog: 18 mg/kg bw/day (renal effects) 90-day rat: 50 mg/kg bw/day 90-day mouse: 10 mg/kg bw/day (LOAEL: 100 mg/kg bw/day)	
Relevant dermal NOAEL ‡	28-day rat: ≥ 1000 mg/kg bw/day (highest dose tested)	
Relevant inhalation NOAEL ‡	No data – not required	

Genotoxicity (Annex IIA, point 5.4)

No genotoxic potential

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

Target/critical effect ‡	Kidney: Increase severity of chronic progressive glomerulonephropathy and histopathological changes in the kidneys associated to changes in clinical pathology parameters in male rats. Liver: increased liver weight with hepatocellular hypertrophy (male mice)	
Relevant NOAEL ‡	2-year rat: 5 mg/kg bw/day 18-month mouse: 10 mg/kg bw/day	
Carcinogenicity ‡	No treatment-related tumours in rats or mice	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No reproductive toxicity at parentally toxic doses. Offspring: decreased body weight throughout lactation at parental toxic dose (increased organ weight with histopathological changes in the liver and kidneys)	
Relevant parental NOAEL ‡	30 mg/kg bw/day	
Relevant reproductive NOAEL ‡	300 mg/kg bw/day (highest dose tested)	
Relevant offspring NOAEL ‡	100 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Rat: no developmental toxicity or teratogenicity, at maternal toxic dose (decreased body weight gain and increased kidney weight) Rabbit: slight increase in resorption rate parameters at maternal toxic dose (gastro-intestinal upset and decreased body weight gain)	
Relevant maternal NOAEL ‡	Rat: 500 mg/kg bw/day Rabbit: 25 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 1000 mg/kg bw/day Rabbit: 25 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No neurotoxic effect. NOAEL : 2000 mg/kg bw (highest dose tested in rat)
Repeated neurotoxicity ‡	No neurotoxic effect following 1-year exposure (rat). NOAEL: 250 mg/kg bw/day
Delayed neurotoxicity ‡	No data – not required

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data – not required
Studies performed on metabolites or impurities ‡	**Metabolite 5-OH-penoxsulam:** Ames test: negative CHO/HGPRT test: negative Chromosomal aberration in rat lymphocytes: negative **Metabolite BSTCA:** Ames test: negative CHO/HGPRT test: negative Chromosomal aberration in rat lymphocytes: negative **Metabolite BST:** Ames test: negative CHO/HGPRT test: negative Chromosomal aberration in rat lymphocytes: negative

Medical data (Annex IIA, point 5.9)

Limited; new active ingredient. There have been no reports of alleged human health effects associated with penoxsulam reported to the US EPA by Dow AgroSciences. Exposure to penoxsulam may cause slight eye irritation without corneal injury. Skin exposure is unlikely to cause irritation, and sensitization is unlikely. Ingestion of small amounts is not anticipated to cause harmful effects. Repeated ingestion of significant amounts may have liver and kidney effects. No adverse effects are expected from a single exposure to dust; repeated or prolonged dust exposure may cause respiratory irritation.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI	0.05 mg/kg bw/day	2-year rat	100
AOEL	0.18 mg/kg bw/day	90-day dog	100
ARfD (acute reference dose)	Not required	-	-

Dermal absorption (Annex IIIA, point 7.3)

Formulation (GF-657, 20.4 g penoxsulam/L OD)	10% for both diluted and undiluted formulation (default value supported by an *in vivo* rat study conducted with the representative formulation)

Acceptable exposure scenarios (including method of calculation)

Operator	The estimated exposure for GF-657 is below the AOEL even when no PPE is used (application rate 0.04 kg penoxsulam/ha) with tractor mounted equipment: German model No PPE 2.9 % of AOEL UK model No PPE 14.4 % of AOEL
Workers	In accordance with normal rice agricultural practices, re-entry to the crop prior to harvest is not necessary. Residues of penoxsulam at harvest are negligible and will lead to insignificant worker exposure.
Bystanders	Recommended uses of GF-657 may potentially result in incidental, brief exposure of bystanders to a highly diluted water-based spray drift, but the predicted exposure should present a negligible hazard and risk (~ 0.2 % of AOEL).

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

	RMS/peer review proposal
Substance classified (penoxsulam)	None

RESIDUES

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

Plant groups covered	Rice
Rotational crops	Wheat, kale and potatoes
Plant residue definition for monitoring	Penoxsulam
Plant residue definition for risk assessment	Penoxsulam
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Lacting goat , laying hen
Animal residue definition for monitoring	Not required for the notified use
Animal residue definition for risk assessment	Not required for the notified use; however assessment is not finalised with regard to potential livestock exposure to residues in rotational crops other than cereals
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Not applicable.
Fat soluble residue: (yes/no)	No

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

.....	Wheat, kale, and potatoes planted into soil 90 days after treatment with PH or TP-labeled penoxsulam at target rates of 50 and 100 g a.i./ha contained total radioactive residues ranging from less than the LOD to 0.062 mg/kg penoxsulam equivalents. A metabolite BSTCA (not occurring in the primary crop and in rat metabolism) was identified in significant amounts. Further data to address residues in rotational crops are required.

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

.....	Residues of penoxsulam are stable in rice grain, straw, and immature forage when stored frozen at -20°C for up to 210 days. Residues of penoxsulam are stable in rice bran, hulls and polished rice when stored frozen at -20°C for up to 197 days. Data for storage period up to 732 days (rice grain, straw, immature forage) and 390 days (rice bran, hulls and polished rice) available, but not peer reviewed

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

Intakes by livestock ≥ 0.1 mg/kg diet/day: [43]	Ruminant: no	Poultry: no	Pig: no
Muscle	No study required	No study required	No study required
Liver	No study required	No study required	No study required
Kidney	No study required	No study required	No study required
Fat	No study required	No study required	No study required
Milk	No study required	No study required	No study required
Eggs	No study required	No study required	No study required

[43] Note: assessment is not finalised with regard to potential livestock exposure to residues in rotational crops other than cereals

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)
Rice	Mediterranean	11 x <LOQ of 0.01 mg/kg [11 x Not detected , i.e.<0.002 mg/kg]	MRL corresponding to LOQ	0.01* mg/kg	<0.01 mg/kg

