CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance metosulam[1]

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SUMMARY

Metosulam is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by France, being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of metosulam in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 5 December 2008 (2008/934/EC)[5] concerning the non-inclusion of metosulam in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Bayer CropScience AG made a resubmission application for the inclusion of metosulam in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, France, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 7 August 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 10 August 2009. The DAR was also distributed to Member States for comments in view of the fact that the original peer review had been terminated following the applicant's notification of withdrawal of support. The EFSA collated and forwarded all comments received to the Commission on 23 September 2009.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the areas of mammalian toxicology and ecotoxicology, and deliver its conclusions on metosulam.

1 On request from the European Commission, Question No EFSA-Q-2009-00891, issued on 23 April 2010.
2 Correspondence: praper@efsa.europa.eu
3 OJ L224, 21.08.2002, p.25
4 OJ L 246, 21.9.2007, p. 19
5 OJ L 333, 11.12.2008, p.11
6 OJ L 15, 18.01.2008, p.5
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The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of metosulam as a herbicide on maize, wheat and barley, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

The specification is not agreed and a data gap is identified for batch data. A data gap has also been identified for data to support the tank cleaning recommendations in the section for identity, physical chemical and technical properties.

A data gap is identified in the mammalian toxicology section to address the genotoxic potential of an impurity present in the technical specification and not adequately tested in the toxicological studies. As there is no agreed technical specification covered by the toxicological assessment, and the genotoxic potential of this impurity is not finalised, an area of concern was identified on this issue.

Based on the metabolism studies performed in wheat and potato, the plant residue definition for monitoring and risk assessment is metosulam alone. A sufficient number of supervised residue trials were provided to propose maximum residue limits (MRLs) on wheat, barley and maize. No risk for the consumer resulting from the representative uses was identified, and no data gaps or areas of concern were identified in the residues section.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at EU level for the representative uses, with the notable exception that information is missing regarding the potential pH dependence of adsorption of the metabolites 7-OH-metosulam (M02) and ATSA (M01). Consequently, the groundwater, surface water and sediment exposure assessments for these metabolites are not finalised.

The risk to birds, mammals, bees, non-target arthropods, earthworms, soil-dwelling macro- and micro-organisms, and biological methods of sewage treatment was assessed as low. A high risk was identified for the aquatic environment. No-spray buffer zones/vegetated filter strips of 10 and 20m are needed to mitigate the risk to aquatic organisms, however, for the environmental conditions represented by some FOCUS scenarios, the maximum mitigation afforded by combined 20m no-spray buffer zones and vegetative strips was insufficient to demonstrate low aquatic risk (maize R4; cereals D1, D2, R1stream, R3stream). A potential high risk was identified for non-target plants in the off-field area. Risk mitigation measures such as a 5m in-field no-spray buffer zone are necessary to protect non-target terrestrial plants in the off-field area.

KEY WORDS

Metosulam, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[9] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant(s) for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

Peer review conducted in accordance with Commission Regulation (EC) No 1490/2002

Metosulam is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR (France, 2006) provided by the designated rapporteur Member State, France, which was received by the EFSA on 21 July 2006.

The peer review was initiated on 8 October 2007 by dispatching the DAR to the applicant Bayer CropScience AG for comments. In addition, the EFSA conducted a public consultation on the DAR.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of metosulam in Annex I to Council Directive 91/414/EEC.

Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 5 December 2008 (2008/934/EC)[10] concerning the non-inclusion of metosulam in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Bayer CropScience AG, made a resubmission application for the inclusion of metosulam in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18, France, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (France, 2009). The Additional Report was received by the EFSA on 7 August 2009.

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 10 August 2009. The DAR was also distributed to Member States for comments in view of the fact that it had not previously been distributed for consultation. In addition, the EFSA conducted a public consultation on the Additional Report. The EFSA collated and

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 333, 11.12.2008, p.11

forwarded all comments received to the Commission on 23 September 2009. The collated comments were also forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 26 October 2009, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on metosulam within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 22 October 2009; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology and ecotoxicology, and that there was no need to request further information from the applicant.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in March 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a herbicide on maize, wheat and barley, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2010) comprises the following documents:

- the comments received,
- the Reporting Table (revision 1-1; 23 October 2009),
- the Evaluation Table (7 April 2010),
- the report(s) of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of April 2010 containing all individually submitted addenda) (France, 2010) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Metosulam is the ISO common name for 2′,6′-dichloro-5,7-dimethoxy-3′-methyl[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonanilide (IUPAC).

The representative formulated product for the evaluation was 'Tacco SC 100', a suspension concentrate (SC), containing 100 g/L metosulam.

The representative uses evaluated comprise of foliar spraying for broadleaf weed control in maize, wheat and barley. Full details of the GAP can be found in the list of end points in Appendix A of this conclusion.

CONCLUSIONS OF THE EVALUATION

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

The specification for metosulam could not be agreed, as the batch data were not considered representative of the current production and therefore a data gap is identified. No relevant impurities were identified from the data provided, however a data gap has been identified by the mammalian toxicology section with regard to one impurity. There is no FAO specification for metosulam. The main data regarding the identity of metosulam and its physical and chemical properties are given in Appendix A.
A data gap is also identified for supporting data for the tank washing procedure.

Metosulam in plants can be determined with a multi-residue method (DFG S19). Analytical methods for food of animal origin are not required as an MRL is not proposed, nonetheless it should be noted that some methods were provided and were found to be acceptable. Soil can be analysed for metosulam with HPLC-UV and HPLC-MS/MS methods. Water is analysed by LC-MS/MS for metosulam, and air can be monitored for metosulam using a HPLC-DAD method.

2. Mammalian toxicity

The technical specification was not agreed in section 1; from a toxicological point of view, the specification would be covered by the toxicological assessment if it complies with the proposal from the applicant presented in the Additional Report (France, 2009) and if the uncertainty over the genotoxic properties of one impurity would be addressed by a new genotoxicity study. A data gap is identified for a new genotoxicity study with an adequate level of this impurity in the test material; if this test is not negative then further investigations may be required. As the technical specification is not agreed and the genotoxic potential of this impurity is not finalised, a critical area of concern was identified on the issue.

Metosulam has low acute toxicity when administered either by the oral, dermal or inhalation routes; no skin or ocular irritation, and no potential for skin sensitisation was observed. The main target organs of metosulam upon short-term exposure are the kidneys in rats, dogs and rabbits, the liver in dogs and mice, and ocular lesions including retinal detachment, necrosis and atrophy in dogs. The relevant NOAEL is around 10 mg/kg bw/day from the 90-day rat and 1-year dog studies. The dog is the most sensitive species showing severe ocular and renal effects (including tubular necrosis and mineralisation, fibrosis, mononuclear aggregates, renal collecting ducts degeneration), when exposed to dose levels below 50 mg/kg bw/day. Accordingly, the risk phrase R48/22 "**Harmful: danger of serious damage to health by prolonged exposure if swallowed**" is proposed. No genotoxic potential was attributed to metosulam administration, based on both *in vitro* and *in vivo* studies. Upon long-term exposure, the kidneys were affected in both rats and mice, but in the latter species at higher dose levels. Additionally, renal tumours were found in male rats at the high dose level of 100 mg/kg bw/day. Tubular epithelial degeneration and regeneration, as shown by increased mitotic activity in a mechanistic study, are expected to cause epithelial cell pleomorphism, multifocal hyperplasia or tumours; metosulam is therefore considered as a non-genotoxic carcinogen, and the risk phrase R40

"**Limited evidence of a carcinogenic effect**" is proposed. The NOAEL for carcinogenicity was set at 30 mg/kg bw/day, and the NOAEL for chronic toxicity was the dose level of 5 mg/kg bw/day from the 2-year study in rats. Fertility and overall reproductive performance were not impaired by metosulam administration; no teratogenicity or developmental toxicity was observed in either rats or rabbits, up to dose levels inducing maternal toxicity. No potential for neurotoxicity was observed in the standard toxicity studies.
The acceptable daily intake (ADI) of metosulam is set at 0.05 mg/kg bw/day, based on the 2-year study in rats and applying a safety factor of 100; the acceptable operator exposure level (AOEL) is 0.02 mg/kg bw/day, based on the short-term dog study with a NOAEL of 10 mg/kg bw/day, applying a safety factor of 100, and a correction for low oral absorption (in dogs) of 20 %. The acute reference dose (ARfD) is 0.25 mg/kg bw based on a 2-week feeding study in dogs, showing severe ocular lesions at 100 mg/kg bw/day at the end of the 2-week treatment period; the NOAEL was 25 mg/kg bw/day and a safety factor of 100 was applied. The estimated operator exposure is below the AOEL without using personal protective equipment (PPE) according to both the German and the UK POEM models. No risk is anticipated for workers or bystanders.