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

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

ADI	0.05 mg/kg body weight
TMDI (European Diet) (% ADI)	0.003 (FAO Standard Diet)
NEDI (% ADI)	0.1 (UK Model – toddlers and 7-10 yr olds)
Factors included in NEDI	Not applicable
ARfD	Not allocated
Acute exposure (% ARfD)	Not applicable

The exposure and risk assessment is not finalized with regard to metabolite BSTCA that is both a plant metabolite in succeeding crops and a ground water metabolite. Guidance document Sanco/221/2000 – rev.10 requires ensuring the total exposure of consumers to the metabolite will not exceed the threshold-of-concern of 0.02 µg/kg bw/day. There is an indication the threshold might be exceeded, however, a sound prediction is not possible with the data that are currently available.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Not relevant. The concentration of residues in the treated crops is <0.01 mg/kg			

* 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)

rice.....	0.01* mg/kg

FATE AND BEHAVIOUR IN THE ENVIRONMENT

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

Mineralisation after 100 days	Triazolopyrimidine ring label: Average = 0.9% AR (120 days) (range 0.5 – 1.4% AR) Phenyl ring label: 0.3% AR
Non-extractable residues after 100 days	Triazolopyrimidine ring label: Average = 12.7% AR (120 days) (range 10.2 – 15.6% AR) Phenyl ring label: 11.9% AR
Major metabolites - name and/or code, % of applied (range and maximum)	5-OH-DE-638 (range 15.3 – 40.5% AR at 14-58 days) BSTCA (range 29.4 – 53.0% AR at 14-120 days)

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

Anaerobic degradation	Mineralization: ≤1% AR (120 days, both TP and PH radiolabels) NER: Average = 64.1% AR (120 days, 65.3% TP radiolabel, 62.9% PH radiolabel) Major metabolites: 5-OH-DE-638 (33.4% AR at 14 days), BSTCA (19.1% AR at 120 days)
Soil photolysis	Photolysis on moist soil, 25 °C, 40 °N latitude, summer sunlight Mineralization: <1% AR (37 days, both TP and PH radiolabels) NER: Average = 24.4% AR (37 days, 30.9% TP radiolabel, 17.9% PH radiolabel) Major metabolites: BSTCA (11.1% AR at 30 days), 2-amino-TP (10.4% AR at 37 days)

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

Method of calculation	Linear first-order kinetics for parent compound. Non-linear first-order kinetics used for 5-OH-DE-638 and BSTCA metabolites.
Laboratory studies (range or median, with n value, with r^2 value)	DT_{50lab} (20 °C, aerobic): Average = 32 days (range 22 - 58 days, n = 4, r^2 = 0.96 - 0.99) 5-OH-DE-638 DT_{50lab} (20 °C, aerobic): Average = 26 days (range 19 - 37 days, n = 4, r^2 = 0.97 - 0.99) BSTCA DT_{50lab} (20 °C, aerobic): Average = 79 days (range 61 – 118 days, n = 4, r^2 = 0.97 - 0.99)
	DT_{90lab} (20 °C, aerobic): Average = 107 days (range 74 - 192 days, n = 4, r^2 = 0.96 - 0.99)
	DT_{50lab} (6 °C, aerobic): 137 days (n = 1, r^2 = 0.95)
	DT_{50lab} (20 °C, anaerobic): 6.6 days (total system, n = 1, r^2 = 0.98), 5.3 days (water only, n = 1, r^2 = 1.00), 8.8 days (soil only, n = 1, r^2 = 0.91) 5-OH-DE-638 DT_{50lab} (20 °C, anaerobic): 5.1days (total system, n = 1, r2 = 0.80)
	DT_{50lab} (photolysis on moist soil, 25 °C, 40 °N latitude, summer sunlight): 19 days (n = 1, r^2=0.90)
	Degradation in the saturated zone: Data not submitted, not required.
Field studies (state location, range or median with n value)	DT_{50f} (Italy, Spain, water): median 5.9 days (n = 2, range 5.6 - 6.1 days) DT_{50f} (Italy, Spain, soil): <1 day
	DT_{90f} (Italy, Spain, water): median 19.5 days (n = 2, range 19 - 20 days)
Soil accumulation and plateau concentration	Data not submitted, not required.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc}
K_d
pH dependence (yes / no)
(if yes type of dependence)

	penoxsulam			
Soil	K_f	1/n	K_d (L/kg)	K_{doc} (L/kg)
Greggio (Italy)	1.96	0.90	2.50	253
Ottobaiano (Italy)	0.32	0.89	0.38	45
Charentilly (France)	0.48	0.88	0.63	65
Marcham (UK)	0.16	0.93	0.20	12
Average[1]	0.73	0.90	0.93	94
Median[1]	0.40	0.90	0.51	55
Supplemental Information				
Wagram-Troup (USA)	0.27	1.02	0.31	77
Amagon (USA)	0.30	0.91	0.39	40
Oswald (USA)	0.49	0.94	0.47	19
Glyndon-Tiffany (USA)	0.45	0.88	0.57	21
Chernozemic (Canada)	nm	nm	1.44	72
Ryerson (Canada)	nm	nm	0.67	19
Glu Humid (Brazil)	nm	nm	0.63	14
Red Latisoil (Brazil)	nm	nm	0.13	13
Purple Latisoil (Brazil)	nm	nm	0.50	35
Volcanic/Upland (Japan)	0.59	0.86	0.81	22
Non-Volcanic/Upland (Japan)	0.56	0.86	0.85	39
Volcanic/Rice (Japan)	4.69	0.80	10.40	305
Non-Volcanic/Rice (Japan)	1.55	0.83	2.49	194
Average[3]	0.99	0.89	1.38	73
Median[3]	0.49	0.89	0.63	39.5

[1] Average and median values for 4 European soils

[2] nm = Freundlich coefficients were not measured for these soils

[3] Average and median values for all reported soils

pH dependence: Yes. Sorption increases with decreasing pH. As soil pH decreases, sorption of penoxsulam is increasingly dependent on the soil organic carbon content.

K_f /K_{oc}
K_d
pH dependence (yes / no)
(if yes type of dependence)

	5-OH-DE-638		
Soil	K_f	K_d (L/kg)	K_{doc} (L/kg)
Greggio (Italy)	nm[1]	1.42	144
Ottobaiano (Italy)	nm	0.40	41
Charentilly (France)	nm	0.28	17
Marcham (UK)	nm	0.30	34
Average[2]	n/a	0.60	59
Median[2]	n/a	0.35	37
Supplemental Information			
Wagram-Troup (USA)	nm	0.14	34
Amagon (USA)	nm	0.32	33
Oswald (USA)	nm	0.46	19
Glyndon-Tiffany (USA)	nm	1.03	38
Average[3]	n/a	0.54	45
Median[3]	n/a	0.36	34
[1] nm = Freundlich coefficients were not measured for these soils			
[2] Average and median values for 4 European soils [3] Average and median values for all reported soils			
pH dependence: No.			

K_f /K_{oc}
K_d
pH dependence (yes / no)
(if yes type of dependence)

	BSTCA		
Soil	K_f	K_d (L/kg)	K_{doc} (L/kg)
Greggio (Italy)	nm[1]	4.39	444
Ottobaiano (Italy)	nm	0.72	74
Charentilly (France)	nm	0.09	5
Average[2]	n/a	1.73	174
Median[2]	n/a	0.72	74
Supplemental Information			
Wagram-Troup (USA)	nm	0.18	46
Amagon (USA)	nm	1.52	156
Oswald (USA)	nm	0.60	25
Average[3]	n/a	1.25	125
Median[3]	n/a	0.66	60
[1] nm = Freundlich coefficients were not measured for these soils			
[2] Average and median values for 3 European soils [3] Average and median values for all reported soils			
pH dependence: No.			

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

Column leaching	Sandy loam soil (free draining), leached for 2 d at 10 cm water/d 9.7% 0-5 cm soil layer 95.8% total in soil (0-30 cm) 3.1% in leachate Sandy loam soil (saturated), leached for 2 d at 10 cm water/d 20.9% 0-5 cm soil layer 97.5% total in soil (0-30 cm) 0.2% in leachate Clay loam soil (free draining), leached for 2 d at 10 cm water/d 102.9% 0-5 cm soil layer 102.9% total in soil (0-30 cm) <LOD in leachate Clay loam soil (saturated), leached for 2 d at 10 cm water/d 35.7% 0-5 cm soil layer 97.1% total in soil (0-30 cm) 1.0% in leachate Sandy silt loam soil (free draining), leached for 2 d at 10 cm water/d 40.2% 0-5 cm soil layer 100.2% total in soil (0-30 cm) <LOD in leachate Silt loam soil (free draining), leached for 2 d at 20 cm water/d 86.1% 0-5 cm 98.2% total in soil (0-30 cm) <LOD in leachate
Aged residues leaching	Data not submitted, not required.
Lysimeter/ field leaching studies	Data not submitted, not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	Modelling as per Guidance Document for Environmental Risk Assessment of Active Substances used on Rice in the EU (Sanco/1090/2000-rev0) No crop interception, Koc 94 L/kg (average from 4 European soils), DT_{50} 8.8 days (soil phase of anaerobic study - worst case compared to the field study where the DT50 was <1 day).
Application rate	40 g a.s./ha

Parent

PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	29.83 µg/kg (clay) 20.70 µg/kg (sand)	not applicable not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
Short term 24h	27.57 µg/kg (clay) 19.14 µg/kg (sand)	28.68 µg/kg (clay) 19.91 µg/kg (sand)		
2d	25.48 µg/kg (clay) 17.69 µg/kg (sand)	27.60 µg/kg (clay) 19.16 µg/kg (sand)		
4d	21.77 µ/kg (clay) 15.11 µg/kg (sand)	25.59 µg/kg (clay) 17.76 µg/kg (sand)		
Long term 7d	17.19 µg/kg (clay) 11.93 µg/kg (sand)	22.93 µg/kg (clay) 15.91 µg/kg (sand)		
28d	3.29 µg/kg (clay) 2.28 µg/kg (sand)	12.03 µg/kg (clay) 8.35 µg/kg (sand)		
50d	0.58 µg/kg (clay) 0.40 µg/kg (sand)	7.43 µg/kg (clay) 5.15 µg/kg (sand)		
100d	0.01 µg/kg (clay) 0.01 µg/kg (sand)	3.79 µg/kg (clay) 2.63 µg/kg (sand)		

Metabolite

Method of calculation	5-OH-DE-638: max formation from parent = 33% (from anaerobic aquatic study) and correction for molecular weight BSTCA: max formation from parent = 53% (from aerobic soil study) and correction for molecular weight
Application rate	40 g a.s./ha

Maximum PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
5-OH-DE-638	9.56 µg/kg (clay) 6.63 µg/kg (sand)	not applicable not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
BSTCA	13.62 µg/kg (clay) 9.45 µg/kg (sand)	not applicable not applicable		

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)		pH 5, 25 °C: stable
		pH 7, 25 °C: stable
		pH 9, 25 °C: stable
Photolytic degradation of active substance and relevant metabolites		DT_{50} = 2 days (summer, 40 °N latitude, sterile pH 7 buffer and natural water) Major metabolites: TPSA: 56% AR at 1 day, DT_{50} = 4.7 days (buffer), 2.0 days (natural water) 2-amino-TP: 18% AR at 1 day, DT_{50} = 0.6 days (buffer), 0.6 days (natural water) 5-OH-2-amino-TP: 23% AR at 14 days (natural water) BSA: 36% at 1.5 days, DT_{50} = 0.9 days (buffer), 0.7 days (natural water)
Readily biodegradable (yes/no)		No
Degradation in water/sediment	DT_{50} water	Average = 15 days (n = 2, range 10 – 20 days, r^2 = 0.90 - 0.96)
	DT_{90} water	Average = 50 days (n = 2, range 34 – 65 days, r^2 = 0.90 - 0.96
	DT_{50} whole system	penoxsulam Average = 23 days (n = 2, range 11 – 34 days, r^2 = 0.78 - 0.91) 5-OH-DE-638 Average = 50 days (n = 2, range 24 – 75 days, r^2 = 0.89 - 0.93)
	DT_{90} whole system	Average = 76 days (n = 2, range 37 – 114 days, r^2 = 0.78 - 0.91
Mineralisation		Average = 1.6% AR (n = 2, range 0.8 – 2.4% AR, 99 days)
Non-extractable residues		Average = 39.4% AR (n = 2, range 20.8 – 57.9% AR, 99 days)
Distribution in water / sediment systems (active substance)		Water Phase: Maximum of 87.5 – 91.5% AR at 0 DAT (days after treatment) decreasing to 0.4 – 3.9% AR at 99 DAT Sediment Phase: 0% AR at 0 DAT, maximum of 2.5 – 20.9% AR at 4 DAT
Distribution in water / sediment systems (metabolites)		Major Metabolites (water): 5-OH-DE-638 (18.6% AR), BSTCA (23.7% AR) Major Metabolites (sediment): 5-OH-DE-638 (15.6% AR)