3. Residues

The metabolism of metosulam was investigated using radiolabelled compound in wheat and potato, representing the cereal and root/tuber crop groups. The parent compound metosulam was the major component of the residues in forage (up to 60 % TRR; 0.14 mg/kg at PHI 14 days) and in straw at harvest (20 % TRR; 0.009 mg/kg), and none of the metabolites accounted for more than 5% TRR. At harvest the radioactivity in grains was extremely low (0.006 mg/kg), and was not further characterized. There was also little evidence of uptake of metosulam from the soil or translocation into the grain. Very low amounts were recovered following the treatment at the application rate of 30 g a.s./ha in potato foliage and tubers (max. 0.0022 mg/kg). Based on these findings the residue definition for monitoring and risk assessment is metosulam parent compound.
On the basis of the limited DT_{50}, and the metabolism studies on primary crops conducted with applications mainly directed to the soil, where the residue uptake was shown to be limited, it was concluded that significant residues of metosulam or its metabolites are highly unlikely to be present in succeeding crops, when the compound is applied according to the representative GAP.
A sufficient number of supervised residue studies were conducted in accordance with the representative uses. As the use on maize in southern Europe is not envisaged in the GAP, the results of the trials from this region were not taken into account. No residues above the LOQ (0.01 mg/kg for cereal grains and maize cobs, and 0.10 mg/kg for straw and silage) were detected. Thus, the proposed MRLs of 0.01* mg/kg in wheat, barley and maize are sufficiently supported by the data.
Storage stability data demonstrated that metosulam was stable when stored deep-frozen for up to 13 months in straw, and 18 months in grains. As no significant residues were present in raw commodities when metosulam was applied according to the representative GAP, the effect of processing and household preparation does not need to be investigated, and neither does the metabolism and magnitude of residues in animals.

No risk for the consumer resulting from the representative uses of metosulam was identified. Based on the EFSA PRIMo rev. 2 model and the proposed MRLs, the TMDI is 0.2 % of the ADI, and the IESTI is less than 0.1% of the ARfD.

4. Environmental fate and behaviour

In soil laboratory incubations under aerobic conditions in the dark, metosulam exhibited low to moderate persistence, forming the major (>10% applied radioactivity (AR)) metabolites 7-OH-metosulam (M02, max. 22 % AR) and ATSA (M01, max. 26 % AR), which exhibited very low to low and low to high persistence, respectively. Mineralisation of the aniline ring radiolabel to carbon dioxide accounted for 2 - 10 % AR after 122 days. The formation of unextractable residues for this

* MRL is proposed at the limit of quantification (LOQ)

radiolabel accounted for 52 – 66 % AR after 122 days. In anaerobic soil incubations metosulam was essentially stable. Metosulam exhibited high to medium mobility in soil. 7-OH-metosulam (M02) exhibited high to medium soil mobility and ATSA (M01) exhibited high soil mobility, but for these two metabolites only a narrow pH range was investigated, and adsorption might be expected to be pH dependent for these compounds. Therefore a data gap is identified to address the pH dependent adsorption of these metabolites. It was concluded that the adsorption of metosulam was not pH dependent. In satisfactory field dissipation studies carried out at 3 sites in Germany and 1 in the UK (spray application to the soil surface on bare soil plots in late spring) metosulam exhibited moderate persistence. Sample analyses were only carried out for the parent metosulam.
In a lysimeter study of two years duration all chromatographically resolved components in leachate accounted for < 0.075 µg/L, as annual average concentrations. It should be noted that this study may not cover the higher leaching potential for metabolites that might be encountered under neutral or alkaline soil conditions.

In laboratory incubations in dark aerobic natural sediment water systems, metosulam exhibited low persistence, forming the major metabolites 7-OH-metosulam (M02, max. ca. 17 % AR in both water and sediment, exhibiting moderate persistence), ATSA (M01, max. ca. 16 % AR in both water and sediment, exhibiting high persistence), and 5,7-OH-metosulam (M04, max. 16 % AR in water but only 4% max. in sediment, that exhibited moderate persistence). The unextractable sediment fraction was the major sink for the aniline ring C^{14} radiolabel, accounting for 59 – 67 % AR at study end (120 days). Mineralisation of this radiolabel accounted for only 0.9 - 3.6 % AR at the end of the study. The rate of decline of metosulam in a laboratory sterile aqueous photolysis experiment was slow relative to that occurred in the aerobic sediment water incubations. No chromatographically resolved component (excluding metosulam) accounted for > 8% AR. The necessary surface water and sediment exposure assessments (Predicted environmental concentrations (PEC)) in surface water and sediment were carried out for the metabolites 5,7-OH-metosulam (M04), 7-OH-metosulam (M02), and ATSA (M01), using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the Steps 1-2 in FOCUS calculator). However, a data gap is identified for further PEC values for M02 and M01, consequent to clarification of their pH dependent adsorption behaviour. For the active substance metosulam, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available[11]. The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of up to 20 m being implemented for the drainage scenarios (representing a 91 – 93 % spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80 %) being implemented for the run-off scenarios. The SWAN tool (version 1.1.4) was appropriately used to implement these mitigation measures in the simulations. However, it should be noted that whilst run-off mitigation is included in the step 4 calculations available, the FOCUS (FOCUS, 2007) report acknowledges that for substances with K_{Foc} < 2000 mL/g (i.e. metosulam), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.
The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2000) scenarios and the models PEARL 3.3.3 and PELMO 3.3.2[12] for the active substance metosulam. The potential for groundwater exposure from the representative uses by metosulam above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. For the metabolites 7-OH-metosulam (M02) and ATSA (M01) the groundwater exposure assessment cannot be finalised before the pH dependent adsorption behaviour of these metabolites has been clarified. Therefore a data gap is identified to address the groundwater leaching potential of these metabolites. For groundwater aquifers, where the overlying soils are predominantly in the pH range 6.3 to 6.7, it is possible to conclude that the potential for groundwater exposure for these metabolites from the representative uses would be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios.

[11] Simulations correctly utilised the agreed Q10 of 2.58 (following EFSA, 2007) and Walker equation coefficient of 0.7
[12] Simulations complied with EFSA (EFSA, 2004) and correctly utilised the agreed Q10 of 2.58 (following EFSA, 2007) and Walker equation coefficient of 0.7

The PEC in soil, surface water, sediment, and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

5. Ecotoxicology

The risk to birds was assessed as low for dietary exposure for the representative uses evaluated. A risk assessment for secondary poisoning of birds and mammals was not triggered, since the log Pow is < 3. For mammals the TER values for acute and long-term dietary exposure exceeded the Annex VI trigger values for all representative uses. In the resubmission the long-term (reproductive) end point was increased from 5 mg a.s./kg bw/day to 30 mg a.s./kg bw/day. A long-term end point of 5 mg a.s./kg bw/day was used in the mammalian toxicology section for general toxicity, based on histopathological effects on kidneys. Effects on body weight of up to 30 % were observed during gestation at a dose of 30 mg a.s./kg bw/day. The applicability of the end point refinement was discussed in an experts' teleconference (PRAPeR TC 28, January 2010). The experts were of the opinion that the long-term end point of 30 mg a.s./kg bw/day would be acceptable taking into consideration that the effects on body weight decreased towards the end of the gestation, and that reproductive parameters (litter size and survival) were not affected. However, it was noted that animals may not be able to compensate for effects on body weight during gestation in nature if they are exposed to environmental stressors such as cold and wet weather conditions, food shortage and parasites. The long-term TERs for the representative uses evaluated were clearly above the Annex VI trigger values, indicating a low risk. However, Member States should take into consideration that the end point of 30 mg a.s./kg bw/day is not conservative when the margin of safety is discussed for uses where the TERs are close to the Annex VI trigger values.

Metosulam is very toxic to aquatic organisms. Effects on higher aquatic plants (ErC_{50} = 0.789 µg a.s./L) were driving the aquatic risk assessment. No full FOCUS step 3 scenario resulted in TERs above the Annex VI trigger values. Risk mitigation such as vegetated filter strips and no-spray buffer zones of up to 10 m and 20 m were suggested in the risk assessment. The TER values were above the trigger for all drainage scenarios (D3, D4, D5, D6), and the majority of the run-off scenarios for the use on maize. For the use on cereals the TER values were above the trigger for 4 out of 6 full drainage scenarios, and for one full run-off scenario out of 3. For most of the scenarios which failed the Annex VI trigger also a no-spray buffer zone/vegetated filter strip of 20 m was not sufficient (maize: R4, cereals: D1, D2, R1 stream, R3 stream). The efficiency of a vegetated filter strip for run-off mitigation for substances with a Koc < 2000 is uncertain. The risk from the metabolite 5,7-OH metosulam (M04) was assessed as low for all representative uses. The risk assessment for ATSA (M01) and 7-OH metosulam (M02) was not finalised. However, given the low toxicity (more than 3 orders of magnitude less than the parent metosulam), and indicative TER values which exceeded the Annex VI trigger by more than 3 orders of magnitude, the risk is likely to be low.