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

Parent

Method of calculation	Modelling as per Guidance Document for Environmental Risk Assessment of Active Substances used on Rice in the EU (Sanco/1090/2000-rev1) No crop interception, Koc 94 L/kg, DT50 in paddy of 6.6 days (anaerobic whole system) and DT50 in surface water 15 days (aerobic aquatic water phase). Dilution factor of 10 for outflow from paddy to drainage channel after 5 days. Calculation was refined using measured paddy water concentrations from field studies 5 days after application.
Application rate	40 g a.s./ha
Main routes of entry	Outflow of paddy water to drainage canals 5 days after application (major route). Spray drift at application (minor route).

PEC$_{(sw)}$		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		1.14 µg/L	Not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
Short term	24h	1.09 µg/L	1.11 µg/L		
	2d	1.04 µg/L	1.09 µg/L		
	4d	0.95 µg/L	1.04 µg/L		
Long term	7d	0.82 µg/L	0.97 µg/L		
	14d	0.60 µg/L	0.84 µg/L		
	21d	0.43 µg/L	0.73 µg/L		
	28d	0.31 µg/L	0.64 µg/L		
	42d	0.16 µg/L	0.50 µg/L		

Metabolite

Method of calculation	Calculated using maximum PEC_{SW} for parent at Step 1b corrected for molecular weight and max amount formed in aerobic aquatic study (5-OH-DE-638 = 30% and BSTCA = 24%) or aqueous photolysis study (BSA = 36%, TPSA= 56%, 2-amino-TP = 18% and 5-OH-2-amino-TP = 23%)

Max $PEC_{(sw)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
5-OH-DE-638	0.55 µg/L	Not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
BSTCA	0.39 µg/L	Not applicable		
BSA	0.43 µg/L	Not applicable		
TPSA	0.60 µg/L	Not applicable		
2-amino-TP	0.14 µg/L	Not applicable		
5-OH-2-amino-TP	0.18 µg/L	Not applicable		

PEC (sediment)

Parent

Method of calculation	Modelling as per Guidance Document for Environmental Risk Assessment of Active Substances used on Rice in the EU (Sanco/1090/2000-rev1). Calculated using outflow and drift PEC_{SW} for parent at Step 1b Partitioning to sediment with Koc of 94 L/kg and DT50 of 23 days (aerobic aquatic whole system).
Application rate	40 g a.s./ha

PEC$_{(sed)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	2.08 µg/kg	Not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
Short term 24h 2d 4d	2.02 µg/kg 1.96 µg/kg 1.84 µg/kg	2.05 µg/kg 2.02 µg/kg 1.96 µg/kg		
Long term 7d 14d 21d 28d 42d	1.68 µg/kg 1.36 µg/kg 1.10 µg/kg 0.89 µg/kg 0.59 µg/kg	1.88 µg/kg 1.70 µg/kg 1.54 µg/kg 1.40 µg/kg 1.18 µ/kg		

Metabolite

Method of calculation	Calculated using maximum PEC_{SW} for parent at Step 1b corrected for molecular weight and max amount formed in sediment in aerobic aquatic study (5-OH-DE-638 = 16%, BSTCA = 2.2%), PCA-5-OH = 16%, OH-BSTCA = 16%

Max PEC$_{(SED)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
5-OH-DE-638	0.33 µg/kg	Not applicable	Not calculated . One application per growing season	Not calculated . One application per growing season
BSTCA	0.05 µg/kg	Not applicable		
PCA-5-OH	0.33 µg/kg	Not applicable		
OH-BSTCA	0.33 µg/kg	Not applicable		

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Modelling as per Guidance Document for Environmental Risk Assessment of Active Substances used on Rice in the EU (Sanco/1090/2000-rev0) Parent: Koc = 94 L/kg (average from 4 European soils) and DT50 = 5.3 days (anaerobic water phase value, comparable to that seen in the water phase of the field study). 5-OH: formation 33%, DT50 = 5.1 days (anaerobic whole system value, worst case compared to field study where water concentrations were not detectable, <3µg/L) and Koc = 59 L/kg. BSTCA: formation 50% (conservative estimate), DT50 = 100 days (estimated value) and Koc = 174 L/kg
Application rate	40 g a.s./ha

$PEC_{(gw)}$

Maximum concentration	Not evaluated
Average annual concentration (active substance)	< 0.0001 µg/L (clay soil) 0.0013 µg/L (sandy soil)
Average annual concentration (5-OH metabolite)	< 0.0001 µg/L (clay soil) 0.0001 µg/L (sandy soil)
Average annual concentration (BSTCA metabolite)	< 0.0001 µg/L (clay soil) 0.234 µg/L (sandy soil)

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

Direct photolysis in air		Not evaluated		
Quantum yield of direct phototransformation		0.180 (measured in water)		
Photochemical oxidative degradation in air (DT_{50})		Latitude: N/A	Season: N/A	DT_{50}: 2.1 hours
Volatilisation	from plant surfaces:	Not evaluated		
	from soil:	Not evaluated		

PEC (air)

Method of calculation	No method of calculation available

$PEC_{(a)}$

Maximum concentration	No method of calculation available

Definition of the Residue (Annex IIA, point 7.3)

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: penoxsulam, 5-OH-penoxsulam, BSTCA Surface water: penoxsulam, 5-OH-penoxsulam, BSTCA. Sediment: penoxsulam, 5-OH-penoxsulam, PCA-5-OH, OH-BSTCA Ground water: penoxsulam, 5-OH penoxsulam, BSTCA Air: penoxsulam

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

Soil (indicate location and type of study)	None
Surface water (indicate location and type of study)	None
Ground water (indicate location and type of study)	None
Air (indicate location and type of study)	None

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data on penoxsulam	Candidate for R 53.