The risk to bees from oral and contact exposure to the technical active substance was assessed as low, as well as oral exposure to the formulation. Since a reliable contact toxicity end point from a study with the representative formulation was missing, the rapporteur Member State suggested that such a study should be submitted at Member State level. The HQ values for the technical active substance were significantly below the Annex VI trigger, and the acute oral end point for the formulation suggest that there is no significant increase of toxicity. Therefore EFSA is of the opinion that the available information is sufficient to conclude that the risk to bees is low for the representative uses evaluated.

A potential high risk was identified for non-target plants for the representative uses in the off-field area. Risk mitigation comparable to a 5 m in-field no-spray buffer zone is needed to protect non-target plants in the off-field area.

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

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

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
metosulam	low to moderate persistence Single first-order DT_{50} 4.2-33.3 days (20ºC pF 2 soil moisture) Northern European field dissipation studies single first-order DT_{50} 20-47 days	Very low toxicity to earthworms and other soil macro-organisms. The risk to soil-dwelling organisms was assessed as low.
ATSA (M01)	low to high persistence Biphasic kinetics DT_{50} 2.8-85 days (DT_{90} 25-513 days, 20ºC 40% MWHC)	Very low toxicity to earthworms and other soil macro-organisms. The risk to soil-dwelling organisms was assessed as low.
7-OH-metosulam (M02)	very low to low persistence Single first-order and biphasic kinetics DT_{50} 0.6-2.4 days (DT_{90} 2.1-14.2 days, 20ºC 40% MWHC)	Very low toxicity to earthworms and other soil macro-organisms. The risk to soil-dwelling organisms was assessed as low.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
metosulam	high to medium mobility K_{Foc} 51-265 mL/g	No	Yes	Yes	Very toxic to aquatic organisms (*Lemna minor* ErC_{50} = 0.000789 mg a.s./L). The risk to aquatic organisms was assessed as high.
ATSA (M01)	currently high mobility K_{Foc} 36-80 mL/g , but data gap regarding pH dependence	Assessment not finalised	No	Oral 90-day, rat: NOAEL = 1000 mg/kg bw/day (no relevant adverse effect) Ames test: negative As the parent compound is proposed to be classified with R40 (Carc. Cat 3), further toxicological assessment would be necessary in case the level in groundwater would exceed 0.1 µg/L.	More than 3 orders of magnitude less toxic to aquatic organisms than metosulam (*Lemna minor* ErC_{50} >10 mg a.s./L). Risk to aquatic organisms is not finalised but it is expected to be low.

7-OH-metosulam (M02)	currently high to medium mobility K_{Foc} 78-134 mL/g , but data gap regarding pH dependence	Assessment not finalised	No	Rat oral LD_{50} > 2000 mg/kg bw Ames test: negative As the parent compound is proposed to be classified with R40 (Carc. Cat 3), further toxicological assessment would be necessary in case the level in groundwater would exceed 0.1 µg/L.	More than 3 orders of magnitude less toxic than metosulam (*Lemna minor* EbC_{50} = 16 mg a.s./L). Risk to aquatic organisms is not finalised but it is expected to be low.

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
metosulam	Very toxic to aquatic organisms (*Lemna minor* ErC_{50} = 0.000789 mg a.s./L). No full FOCUS step3 scenario resulted in TERs above the Annex VI trigger. Risk mitigation needed such as a no-spray buffer zone of at least 10 m. The efficiency of run-off mitigation is uncertain, but effective run-off mitigation would be necessary.
ATSA (M01)	More than 3 orders of magnitude less toxic to aquatic organisms than metosulam (*Lemna minor* ErC_{50} >10 mg a.s./L). Risk to aquatic organisms is not finalised as the exposure assessment is not finalised, but risk is expected to be low.
7-OH-metosulam (M02)	More than 3 orders of magnitude less toxic than metosulam (*Lemna minor* EbC_{50} = 16 mg a.s./L). Risk to aquatic organisms is not finalised as the exposure assessment is not finalised, but risk is expected to be low.
5,7-OH-metosulam (M04) for water only	More than 3 orders of magnitude less toxic than metosulam (*Lemna minor* ErC_{50} = 7.95 mg a.s./L). Risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
metosulam	Rat LC_{50} inhalation, 4-hour exposure > 1.9 mg/L air (no classification required)

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

- New batch data that support the current production (relevant for all representative uses evaluated, submission date proposed by the applicant: unknown; see section 1).

- Supporting data for the tank cleaning procedure (relevant for all representative uses evaluated; data submitted and evaluated by the RMS in the addendum to Volume 3 B3 of November 2009, but not considered during the peer review in view of the restrictions concerning the acceptance of newly submitted studies after the submission of the Additional Report, as laid down in Commission Regulation (EC) No. 33/2008; see section 1).

- Applicant to submit an Ames test with adequate levels of one impurity in the test material (relevant for all representative uses evaluated; study submitted and evaluated by the RMS in an addendum to Volume 4 of November 2009, but not considered during the peer review in view of the restrictions concerning the acceptance of newly submitted studies after the submission of the Additional Report, as laid down in Commission Regulation (EC) No. 33/2008; see section 2).

- Applicant to address the pH dependent adsorption of metabolites 7-OH-metosulam (M02, a phenol) and ATSA (M01, an amine). Either batch adsorption experiments with soils investigated at pH > 7 and < 6, and/or pKa / pKb investigations are necessary (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 4)

- Applicant to address the groundwater leaching potential of metabolites 7-OH-metosulam (M02) and ATSA (M01), consequent to the information on the pH dependence of their adsorption (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 4).

- Applicant to address the surface water exposure of metabolites 7-OH-metosulam (M02) and ATSA (M01), consequent to the information on the pH dependence of their adsorption (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 4).

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

- Risk mitigation such as no-spray buffer zones and run-off vegetated buffer strips are required to protect the aquatic environment. In situations represented by some FOCUS scenarios, the maximum mitigation afforded by combined 20m no-spray zones and vegetative strips was insufficient to demonstrate low aquatic risk (maize R4; cereals D1, D2, R1&R3). In most other FOCUS scenario represented situations, low risk could be identified with the mitigation proposed to be afforded by a 10m wide buffer / strip.

- Risk mitigation comparable to a 5m in-field no-spray buffer zone is needed to protect non-target plants in the off-field area.

ISSUES THAT COULD NOT BE FINALISED

Overall, the risk assessment could not be finalised for any of the representative uses. See summary of the representative uses in Appendix A as well as the list below for further details of the issues that are not finalised for the individual uses.

- The technical specification for the physical-chemical area could not be finalised because the available data did not support it (see section 1).

- The genotoxic potential of one impurity present in the technical specification could not be finalised (see section 2).

- The groundwater, surface water and sediment exposure assessments for the metabolites 7-OH-metosulam (M02) and ATSA (M01) are not finalised (see section 4). As a consequence,
  - the aquatic risk assessment for these metabolites is not finalised (see sections 5 and 6).
  - as the proposal for classification of the active substance includes a carcinogenic categorisation, the existing toxicity information on these metabolites would be insufficient to conclude that they are not relevant (see section 6), should any subsequent exposure assessment indicate that the parametric drinking water limit (0.1 µg/L) might be exceeded in groundwater.

CRITICAL AREAS OF CONCERN

- There is no agreed technical specification covered by the toxicological assessment. Furthermore, the genotoxic potential of one impurity present in the technical specification could not be finalised (refer to data gap for an Ames test with adequate levels of the impurity in the test material).

REFERENCES

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models comparability and the consistency of this risk assessment of groundwater contamination. The EFSA Journal (2004) 93, 1-20.

EFSA (European Food Safety Authority), 2007. Scientific Opinion of the Panel on Plant Protection Products and their Residues on a request from EFSA related to the default *Q*10 value used to describe the temperature effect on transformation rates of pesticides in soil. The EFSA Journal (2007) 622, 1-32.

EFSA (European Food Safety Authority), 2010. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance metosulam.

FOCUS, 2000. "FOCUS Groundwater Scenarios in the EU review of active substances". Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-rev.2. 202 pp, as updated by the Generic Guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

FOCUS, 2001. "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

FOCUS, 2007. "Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 1. Extended Summary and Recommendations". Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 169 pp.

France, 2006. Draft Assessment Report (DAR) on the active substance metosulam prepared by the rapporteur Member State France in the framework of Directive 91/414/EEC, July 2006.

France, 2009. Additional Report to the Draft Assessment Report on the active substance metosulam prepared by the rapporteur Member State France in the framework of Commission Regulation (EC) No 33/2008, August 2009.

France, 2010. Final Addendum to the DAR and Additional Report on metosulam, compiled by EFSA, April 2010.

APPENDICES

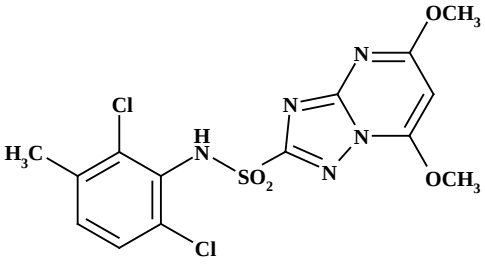
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Metosulam
Function (*e.g.* fungicide)	Herbicide

Rapporteur Member State	France
Co-rapporteur Member State	/

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2′,6′-dichloro-5,7-dimethoxy-3′-methyl[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonanilide
Chemical name (CA) ‡	[1,2,4]Triazolo[1,5-*a*]pyrimidine-2-sulfonamide, *N*-(2,6-dichloro-3-methylphenyl)-5,7-dimethoxy-
CIPAC No ‡	707
CAS No ‡	139528-85-1
EC No (EINECS or ELINCS) ‡	not allocated
FAO Specification (including year of publication) ‡	Not allocated
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	$C_{14}H_{13}Cl_2N_5O_4S$
Molecular mass ‡	418.26
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	No melting point before decomposition
Boiling point (state purity) ‡	No boiling point before decomposition
Temperature of decomposition (state purity)	190°C (99.1 %)
Appearance (state purity) ‡	Cream-coloured powder (purity 99.1%)
Vapour pressure (state temperature, state purity) ‡	$1*10^{-12}$ Pa (25°C, 99.1 %)
Henry's law constant ‡	$8*10^{-13}$ $Pa.m^3.mol^{-1}$
Solubility in water (state temperature, state purity and pH) ‡	0.2 g/L (20°C, 99.1 %, in distillate water un buffered) 0.1 g/l (20°C, 99.1 %, pH 5) 0.7 g/l (20°C, 99.1 %, pH 7) 5.6 g/l (20°C, 99.1 %,pH 9)
Solubility in organic solvents ‡ (state temperature, state purity)	At 20°C (purity 99.1%) : acetonitrile : 10 g/l methanol : 1.9 g/l 1-octanol : 0.2 g/l n-hexane : < 0.2 g/l toluene : <0.2g/l methylene chloride : 6.0 g/l acetone: 7.8 g/l Ethyl acetate: 1.0 g/l
Surface tension ‡ (state concentration and temperature, state purity)	69.6 mN/m (20°C, 96 %) at 202 mg/L 71.6 mN/m (20°C, 96%) at 101 mg/L
Partition co-efficient ‡ (state temperature, pH and purity)	At 20°C , purity 99.3% : pH 4 : Log P_{OW} = 1.8 pH 7 : Log P_{OW} = 0.2 pH 9 : Log P_{OW} = -1.1
Dissociation constant (state purity) ‡	5.5 (99.3 %)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	ε = 5.5 x 10^4 $l.mol^{-1}.cm^{-1}$at 206 nm at pH 4, 99.5 % ε = 6.7 x 10^4 $l.mol^{-1}.cm^{-1}$at 212 nm at pH 7, 99.5 % ε = 7.1 x 10^4 $l.mol^{-1}.cm^{-1}$at 212 nm at pH 9, 99.5 %
Flammability ‡ (state purity)	Metosulam is not highly flammable (96 %)
Explosive properties ‡ (state purity)	Metosulam is not explosive (96 %)
Oxidising properties ‡ (state purity)	Metosulam is non-oxidising (96 %)

Summary of representative uses evaluated *(METOSULAM)* representative formulation 'Tacco SC 100'

Crop and/ or situation (a)	Member state or country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Maize	Austria Germany	'Tacco SC 100'	F	Dicotyledonous plants	SC	100 g/L	Spray appl. with tractor mounted boom sprayer	BBCH 00 – 16, Pre – post emergence	1	n/a	0.005 – 0.015	200 - 400	0.02–0.03	n/a	[I], [II]
Cereals (wheat, barley) (spring and winter)	UK Italy	'Tacco SC 100'	F	Dicotyledonous plants	SC	100 g/L	Spray appl. with tractor mounted boom sprayer	BBCH 13 – 32 post-emergence	1	n/a	0.002 – 0.013	150 - 500	0.01-0.02	n/a	[I], [II]

[I] The groundwater, surface water and sediment exposure assessments for metabolites 7-OH-metosulam (M02) and ATSA (M01) are not finalised (refer to section '*Issues that could not be finalised*' of the Conclusion).

[II] There is no agreed specification covered by the toxicological assessment.

* For uses where the column „Remarks" in marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha

(m) PHI - minimum pre-harvest interval

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV (214 nm)
Impurities in technical as (analytical technique)	HPLC-UV (214 nm) GC-FID Karl Fisher titration GC-ECD (ion chromatography)
Plant protection product (analytical technique)	HPLC-UV (230 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Metosulam
Food of animal origin		Not required as no definition was defined
Soil		Metosulam
Water	surface	Metosulam
	drinking/ground	Metosulam
Air		Metosulam

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-UV: LOQ = 0.1 mg/kg maize whole plant and rest of plant, barley and wheat (grain and straw), barley whole plant, wheat and barley (rest of plant, whole plant, ears and straw. LOQ = 0.01 mg/kg maize cobs, wheat grain and barley grain HPLC-MS/MS: LOQ = 0.01 mg/kg barley grain, orange fruit, tomato fruit and rape seed DFG S 19 applicable LOQ = 0.01 mg/kg oilseed rape seed, watery plant material, acidic plant material, dry plant material, fatty plant
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-UV : LOQ = 0.01 mg/kg milk, cream LOQ = 0.01 mg/kg fat, kidney, liver, muscle DFG S 19 applicable LOQ = 0.01 mg/kg milk, egg, muscle, liver, kidney, fat No residue definition.
Soil (analytical technique and LOQ)	HPLC-UV: LOQ = 0.2 µg/kg HPLC-MS/MS: LOQ = 0.2 µg/kg

Water (analytical technique and LOQ)	LC-MS/MS: LOQ = 0.05 µg/L surface and drinking water
Air (analytical technique and LOQ)	HPLC-DAD: LOQ = 1 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not required as the active substance is neither toxic nor very toxic

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	**Rats** (both sexes): Tmax = 4h, the oral absorption being at 5 mg/kg bw: 68.4-76.2% in males 83.4-89.7% in females enhanced by repeated dosing at 100 mg/kg bw: 59.1% in males 70.6% in females **Mice** (males): Tmax = 6h, 20.6% oral absorption (at 100 mg/kg bw) **Dogs** (males): Tmax = 4h, 19.2% oral absorption (at 100 mg/kg bw)
Distribution ‡	Widely distributed throughout the body (rats, dogs), maximal residue concentration in the plasma.
Potential for accumulation ‡	Ratios of tissue/plasma levels lower than 1, suggesting no potential storage of residues in tissues.
Rate and extent of excretion ‡	**Rats**: biphasic elimination initial and terminal depuration half-lives: 9h and 60h elimination via urine (21% in males, 65% in females) and faeces (28% in males, 14% in females); quicker in females (ca. 80% within 48 hours) than in males (ca. 50% within 48 hours) **Dogs** (males) : monophasic elimination (half-life: 73h) 4.2% eliminated in urine and 73% via faeces within 24 hours **Mice** (males) : monophasic elimination (half-life: 54h) 11% eliminated in urine and 80% via faeces within 24 hours **Goats:** very low excretion in milk (0.05%)
Metabolism in animals ‡	**Rats :** Main urinary component is unchanged metosulam. Aliphatic oxidation to form 3-OH metosulam, O-demethylation to form 5-OH metosulam and aniline phenyl oxidation to form 4-OH metosulam, which is secondarily conjugated with glucose or sulfate. **Mice** (males) : extensively metabolized (4% of urine radioactivity as unchanged metosulam) **Dogs** (males) :

	minimal metabolism in dogs (75-88% of urine radio-activity as unchanged metosulam)	
Toxicologically relevant compounds ‡ (animals and plants)	Metosulam	
Toxicologically relevant compounds ‡ (environment)	Metosulam	

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 1.9 mg/L air (4h/nose only, twice ground particles aerosol); maximal attainable concentration	
Skin irritation ‡	Not irritating	
Eye irritation ‡	Not irritating	
Skin sensitisation ‡	Not sensitizing (M&K and Buehler methods)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	**Retina** (detachment and degeneration in dogs) *< 50 mg/kg bw* **Kidneys** (tubular epithelium degeneration ± inflammation in rats, dogs and rabbits) *< 50 mg/kg bw in dogs* **Gallbladder** (mucin accumulation in dogs, degeneration ± inflammation in rabbits) **Liver** (inflammation ± necrosis in mice and dogs)	
Relevant oral NOAEL ‡	10 mg/kg bw/day (1-year, dog) 9.4 mg/kg bw/day (90-day, rats) 250 mg/kg bw/day (90-day, mice) < 300 mg/kg bw/day (14-day, rabbit)	**Xn R48/22**
Relevant dermal NOAEL ‡	Systemic NOAEL: 1000 mg/kg bw/day (21-day, rabbits) Local NOAEL: < 100 mg/kg bw/day (epidermic hyperplasia at the test site)	
Relevant inhalation NOAEL ‡	No data - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential (*in vitro* and *in vivo*)	