ECOTOXICOLOGY

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

Acute toxicity to mammals	Rat penoxsulam acute oral LD_{50} **> 5000** mg a.s./kg bw/day GF-237 acute oral LD_{50} > 5000 mg product/kg bw/day
Reproduction toxicity to mammals	Rat-2 Generation Reproduction Study penoxsulam Body weight NOAEL = 100 mg a.s./kg bw/day penoxsulam Reproduction NOAEL = 300 mg a.s./kg bw/day Rabbit Developmental Toxicity Study penoxsulam Maternal body weight NOAEL = 25 mg a.s./kg bw/day penoxsulam Developmental NOAEL* = **25** mg a.s./kg bw/day
Acute toxicity to birds	Bobwhite quail DE 638 acute oral LD_{50} > 2025 mg a.s./kg bw/day Mallard duck penoxsulam acute oral **LD_{50} > 2000** mg a.s./kg bw/day GF-237 acute oral LD_{50} > 2000 mg product/kg bw/day (> 54 mg a.s./kg bw/day)
Dietary toxicity to birds	Bobwhite quail penoxsulam 8 day LC50 > 5063 mg a.s./kg diet **(> 804** mg a.s./kg bw/day) Mallard duck penoxsulam 8 day LC50 > 5063 mg a.s./kg diet (> 1116 mg a.s./kg bw/day)
Reproductive toxicity to birds	Bobwhite quail penoxsulam NOEL = 1000 mg a.s./kg diet (= **80.1** mg a.s./kg bw/day, females) (= 82.5 mg a.s./kg bw/day, males)

* Endpoint used in long-term risk assessment

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

BIRDS					
Application rate (kg as/ha)	**Crop-Scenario**	**Category (*e.g.* insectivorous bird)**	**Time-scale**	**TER**	**Annex VI Trigger**
0.040	Rice-Paddy	Insectivorous bird – Wren	Acute	>920	10
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% large insects)	Acute	>13000	10
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% aquatic plants)	Acute	>450	10
0.040	Rice-Paddy	Large herbivorous bird	Acute	>790	10
0.040	Rice-Paddy	Piscivorous bird	Acute	>130000	10
0.040	Rice-Paddy	Insectivorous bird - Wren	ST	>670	10
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% large insects)	ST	>13500	10
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% aquatic plants)	ST	>630	10
0.040	Rice-Paddy	Large herbivorous bird	ST	>590	10
0.040	Rice-Paddy	Piscivorous bird	ST	>52000	10
0.040	Rice-Paddy	Insectivorous bird - Wren	LT	125	5
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% large insects)	LT	1350	5
0.040	Rice-Paddy	Omnivorous bird – Mallard (100% aquatic plants)	LT	120	5
0.040	Rice-Paddy	Large herbivorous bird	LT	110	5
0.040	Rice-Paddy	Piscivorous bird	LT	5200	5
0.040	Rice-Off crop drift	All indicator species	*	*	*
0.040	Rice-Metabolites	All indicator species	**	**	**

* Since acceptable TER values for all rice paddy scenarios cover off crop drift scenarios, it is not necessary to present TER values for off crop drift scenarios. TER values have been calculated based on the sum of dietary and drinking water ETE values.

** All TER values for metabolites were well above Annex VI trigger values for acute, short term and long term exposure. Risk assessment based on worst case exposure that would result from ingestion of metabolites occurring in treated rice plants. Drinking water exposure was also included in the ETE calculation. Toxicity of the parent material was assumed to be equal to the metabolites.

MAMMALS					
Application rate (kg as/ha)	**Crop-Scenario**	**Category (*e.g.* insectivorous bird)**	**Time-scale**	**TER**	**Annex VI Trigger**
0.040	Rice-Paddy	Small herbivorous mammal-Water vole	Acute	>1400	10
0.040	Rice-Paddy	Insectivorous mammal-Water shrew	Acute	>10000	10
0.040	Rice-Paddy	Piscivorous mammal-Otter	Acute	>140000	10
0.040	Rice-Paddy	Small herbivorous mammal-Water vole	LT	25	10
0.040	Rice-Paddy	Insectivorous mammal-Water shrew	LT	140	10
0.040	Rice-Paddy	Piscivorous mammal-Otter	LT	720	10
0.040	Rice-Off crop drift	All indicator species	*	*	*
0.040	Rice-Metabolites	All indicator species	**	**	**

* Since acceptable TER values for all rice paddy scenarios cover off crop drift scenarios, it is not necessary to present acceptable TER values for off crop drift scenarios. TER values have been calculated based on the sum of dietary and drinking water ETE values.

** All TER values for metabolites were well above Annex VI trigger values for acute, short term and long term exposure. Risk assessment based on worst case exposure that would result from ingestion of metabolites occurring in treated rice plants. Drinking water exposure was also included in the ETE calculation. Toxicity of the parent material was assumed to be equal to the metabolites.

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 (mga..s./l)
Laboratory tests – Active substance and formulation				
Fish - Rainbow trout *(Lepomis macrochirus)*	penoxsulam	96 hours	LC_{50}	>100 [a]
Fish - Rainbow trout	GF-237	96 hours	LC_{50}	>100 [a] mg product/l (> 2.7 mg a.s./l)
Fish – Fathead minnow *(Oncorhynchis mykiss)*	penoxsulam	36 days	Early life stage NOEC	10 [a]
Crustaceans – Daphnia (*Daphnia magna)*	penoxsulam	48 hours	EC_{50}	>100 [a]
Crustaceans - Daphnia	GF-237	48 hours	EC_{50}	404 [a] mg product/l (10.9 mg a.s./l)
Crustaceans - Daphnia	penoxsulam	21 days	NOEC	3.33 [a]
Molluscs Snail	~~DE-638~~ penoxsulam	96 hours	LC_{50}	>120 [a]
Sediment dweller - Midge	penoxsulam	28 days	Sediment NOEC	810 [b] (mg a.s./kg sed)
Sediment dweller - Midge	penoxsulam	28 days	Water NOEC	61 [b]
Algae – *Pseudokirchis. subcapitata*	penoxsulam	96 hours	Cell density E_rC_{50}	0.0864 [c]
Algae – *Pseudokirchis. subcap tata*	GF-237	96 hours	Biomass E_bC_{50}	2.6 mg product/l [a] (0.0676 mg a.s./l)
Aquatic plant – *Lemna gibba*	penoxsulam	14 days	EC_{50}	0.00329 [c]
Aquatic plant – *Lemna gibba*	GF-657	28 days outdoor study in w/s system	E_rC_{50} E_bC_{50}	0.587 mg prod./L [a] (0.0126 mg a.s./L) 0.232 mg prod./L (0.00499 mg a.s./L)