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

Target/critical effect ‡	**Kidneys :** - renal epithelium hyperplasia (rats and mice) - renal tumours in male rats (cortical adenomas and adeno-carcinomas, 50% metastatic, induced by nephrotoxicity)	
Relevant NOAEL ‡	**Chronic toxicity** : 5 mg/kg bw/day (2-year, rat) 300 mg/kg bw/day (18-month, mouse) **Carcinogenicity** : 30 mg/kg bw/day (rat) > 1000 mg/kg bw/day, no carcinogenic effect in mouse	
Carcinogenicity ‡	Renal tumours in male rats	**R40** **(Cat. 3 carcinogen)**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No relevant effect on reproduction and offspring (rat) ***Main toxic effects in parents :*** Lower food intake and body weight gain **Kidneys** : nuclear pleomorphism and hypertrophy & lower kidney weight	
Relevant parental NOAEL ‡	30 mg/kg bw/day	
Relevant reproductive NOAEL ‡	100 mg/kg bw/day	
Relevant offspring NOAEL ‡	100 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	No relevant developmental effect (rat & rabbit) ***Main toxic effects in parents :*** Lower body weigh gain (rat & rabbit)/body weight loss (rabbit) **Kidneys** : degeneration/necrosis of renal epithelium (rabbit) **Gallbladder** : inflammation/necrosis (rabbit)	

Relevant maternal NOAEL ‡	Rat: 100 mg/kg bw/day Rabbit: 30 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 1000 mg/kg bw/day (highest dose-level) Rabbit: 300 mg/kg/day (highest dose-level)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, not required	
Repeated neurotoxicity ‡	No data-not required	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	***Mechanism of action of the carcinogenic effect*** Renal tubular necrosis, degeneration & regeneration of tubules , increased mitotic figures (BrDU incorporation) and nuclear pleomorphism occurred in rats given 100 mg/kg bw/day metosulam for 7 to 14 days ***14-day topical ocular application in dogs:*** No retinal lesions were observed. ***6-week gavage study in monkey:*** LOAEL = 100 mg/kg bw/day based on pale faeces and diarrhoea, no ocular lesions were found.
Studies performed on metabolites or impurities ‡	***Studies performed on metabolites :*** **M01 :** ➢ NOAEL (90-day, rat) : 1000 mg/kg bw/day (the highest dose tested) ➢ Ames test: negative **M02 :** ➢ DL_{50} oral (rat) : > 2000 mg/kg bw ➢ Ames test: negative **M04 :** ➢ DL_{50} oral (rat) : > 2000 mg/kg bw ➢ Ames test: negative

Medical data ‡ (Annex IIA, point 5.9)

No reported incidents of adverse reactions during the manufacture or formulation of metosulam

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.05 mg/kg bw/day	Rat 2-year study	100
AOEL ‡	0.02 mg/kg bw/day	1-year dog study	Overall 500 100 + 20 (correction for low oral absorption)
ARfD ‡	0.25 mg/kg bw	2-week dog study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation "TACCO SC 100"	0.02 % for concentrate 4.3% for spray dilution Based on an *in vitro* study in human skin

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure according to UK POEM or German BBA model is below the systemic AOEL: Tractor-mounted equipment (application rate 0.03 kg as/ha) UK POEM model: - without PPE: 23.1% German BBA model: - without PPE: 3.8%
Workers	The estimated exposure is 0.004% of the systemic AOEL, without PPE.
Bystanders	The estimated exposure is 0.12% of the systemic AOEL

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

	RMS/peer review proposal
Metosulam	Xn "Harmful" **R48/22 "**Harmful: danger of serious damage to health by prolonged exposure if swallowed" **R40** "Limited evidence of a carcinogenic effect"

Residues

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

Plant groups covered	Cereals (wheat) – post-emergence application Root vegetables (potato) - pre-emergence application
Rotational crops	No study provided and not required
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable
Processed commodities	No study provided and not required
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Metosulam
Plant residue definition for risk assessment	Metosulam
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Ruminants (lactating goats) - Not evaluated
Time needed to reach a plateau concentration in milk and eggs	4 days for milk
Animal residue definition for monitoring	Not proposed (not necessary for notified uses)
Animal residue definition for risk assessment	Not applicable
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

No study provided. None required.

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

Stable in wheat straw (up to 389 days at ≤-16C) and grain (up to 543 days) at ≤-16◦C, in plant extracts (up to 14 days) at +4◦C, in cow's milk (up to 110 days), in bovine fat (up to 394 days) and in bovine kidney and liver tissues (up to 455 days) at ≤-16◦C.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No. (below trigger value)		
Potential for accumulation (yes/no):	-	-	-
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	-	-	-
	No feeding studies required since cattle and poultry are not expected to be exposed to metosulam residues.		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation /comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Cereals (wheat, barley)	N and S Field Spray	12 x<0.01 (wheat) 12 x<0.01 (barley) 2 x <0.01 (rye, oats	-	0.01*	0.01	0.01 Straw: 0.1
Maize	N Field Spray	15 x<0.01	-	0.01*	0.01	0.01

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

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

ADI	0.05 mg/kg bw/day
TMDI (% ADI) according to EFSA PRIMo model	maximum 0.2% ADI (WHO cluster diet B)
TMDI (% ADI) according to French diets	0.1 (all population)
IEDI (WHO European Diet) % ADI)	-
NEDI (specify diet) (% ADI)	-
Factors included in IEDI and NEDI	-
ARfD	0.25 mg/kg bw
IESTI (%ARfD) according to EFSA PRIMo model	maximum 0.1% ARfD (wheat)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	-

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Tranfer factor	Yield factor	
None	-	-	-	-

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

- Wheat	0.01* mg/kg
- Barley :	0.01* mg/kg
- Maize	0.01* mg/kg

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

Fate and behaviour in the environment

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

Mineralization after 122-days ‡	2.0-10.1 % after 122 d, Aniline-[*UL*-^{14}C]-metosulam (n[1]= 4)
Non-extractable residues after 122 days ‡	51.9-65.7 % after 122 d, Aniline-[*UL*-^{14}C]-metosulam (n = 4)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	M01 – 10.3-26.3 % at 63-28 d (n = 4) M02 – 15.9-21.8 % at 7 d (n = 4) Aniline-[*UL*-^{14}C]-metosulam

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

Anaerobic degradation ‡

Mineralization after 100 days	<LOD at 364 d Aniline-[*UL*-^{14}C]-metosulam & Triazole-[2-^{14}C]-metosulam
Non-extractable residues after 100 days	0.27 % after 119 d, Aniline-[*UL*-^{14}C]-metosulam (n = 1) 0.30 % after 119 d, Triazole-[2-^{14}C]-metosulam (n = 1)
Metabolites that may require further consideration for risk assessment – name and/or code, % of applied (range and maximum)	None

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment – name and/or code, % of applied (range and maximum)	Degradation of metosulam 2 times more rapid under irradiation. Metosulam is the major component (62.8 % AR at day 10). Others compounds < 1.1 % AR.

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X^2	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (χ^2)	Method of circulation
Sand		6.4	20 / 40	5.2 / 17.4	4.4	10.49	SFO
Sand		7.7	20 / 40	4.9 / 16.3	4.2	5.96	SFO
Loamy sand		5.9	20 / 40	15.1 / 144*	33.3	1.97	FOMC

[1] n corresponds to the number of soils.

Silty clay loam		8.1	20 / 40	11.3 / 38.3	6.9	8.00	SFO
Geometric mean/median					8.1 / 5.7		

* Co = 88.72, α = 0.955, β = 14.2, normalised DT_{50} derived from DT_{90}/3.32

M01 (ATSA)	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	f. f. # k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (χ^2)	Method of circulation
Loamy sand		5.6 (Ca)	20 / 40	49.4 / 262.2*	0.531	91.2	1.59	HS
Sandy loam		6.3 (w)	20 / 40	84.95 / 513.5**	0.139	134.53	3.34	HS
Clay loam		7.8 (w)	20 / 40	2.8 / 24.9***	0.206	6.57	2.04	FOMC
Silty clay loam		7.2 (w)	20 / 40	45.7 / 215.9****	0.302	73.0	5.04	HS
Geometric mean/median						49.20 / 82.1		

* tb = 15.1, k1 = 0.029, k2 = 0.0076, normalised DT_{50} derived k2
** tb = 10.5, k1 = 0.039, k2 = 0.0038, normalised DT_{50} derived k2
*** Co = 97.12, α = 1.02, β = 2.89, normalised DT_{50} derived from DT_{90}/3.32
**** tb = 16.9, k1 = 0.025, k2 = 0.0095, normalised DT_{50} derived k2
# formation fraction from M02, best fit kinetic for M02, SFO fit for M01

M02 (7-OH-metosulam)	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Loamy sand		5.6 (Ca)	20 / 40	1.4 / 12.53**	-	3.8	4.67	FOMC
Sandy loam		6.3 (w)	20 / 40	2.4 / 7.98	-	1.77	8.52	SFO
Clay loam		7.8 (w)	20 / 40	1.8 / 14.2*	-	3.75	11.06	FOMC
Silty clay loam		7.2 (w)	20 / 40	0.6 / 2.09	-	0.6	9.2	SFO
Geometric mean/median						2.10 / 2.79		

* Co = 96.49, α = 1.13, β = 2.14, normalised DT_{50} derived from DT_{90}/3.32
** Co = 84.44, α = 1.06, β = 1.61, normalised DT_{50} derived from DT_{90}/3.32

Field studies ‡
4 European field trials at application rate 40 g/ha (Herford, Grebin) or 20 g/ha (Crimplesham, Rohr). 7 sampling dates. Only parent was analysed.

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Loam (Bare soil)	Herford (Germany)		6.8	10	20	66	0.98		First order
Loam (Bare soil)	Grebin (Germany)		5.6	10	47	156	0.85		
Loamy sand (Bare soil)	Crimplesham (UK)		7.5	10	27	90	0.92		
Silt loam (Bare soil)	Rohr (Germany)		7.1	10	41	136	0.87		

pH dependence ‡ (yes / no) (if yes type of dependence)	No.
Soil accumulation and plateau concentration ‡	Not required.

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[2]	pH	t. °C / % MWHC	DT_{50}/DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of circulation
Loamy sand		5.7	20	> 1 year			
Geometric mean/median							

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	1.26	5.4			1.491	201.5	1.084
Silty clay loam	3.7	6.5			3.195	146.6	0.8426
Sandy clay loam	29.2	7.4			8.841	51.5	0.8678
Loamy sand	6	5.5			0.927	264.7	0.8898
Arithmetic mean/median					3.61	166.1	0.9211
pH dependence, Yes or No			Not expected in a normal range of agricultural soil				

	pH

M01 ‡							
Soil Type	OC %	Soil pH (Ca)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Silt	2.11	6.7			0.8	36	0.8948
Silt loam	0.83	6.5			0.4	42	0.9009
Sandy loam	1.02	6.3			0.8	80	0.9113
Arithmetic mean/median					0.67	53	0.9023
pH dependence (yes or no)			Data gap				

M02 ‡							
Soil Type	OC %	Soil pH (Ca)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Silt	2.11	6.7			1.6	78	0.9079
Silt loam	0.83	6.5			0.9	110	0.8551
Sandy loam	1.02	6.3			1.4	134	0.9012
Arithmetic mean/median					1.3	107	0.8881
pH dependence (yes or no)			Data gap				

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

Column leaching ‡	3 acidic soils (pH 5.3-6.5) Elution (mm): 200 mm distilled water Time period (d): 2 d Leachate: 0.58-23.92 % total radioactivity in leachate (only active substance). 10-33 % total radioactivity retained in top 12 cm 3 alkaline soils (pH 7.8-8.2) Elution (mm): 200 mm 0.01 M $CaCl_2$ Time period (d): 2 d Leachate: 0.13-0.85 % total radioactivity in leachate (only active substance). 26-58 % total radioactivity retained in 15-25 cm for sand and sandy clay loam soils; > 86 % AR in 0-10 cm fir clay loam soil.
Aged residues leaching ‡	1 acidic soil Aged for (d): 30 d

	Eluation (mm): 200 mm distilled water Time period (d): 2 d Analysis of soil residues post ageing (soil residues pre-leaching): No data. Leachate: 11.7-12.9 % total radioactivity in leachate. >59.5 % total radioactivity retained in top 3 cm 1 alkaline soil Aged for (d): 12-32 d Eluation (mm): 200 mm 0.01 M $CaCl_2$ Time period (d): 2 d Analysis of soil residues post ageing (soil residues pre-leaching): 30&8 % active substance 12&32 d, 18&19 % M01 12&32d, 16&4 % M02 12&32 d. Leachate: 12 days aging: 3.2-3.8 % total radioactivity in leachate, 1 % M01 > 41 % total radioactivity retained in top 5 cm 32 days aging: 6.7-6.8 % total radioactivity in leachate, 1 % M01 > 66 % total radioactivity retained in top 5 cm
Lysimeter/ field leaching studies ‡	Location: Letcombe (UK) Study type: lysimeter (3 lysimeters No 7,8,11, same soil) Soil properties: 0-29 cm, loamy sand, pH = 6.2, OC = 0.6 % 29-50 cm, sand, pH = 6.2, OC = 0.2 % 50-73 cm, sand, pH = 5.4, OC = 0.1 % 73-100 cm, loamy sand, pH = 6.0, OC = 0.1 % Dates of application : Year 1: 21st March 90 (lysimeters 7&8) / 3rd April 90 (lysimeter 11) Year 2: 22nd March 91 (lysimeter 7) Crop : Year 1: Winter barley Year 2: Winter wheat (Lysimeter 7), Winter oilseed rape (Lysimeter 8), Sugarbeet (Lysimeter 11) Number of applications: 1 application per year Duration: 2 years Application rate: 25.6-32.3 g/ha/year Average annual rainfall (mm): 756 (year 1) – 812 (year 2) Average annual leachate volume (mm): 243-307 mm

	(year 1) – 331-444 mm (year 2) % radioactivity in leachate (maximum/year): - Individual annual average concentrations (µg/l): **Active substance** not detected; **M01**: 0.011 (year 1) - 0.052 (year 2) for lysimeter 7; 0.021 (year 1) - 0.077 (year 2) for lysimeter 8; 0.027 (year 1) - 0.029 (year 2) for lysimeter 11; **M02**: 0.007 (year 1) - 0.004 (year 2) for lysimeter 7; 0.010 (year 1) - 0.016 (year 2) for lysimeter 8; 0.012 (year 1) - 0.010 (year 2) for lysimeter 11. **Unidentified radioactivity**, 3 components (µg/L parent equivalents): 0.005-0.027 (year 1) - 0.008-0.053 (year 2) for lysimeter 7; 0.006-0.033 (year 1) - 0.002-0.075 (year 2) for lysimeter 8; nd-0.059 (year 1) - 0.007-0.041 (year 2) for lysimeter 11. Amount of radioactivity in the soils at the end of the study = 60.4-74.6 % AR, mainly unextracted residues.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	The applicant provided new study for PECsoil but it is not validated. Only PECsoil,max (initial) are presented.
Application data	Crop: maize % plant interception: no crop interception Application rate(s): 30 g as/ha Crop: Winter cereals % plant interception: 25 % Application rate(s): 20 g as/ha Depth of soil layer: 5cm Soil bulk density: 1.5g/cm3 Number of applications: 1 Interval (d): -

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial - Maize	0.04		-	
Initial - Winter cereals	0.02		-	
Plateau concentration	Not required			

Metabolite M01 (ATSA)	
Method of calculation	Molecular weight relative to the parent: 0.771 The applicant provided new study for PECsoil but it is not validated. Only PECsoil,max (initial) are presented. Plateau concentration calculated with worst-case kinetic (HS, tb = 10.5, k1 = 0.039, k2 = 0.0038)
Application data	Application rate assumed: assumed M01 is formed at a maximum of 26.3 % of the applied dose.

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial - Maize	0.0081		-	
Initial - Winter cereals	0.0041		-	
Plateau concentration	0.0100 (Maize) 0.0049 (Winter cereals)			

Metabolite M02 (7-OH-metosulam)	
Method of calculation	Molecular weight relative to the parent: 0.966 The applicant provided new study for PECsoil but it is not validated. Only PECsoil,max (initial) are presented.
Application data	Application rate assumed: assumed M01 is formed at a maximum of 21.8 % of the applied dose

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial - Maize	0.0084		-	
Initial - Winter cereals	0.0042		-	
Plateau concentration	Not required			

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5 at 25 °C, for 30 days: Stable pH 7 at 25 °C, for 30 days: Stable pH 9 at 25 °C, for 30 days: Stable
Photolytic degradation of active substance and metabolites above 10 % ‡	Sterile buffer, pH 7, 25 °C, Xe lamp. DT_{50}: 31.1 days.

	Estimated DT_{50} = 140 summer days at Huntington (UK)
Quantum yield of direct phototransformation in water at Σ > 290 nm	Φ = 0.00022
Readily biodegradable ‡ (yes/no)	No.