Laboratory tests – Metabolites				
Crustaceans - Daphnia	5-OH-penoxsulam	48 hours	EC_{50}	>100 [a]
Crustaceans - Daphnia	BSTCA	48 hours	EC_{50}	>100 [a]
Crustaceans - Daphnia	BST	48 hours	EC_{50}	> 100 [a]
Crustaceans - Daphnia	BSA	48 hours	EC_{50}	>1.6 [d]
Crustaceans - Daphnia	TPSA	48 hours	EC_{50}	>1.4 [d]
Crustaceans - Daphnia	2-Amino-TP	48 hours	EC_{50}	>1.0 [d]
Crustaceans - Daphnia	5-OH-2-Amino-TP	48 hours	EC_{50}	>1.0 [d]
Algae – *P. subcapitata*	5-OH-penoxsulam	96 hours	Cell density EC_{50}	>10 [a]
Algae – *P. subcapitata*	BSTCA	96 hours	Cell density EC_{50}	>10 [a]
Algae – *P. subcapitata*	BST	96 hours	Cell density EC_{50}	>10 [a]
Algae – *P. subcapitata*	TPSA	96 hours	Cell density EC_{50}	>1.4 [d]
Algae – *P. subcapitata*	BSA	96 hours	Cell density EC_{50}	>1.6 [d]
Algae – *P. subcapitata*	2-Amino-TP	96 hours	Cell density EC_{50}	>1.0 [d]
Algae – *P. subcapitata*	5-OH-2-Amino-TP	96 hours	Cell density EC_{50}	>1.0 [d]
Aquatic plant - *Lemna*	5-OH-penoxsulam	14 days	EC_{50}	>10 [a]
Aquatic plant - *Lemna*	BSTCA	14 days	EC_{50}	>10 [a]
Aquatic plant - *Lemna*	BST	14 days	EC_{50}	>6.2 [c]
Aquatic plant - *Lemna*	TPSA	14 days	EC_{50}	>1.4 [d]
Aquatic plant - *Lemna*	BSA	14 days	EC_{50}	>1.6 [d]
Aquatic plant - *Lemna*	2-Amino-TP	14 days	EC_{50}	>1.0 [d]
Aquatic plant - *Lemna*	5-OH-2-Amino-TP	14 days	EC_{50}	>1.25 [d]
Microcosm/mesocosm tests:				
Mesocosm test	Not needed			

a: endpoint related to nominal concentrations
b: endpoint related to initial measured concentration
c: endpoint related to mean measured concentrations
d: endpoint related to nominal concentrations, not analytically confirmed

Toxicity/exposure ratio for the most sensitive aquatic organisms - Rice-Paddy Water Scenario (Annex IIIA, point 10.2)

Application rate (kg as/ha)**	Crop–Scenario-Substance	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.040	Rice-Paddy Water-GF-657	Fish	Acute	In crop	>50	*
0.040	Rice-Paddy Water-GF-657	Daphnia	Acute	In crop	202	*
0.040	Rice-Paddy Water penoxsulam	Fish	Acute	In crop	>2500	*
0.040	Rice-Paddy Water penoxsulam	Daphnia	Acute	In crop	>2500	*
0.040	Rice-Paddy Water penoxsulam	Snail	Acute	In crop	>3000	*
0.040	Rice-Paddy Water-5-OH-penoxsulam	Daphnia	Acute	In crop	>7692	*
0.040	Rice-Paddy Water-BSTCA	Daphnia	Acute	In crop	>15385	*
0.040	Rice-Paddy Water-BSA	Daphnia	Acute	In crop	>176	*
0.040	Rice-Paddy Water-TPSA	Daphnia	Acute	In crop	>108	*
0.040	Rice-Paddy Water-2-Amino-TP	Daphnia	Acute	In crop	>345	*
0.040	Rice-Paddy Water-5-OH-2-Amino-TP	Daphnia	Acute	In crop	>286	*
0.040	Rice-Paddy Water penoxsulam	Fish	LT	In crop	250	*
0.040	Rice-Paddy Water penoxsulam	Daphnia	LT	In crop	83	*
0.040	Rice-Paddy Water penoxsulam	Sediment dweller	LT	In crop	1525	*

* Risk assessment for the in-crop scenario should considered at member state level, taking into account specific local conditions, agricultural practices and particular aspects of environmental protection.

** To represent a worst case situation

Toxicity/exposure ratio for the most sensitive aquatic organisms - Rice-Surface Water Scenario (Annex IIIA, point 10.2)

Application rate (kg as/ha)*	Crop–Scenario-Substance	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.040	Rice-Surface Water-GF-657	Fish	Acute	1 m	>2368	100
0.040	Rice- Surface Water-GF-657	Daphnia	Acute	1 m	9561	100
0.040	Rice- Surface t Water penoxsulam	Fish	Acute	1 m	>87000	100
0.040	Rice- Surface Water penoxsulam	Daphnia	Acute	1 m	>87000	100
0.040	Rice- Surface Water penoxsulam	Snail	Acute	1 m	>100000	100
0.040	Rice- Surface Water-5-OH-penoxsulam	Daphnia	Acute	1 m	>181000	100
0.040	Rice- Surface Water-BSTCA	Daphnia	Acute	1 m	>256000	100
0.040	Rice- Surface Water-BSA	Daphnia	Acute	1 m	>3720	100
0.040	Rice- Surface Water-TPSA	Daphnia	Acute	1 m	>2330	100
0.040	Rice- Surface Water-2-Amino-TP	Daphnia	Acute	1 m	>7140	100
0.040	Rice- Surface Water-5-OH-2-Amino-TP	Daphnia	Acute	1 m	>5000	100
0.040	Rice- Surface Water penoxsulam	Fish	LT	1 m	8800	10
0.040	Rice- Surface Water penoxsulam	Daphnia	LT	1 m	2900	10
0.040	Rice- Surface Water penoxsulam	Sediment dweller	LT	1 m	53500	10