Degradation in water / sediment

Parent	Distribution (max in water 89.7-96.8 % after 0 d; max. sed 11.5-19.6 % after 1-3 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	St. (χ^2)	DT_{50}-DT_{90} sed	St. (χ^2)	Method of calculation
Loamy sand	6.7	7.1	20	8.2 / 27.1	7.03	7.5 / 24.8	8.53	4.56 / 49.1*	15.6	SFO
Loam	5.3-6.2*	5.7	20	8.1 / 26.8	6.75	5.9 / 19.6	7.51	31.0 / 103.1	21.7	
Geometric mean/median										

* FOMC

M01	Distribution (max in water 0.9-17.4 % after 60 d; max. sed 11.1-15.7 % after 60-120 d)									
Water / sediment system	pH water phase	pH sed (w)	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Loamy sand	6.7	7.1	20	120 / 399	4.5					SFO
Loam	5.3-6.2*	5.7	20	not determined	10.8					
Geometric mean										
M02	Distribution (max in water 9.9-17.2 % after 14 d; max. sed 6.1-17.8 % after 7-14 d)									
Water / sediment system	pH water phase	pH sed (w)	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Loamy sand	6.7	7.1	20	14 / 46.6	16.1					
Loam	5.3-6.2*	5.7	20	22.4 / 74.5	22.8					
Geometric mean				20.1 / 66.8						
M04	Distribution (max in water 6.1-15.6 % after 14 d; max. sed 3.6-4.2 % after 14 d)									
Water / sediment system	pH water phase	pH sed (w)	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Loamy sand	6.7	7.1	20	14 / 46.9	23.6					

Loam	5.3-6.2*	5.7	20	13.1 / 43.7	55.7					
Geometric mean										

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed (w)	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Loamy sand	6.7	7.1	3.6 %, 120 d	58.7 %, 120 d	58.7 %, 120 d
Loam	5.3-6.2*	5.7	0.9 %, 120 d	67.5 %, 120 d	67.5 %, 120 d

***** two replicates

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. 1.1 of FOCUS: Molecular weight (g/mol): 418.30 Water solubility (mg/L): 200 (20°C) K_{OC} (L/kg): 166.1 l/kg ; 1/n: 0.92 DT_{50} soil (d): 10.6 d (lab) DT_{50} water/sediment system (d): 8.2 DT_{50} water (d): 8.2 DT_{50} sediment (d): 8.2 Crop interception (%): No interception for maize and minimal crop cover for winter cereals
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: MACRO (v4), PRZM (v1), TOXSWA (v2) Q10 of 2.58 used, corresponding to Ea of 65.4 $kJ.mol^{-1}$
Application rate	Number of applications: 1 Interval (d): - Application rate: Maize: 30 g/ha with no interception Winter cereals: 20 g/ha with minimal crop cover Application rate(s): 1500 g as/ha Application date: Maize: March-May in FOCUS Steps 1-2 14 days before crop emergence, 7th to 26th April in FOCUS Step 3

		Winter cereals : October - February in FOCUS Steps 1-2 4th to 27th February in FOCUS Step 3			
FOCUS STEP 2 Scenario Maize	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	1.432		2.284	
	21 d		0.666		
Southern EU	0 h	2.693		4.377	
	21 d		1.256		

FOCUS STEP 2 Scenario winter cereals	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	1.690		2.744	
	21 d		0.788		
Southern EU	0 h	1.375		2.220	
	21 d		0.641		

FOCUS STEP 3 Scenario - Maize	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	Ditch	0 h (max)	0.157		0.046	
D4	Pond	0 h (max)	0.006		0.009	
D4	Stream	0 h (max)	0.133		0.007	
D5	Pond	0 h (max)	0.006		0.008	
D5	Stream	0 h (max)	0.134		0.004	
D6	Ditch	0 h (max)	0.157		0.048	
R1	Pond	0 h (max)	0.008		0.017	
R1	Stream	0 h (max)	0.309		0.069	
R2	Stream	0 h (max)	0.163		0.044	
R3	Stream	0 h (max)	0.154		0.027	
R4	Stream	0 h (max)	0.774		0.241	

FOCUS STEP 3 Scenario – Winter cereals	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D1	Ditch	0 h (max)	0.595		1.202	
D1	Stream	0 h (max)	0.373		0.705	
D2	Ditch	0 h (max)	0.329		0.240	
D2	Stream	0 h (max)	0.207		0.123	
D3	Ditch	0 h (max)	0.126		0.031	
D4	Pond	0 h (max)	0.004		0.007	
D4	Stream	0 h (max)	0.102		0.005	
D5	Pond	0 h (max)	0.004		0.006	
D5	Stream	0 h (max)	0.092		0.002	
D6	Ditch	0 h (max)	0.126		0.026	
R1	Pond	0 h (max)	0.006		0.010	
R1	Stream	0 h (max)	0.362		0.064	
R3	Stream	0 h (max)	0.402		0.088	
R4	Stream	0 h (max)	0.109		0.034	

FOCUS STEP 4 Scenario – Maize 10m buffer / vegetated filter strip	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	Ditch	0 h (max)	0.027		-	
D4	Pond	0 h (max)	0.004		-	
D4	Stream	0 h (max)	0.030		-	
D5	Pond	0 h (max)	0.004		-	
D5	Stream	0 h (max)	0.030		-	
D6	Ditch	0 h (max)	0.028		-	
R1	Pond	0 h (max)	0.004		-	
R1	Stream	0 h (max)	0.131		-	
R2	Stream	0 h (max)	0.073		-	
R3	Stream	0 h (max)	0.034		-	
R4	Stream	0 h (max)	0.352		-	

FOCUS STEP 4 Scenario – Winter cereals 10m buffer / vegetated filter strip	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D1	Ditch	0 h (max)	0.595		-	
D1	Stream	0 h (max)	0.373		-	
D2	Ditch	0 h (max)	0.329		-	
D2	Stream	0 h (max)	0.207		-	
D3	Ditch	0 h (max)	0.018		-	
D4	Pond	0 h (max)	0.003		-	
D4	Stream	0 h (max)	0.020		-	
D5	Pond	0 h (max)	0.003		-	
D5	Stream	0 h (max)	0.018		-	
D6	Ditch	0 h (max)	0.019		-	
R1	Pond	0 h (max)	0.003		-	
R1	Stream	0 h (max)	0.159		-	
R3	Stream	0 h (max)	0.178		-	
R4	Stream	0 h (max)	0.050		-	
FOCUS STEP 4 Scenario – Maize 20m buffer / vegetated filter strip	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	Ditch	0 h (max)	0.014		-	
D4	Pond	0 h (max)	0.003		-	
D4	Stream	0 h (max)	0.015		-	
D5	Pond	0 h (max)	0.003		-	
D5	Stream	0 h (max)	0.016		-	
D6	Ditch	0 h (max)	0.014		-	
R1	Pond	0 h (max)	0.003		-	
R1	Stream	0 h (max)	0.067		-	
R2	Stream	0 h (max)	0.038		-	
R3	Stream	0 h (max)	0.018		-	

R4	Stream	0 h (max)	0.185		-	

FOCUS STEP 4 Scenario – Winter cereals 20m buffer / vegetated filter strip	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D1	Ditch	0 h (max)	0.595		-	
D1	Stream	0 h (max)	0.373		-	
D2	Ditch	0 h (max)	0.329		-	
D2	Stream	0 h (max)	0.207		-	
D3	Ditch	0 h (max)	0.010		-	
D4	Pond	0 h (max)	0.002		-	
D4	Stream	0 h (max)	0.010		-	
D5	Pond	0 h (max)	0.002		-	
D5	Stream	0 h (max)	0.009		-	
D6	Ditch	0 h (max)	0.011		-	
R1	Pond	0 h (max)	0.002		-	
R1	Stream	0 h (max)	0.082		-	
R3	Stream	0 h (max)	0.092		-	
R4	Stream	0 h (max)	0.026		-	

Metabolite M01 (ATSA)	
Parameters used in FOCUSsw step 1 and 2	Version control no. 1.1 of FOCUS: Molecular weight (g/mol): 322.2 Water solubility (mg/L): 175.9 (20°C) K_{OC} (L/kg): 53 L/kg* DT_{50} soil (d): 54.90 d (lab) DT_{50} water/sediment system (d): 120 DT_{50} water (d): 120 DT_{50} sediment (d): 120 Crop interception (%): No interception for maize and minimal crop cover for winter cereals * as pH dependence of adsorption for M01 is not addressed, exposure assessment using this value is only considered indicative.
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Max observed in water sediment studies: 28.50%

Main routes of entry	Max observed in soil studies: 26.30 % -

FOCUS STEP 2 Scenario Maize	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.416		0.219	
	21 d		0.391		
Southern EU	0 h	0.776		0.408	
	21 d		0.730		

FOCUS STEP 2 Scenario Winter cereals	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.487		0.256	
	21 d		0.458		
Southern EU	0 h	0.398		0.209	
	21 d		0.374		

Metabolite M02 (7-OH-metosulam)	
Parameters used in FOCUSsw step 1 and 2	Version control no. 1.1 of FOCUS: Molecular weight (g/mol): 404.2 Water solubility (mg/L): 5.4 (20°C) K_{OC} (L/kg): 107 L/kg* DT50 soil (d): 2.20 d (lab) DT_{50} water/sediment system (d): 22.4 DT_{50} water (d): 22.4 DT_{50} sediment (d): 22.4 Crop interception (%): No interception for maize and minimal crop cover for winter cereals * as pH dependence of adsorption for M02 is not addressed, exposure assessment using this value is only considered indicative.
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Max observed in water sediment studies : 27.8 % Max observed in soil studies : 21.80 %
Main routes of entry	-