* To represent a worst case situation

Toxicity/exposure ratio for the most sensitive aquatic organisms - Rice-Paddy soil and Rice-Surface Water Sediment Scenario (Annex IIIA, point 10.2)

Application rate (kg as/ha)**	Crop–Scenario-Substance	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.040	Rice-Paddy Soil penoxsulam	Sediment dweller	LT	In crop	27180	*
0.040	Rice- Surface Water Sediment- penoxsulam	Sediment dweller	LT	1 m	299000	10

* Risk assessment for the in-crop scenario should considered at member state level, taking into account specific local conditions, agricultural practices and particular aspects of environmental protection.
** To represent a worst case situation

Toxicity/exposure ratio for the most sensitive aquatic organisms - Rice-Surface Water Scenario (Annex IIIA, point 10.2)

Application rate (kg as/ha)*	Crop–Scenario-Substance	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
0.040	Rice- Surface Water-GF-657	Algae	Acute	1 m	46	10
0.040	Rice- Surface Water penoxsulam	Algae	Acute	1 m	76	10
0.040	Rice- Surface Water penoxsulam	Lemna	Acute	1 m	**2.9**	10
0.040	Rice- Surface Water-5-OH-penoxsulam	Algae	Acute	1 m	>18100	10
0.040	Rice- Surface Water-5-OH-penoxsulam	Lemna	Acute	1 m	>18100	10
0.040	Rice- Surface Water-BSTCA	Algae	Acute	1 m	>25600	10
0.040	Rice- Surface Water-BSTCA	Lemna	Acute	1 m	>25600	10
0.040	Rice- Surface Water-BSA	Algae	Acute	1 m	>3720	10
0.040	Rice- Surface Water-BSA	Lemna	Acute	1 m	>3720	10
0.040	Rice- Surface Water-TPSA	Algae	Acute	1 m	>2330	10
0.040	Rice- Surface Water-TPSA	Lemna	Acute	1 m	>2330	10
0.040	Rice- Surface Water-2-Amino-TP	Algae	Acute	1 m	>7140	10
0.040	Rice- Surface Water-2-Amino-TP	Lemna	Acute	1 m	>7140	10
0.040	Rice- Surface Water-5-OH-2-Amino-TP	Algae	Acute	1 m	>5550	10
0.040	Rice- Surface Water-5-OH-2-Amino-TP	Lemna	Acute	1 m	>6940	10

* To represent a worst case situation

Bioconcentration factor (BCF)	
penoxsulam	Not required, Log Kow = -0.602 at pH=7.
5-OH penoxsulam	Not required, Log Kow = 0.43 (estimated from molecular structure)
BSTCA	Not required, Log Kow = -0.71 (estimated from molecular structure)
OH-BSTCA	Not required, Log Kow = -1.19 (estimated from molecular structure)
BSTCA-methyl	Not required, Log Kow = -0.76 (estimated from molecular structure)
PCA-5-OH	Not required, Log Kow = -0.99 (estimated from molecular structure)
BST	Not required, Log Kow = -0.59 (estimated from molecular structure)
TPSA	Not required, Log Kow = -4.92 (estimated from molecular structure)
BSA	Not required, Log Kow = -1.64 (estimated from molecular structure)
2-AMINO-TP	Not required, Log Kow = -0.55 (estimated from molecular structure)
5-OH,2-AMINO-TP	Not required, Log Kow = -1.26 (estimated from molecular structure)
DiFESA	Not required, Log Kow = 0.56 (estimated from molecular structure)
3-AMINO-TCA	Not required, Log Kow = -2.40 (estimated from molecular structure)

Clearance time (CT50) (CT90)	Not applicable
Level of residues (%) in organisms after the 14 day depuration phase	Not applicable

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

Acute oral toxicity	penoxsulam LD50 > 100 µg a.s./bee GF-237 LD50 > 160 µg product/bee
Acute contact toxicity	penoxsulam LD50 > 100 µg a.s./bee GF-237 LD50 > 100 µg product/bee

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.040	Rice penoxsulam	Oral	<0.4	50
0.040	Rice penoxsulam	Contact	<0.4	50
0.040	Rice-GF-657	Oral	<12	50
0.040	Rice-GF-657	Contact	<19	50

Field or semi-field tests: Not needed

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

Species	Stage	Test Substance	Dose (g as/ha)	Endpoints	Adverse Effect*	Annex VI Trigger
Laboratory tests-Glass plates						
Typhlodromus pyri	Protonymph	GF-657	4-40	LR50 Fecundity	LR50=7.46 g a.s./ha; **HQ=5.4** F= 24% at 4 g a.s./ha	HQ>2
Aphidius rhopalosiphi	Adult	GF-657	5-40	LR50 Parasitism	LR50 > 40 g a.s./ha; HQ < 1 M= 7 - 47% P=65% at 40 g a.s./ha	HQ>2
Chrysoperla carnea	Larval	GF-657	1.11-40	LR50 Fecundity	LR50 > 40 g a.s./ha HQ < 1 M= 0 - 20% F= -14% at 40 g a.s./ha	HQ>2
Extended Laboratory tests						
Typhlodromus pyri	Protonymph	GF-657	1.11-40	Mortality Fecundity	M= 7 - 0% F= -9 - +9%	>50%
Aphidius rhopalosiphi	Adult	GF-657	1.11-40	Mortality Parasitism	M=0% P= 0.5 - 26%	>50%

* Negative (-) values indicate positive effect, e.g. fecundity increase versus control.

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

Acute toxicity	penoxsulam 14 day LC50 > 1000 mg a.s./kg d.w. soil GF-237 14 day LC50 > 10000 mg product/kg d.w. soil
Reproductive toxicity	Not required

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

Application rate	Crop-Scenario	Time-scale	TER	Annex VI Trigger
40 g a.s./ha	Rice-Overspray penoxsulam	Acute	>18760	10
1481 g product/ha (40 g a.s./ha)	Rice-Overspray-GF-237	Acute	>5076	10

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

Nitrogen transformation	penoxsulam 0.0% (Day 42) at 2 X 50 g a.s./ha penoxsulam 7.7% (Day 42) at 10 X 50 g a.s./ha No long term effects on nitrogen transformation.
Carbon mineralisation	penoxsulam –9.0% (Day 29) at 2 X 50 g a.s./ha penoxsulam 9.0% (Day 29) at 10 X 50 g a.s./ha No long term effects on carbon mineralisation

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

Test	Most sensitive species	Test Substance	End-point (g a.s./ha)
Seedling emergence	Sugarbeet	penoxsulam	Shoot weight EC50 = 6.2
Vegetative vigor	Soybean	penoxsulam	Shoot weight EC50 = 6.2

Toxicity/exposure ratios for non-target terrestrial plants

Application rate (g a.s./ha)	Crop	Test system	Distance from treated area (m)	Drift (%)	PECdrift (g a.s./ha)	TER	Trigger
40	rice	Seedling emergence/pre-emergence exposure	1	2.77	1.11	5.6	5
40	rice	Vegetative vigor/post-emergence exposure	1	2.77	1.11	5.6	5

Effects on biological methods of sewage treatment (Annex IIA, point 8.7)

Test	Test Substance	Endpoint
Sewage sludge respiration inhibition	penoxsulam	30 min EC50 > 1000 mg a.s./L

Classification and proposed labelling (Annex IIA, point 10)

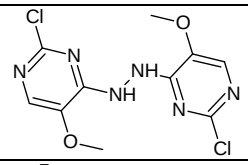
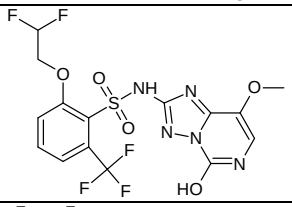
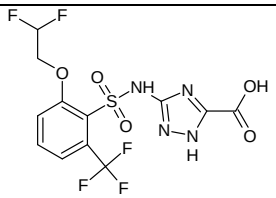
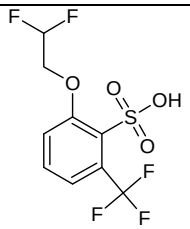
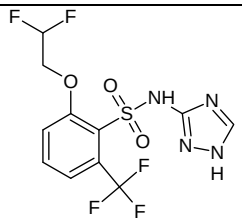
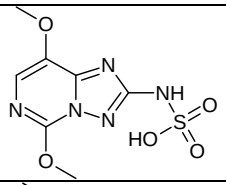
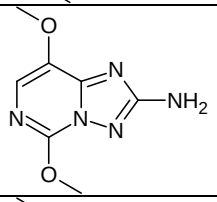
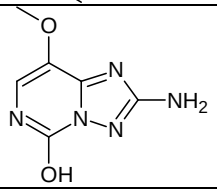
With regard to ecotoxicological data**: Penoxsulam**

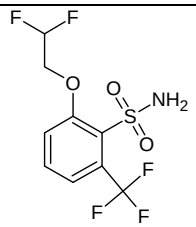
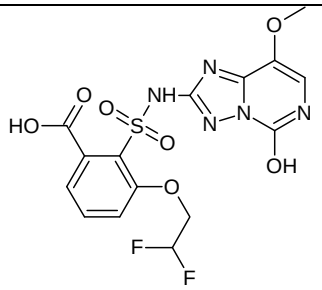
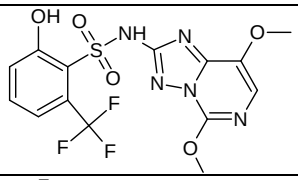
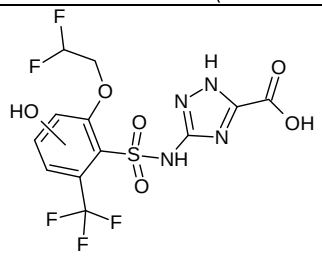
Hazard symbol:	N	Dangerous for the environment
Risk Phrases:	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety Phrases:	S57	Use appropriate containment to avoid environmental contamination

Classification and proposed labelling with regard to ecotoxicological data**: GF-657 OD**

Hazard symbol:	N	Dangerous for the environment
Indication of danger:	Dangerous for the environment	Not readily biodegradable 96 hr LC50 for fish >100 mg a.s./L 48 hr EC50 for Daphnia magna >98.3 mg a.s./L 96 hr EC50 for algae 0.0864 mg a.s./L Therefore in accordance with EC criteria and on the basis of these studies penoxsulam, is classified as 'Dangerous for the environment' and requires R50/53.
Risk Phrases:	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety Phrases:	S57	Use appropriate containment to avoid environmental contamination

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Bis-CHYMP	2-chloro-4-[2-(2-chloro-5-methoxy-4-pyrimidinyl)hydrazino]-5-methoxypyrimidine	
5-OH-penoxsulam 5-OH-DE-638	2-(2,2-difluoroethoxy)-*N*-(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide	
BSTCA	3-({[2-(2,2-difluoroethoxy)-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1*H*-1,2,4-triazole-5-carboxylic acid	
BSA	2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonic acid	
BST	2-(2,2-difluoroethoxy)-*N*-(1*H*-1,2,4-triazol-3-yl)-6-(trifluoromethyl)benzenesulfonamide	
TPSA	(5,8-dimethoxy[1,2,4]triazolo[1,5-c]pyrimidin-2-yl)sulfamic acid	
2-amino-TP	5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-amine	
5-OH-2-amino-TP	2-amino-8-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-5-ol	

sulfonamide	2-(2,2-difluoroethoxy)-6-(trifluoromethyl)benzenesulfonamide	
PCA-5-OH	3-(2,2-difluoroethoxy)-2-[(5-hydroxy-8-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)sulfamoyl]benzoic acid	
2-hydroxyphenyl-penoxsulam 2-OH-DE-638	*N*-(5,8-dimethoxy[1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)-2-hydroxy-6-(trifluoromethyl)benzenesulfonamide	
OH-BSTCA	3-({[2-(2,2-difluoroethoxy)-?-hydroxy-6-(trifluoromethyl)phenyl]sulfonyl}amino)-1*H*-1,2,4-triazole-5-carboxylic acid	

ABBREVIATIONS

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
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
g	gram
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 or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry

LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mg	milligram
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
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
pH	pH-value
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
wk	week
wt	weight
yr	year