FOCUS STEP 2 Scenario Maize	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.16		0.17	
Southern EU	0 h	0.27		0.28	

FOCUS STEP 2 Scenario Winter cereals	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.17		0.18	
Southern EU	0 h	0.14		0.15	

Metabolite M04 (5,7-OH-metosulam)	
Parameters used in FOCUSsw step 1 and 2	Version control no. 1.1 of FOCUS: Molecular weight (g/mol): 390.20 Water solubility (mg/L): 1000 (20°C)* K_{OC} (L/kg): 0 l/kg * DT_{50} soil (d): 1000 d* DT_{50} water/sediment system (d): 14.10 DT_{50} water (d): 14.10 DT_{50} sediment (d): 14.10 Crop interception (%): No interception for maize and minimal crop cover for winter cereals * default value
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Max observed in water sediment studies: 28.50% Max observed in soil studies: 0 %
Main routes of entry	-

FOCUS STEP 2 Scenario Maize	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.049		<0.001	
	21 d		0.031		
Southern EU	0 h	0.049		<0.001	
	21 d		0.031		

FOCUS STEP 2 Scenario Winter cereals	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.033		<0.001	
	21 d		0.021		
Southern EU	0 h	0.033		<0.001	
	21 d		0.021		

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Modelling using FOCUS models, with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PELMO 3.3.2 and PEARL 3.3.3 Q10 of 2.58 used, corresponding to Ea of 65.4 $kJ.mol^{-1}$ Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: Winter cereals Scenarios (list of names): Châteaudun, Hamburg, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: Maize **Metosulam** Geometric mean DT_{50lab} 8.1 d (normalisation to pF2, 20 °C with Q10 of 2.58). K_{DOC}:, arithmetic mean 166.1L/kg, $^{1}/_{n}$= 0.921. Plant uptake factor: 0.5 Vapour pressure: 1 10^{-12} Pa Solubility: 200 mg/L **M01 (ATSA)** Data gap **M02 (7-OH-metosulam)** Data gap

Application rate	Application rate: 30 g/ha for maize 20 g/ha for winter cereals No interception for maize, 25% crop interception for winter cereals No. of applications: 1 Time of application (month or season): Maize : 10 days before the emergence Winter cereals : February 1st

PEC (gw) – FOCUS modelling result (80th percentile annual average concentration at 1m)

	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			7-OH-Metosulam Data gap	ATSA Data Gap	
				Pearl	Pelmo
Winter cereals	Chateaudun	<0.001			
	Hamburg	<0.001			
	Jokioinen	<0.001			
	Kremsmunster	<0.001			
	Okehampton	<0.001			
	Piacenza	<0.001			
	Porto	<0.001			
	Sevilla	<0.001			
	Thiva	<0.001			

	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			7-OH-Metosulam Data gap	ATSA Data gap	
				Pearl	Pelmo
Maize	Chateaudun	<0.001			
	Hamburg	<0.001			
	Kremsmunster	<0.001			
	Okehampton	<0.001			
	Piacenza	<0.001			
	Porto	<0.001			
	Sevilla	<0.001			
	Thiva	<0.001			

PEC (gw) From lysimeter / field studies

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

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

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 1.6 days considering OH radical reaction.
Volatilisation ‡	from plant surfaces (BBA guideline): Not studied - no data requested from soil surfaces (BBA guideline): Not studied - no data requested
Metabolites	None

PEC (air)

Method of calculation	-

PEC (a)

Maximum concentration	No data

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: metosulam, M01, M02 Surface Water: metosulam, M01, M02, M04 Sediment: metosulam, M01, M02 Ground water: metosulam, M01, M02 Air: metosulam

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

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

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

Candidate for R53

Ecotoxicology

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Mallard duck	Metosulam	Acute	> 2,000 mg a.s./kg bw	-
Bobwhite quail	Metosulam	Acute	> 2,250 mg a.s./kg bw	-
	Preparation	Acute	Not required	-
	Metabolite	Acute	Not required	-
Mallard duck	Metosulam	Short-term	> 1923 mg a.s./kg bw/day	> 5620 ppm
Bobwhite quail	Metosulam	Short-term	> 1405 mg a.s./kg bw/day	> 5620 ppm
Bobwhite quail	Metosulam	Long-term	22 mg a.s./kg bw/day	313 ppm
Mammals ‡				
Rat	Metosulam	Acute	> 5000 mg a.s./kg bw	-
	M02 (7-OH metosulam)	Acute	> 5000 mg/kg bw	-
	M04 (5,7-OH metosulam)	Acute	> 5000 mg/kg bw	-
	Metosulam SC 100	Acute	> 5000 mg product/kg bw	-
Rat	Metosulam	Long-term (2-generations study)	30 mg a.s./kg bw/day	-
	M01 (ATSA)	Long-term (13 weeks)	1000 mg /kg bw/day	-
Additional higher tier studies ‡				
Birds: not required				
Mammals: not required				

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

Maize, 0.03 kg a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	1.62	> 1234	10
	Short-term	0.90	> 1561	10
	Long-term	0.90	24.4	5
Tier 1 (Birds)				
Medium herbivorous bird	Acute	1.98	> 1010	10
	Short-term	0.91	> 1544	5
	Long-term	0.48	45.8	10
Higher tier refinement (Birds): not required				
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	0.73	> 6842	10
	Long-term	0.18	170	5
Higher tier refinement (Mammals): not required				

Cereals, 0.02 kg a.s./ha (early crop stage)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	1.08	>1852	10
	Short-term	0.6	>2342	10
	Long-term	0.6	37	5
Tier 1 (Birds)				
Large herbivorous bird	Acute	1.25	>1600	10
	Short-term	0.67	>2097	5
	Long-term	0.35	63	10
Higher tier refinement (Birds): not required				
Tier 1 (Mammals)				
Medium herbivorous mammal	Acute	3.95	>1267	10
	Long-term	1.12	27	5
Higher tier refinement (Mammals) not required				

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1,2] (mg/L)
Laboratory tests ‡				
Fish				
O. mykiss	Metosulam	96 h	LC_{50}	**>29.3 mm**
P. promelas	Metosulam	96 h	LC_{50}	>53.2 mg/L mm
M.beryllina	Metosulam	96 h	LC_{50}	>93.2 mg/L mm
O. mykiss	Metosulam	21d	NOEC	24.4 mm
P .promelas	Metosulam	Fish early life stage toxicity test, 32d	NOEC	**4.24 mm**
O. mykiss	Metosulam SC 100	96 h	LC_{50}	> 80 (a.s.) nom
O. mykiss	Metosulam SC 100	21d	NOEC	25 (a.s.) nom
Aquatic invertebrate				
D. magna	Metosulam	48 h	EC_{50}	>100 nom
Paleomonetes pugio	Metosulam	48 h	EC_{50}	>100.2 mm
Crassostrea virginica	Metosulam	48 h	EC_{50}	87.7 nom
D. magna	Metosulam	21 d	Parental and Reproduction NOEC	2.5 nom
D. magna	Metosulam SC 100	48 h	EC_{50}	**6.4 (a.s.) nom**
D. magna	Metosulam SC 100	21 d	Parental and Reproduction NOEC	**0.25 (a.s.) nom**
Sediment dwelling organisms:				
Chironomus riparius	M01 (ATSA)	28d	NOEC	**100 nom**
Chironomus riparius	M02 (7-OH metosulam)	28d	NOEC	**100 nom**
Algae				
S. subspicatus	Metosulam	72 h 48h	EbC_{50} ErC_{50}	0.075 nom 0.17 nom
N. pelliculosa	Metosulam	72 h	EbC_{50} ErC_{50}	>53.6 mm
S. subspicatus	Metosulam SC 100	72 h 48h	EbC_{50} ErC_{50}	**0.045 (a.s) nom** **1.9 (a.s.) nom**
D subspicatus	M01 (ATSA)	72 h	EbC_{50} ErC_{50}	**> 10 nom**
D. subspicatus	M02 (7-OH metosulam)	72 h	EbC_{50} ErC_{50}	**>100 nom**

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1,2] (mg/L)
D. subspicatus	M04 (5,7-OH metosulam)	72 h	EbC_{50} ErC_{50}	**81 mm** **101 mm**
Higher plant				
L. minor	Metosulam	7 d	EbC_{50} ErC_{50}	**0.0023 mm** **0.000789 mm**
L. minor	Metosulam SC 100	7 d	EbC_{50} ErC_{50}	0.00098 nom 0.00085 nom
L. minor	M01 (ATSA)	7d	ErC_{50}	**> 10 nom**
L. minor	M02 (7-OH metosulam)	7d	EbC_{50} ErC_{50}	**16 nom** **19 nom**
L. minor	M04 (5,7-OH metosulam)	7d	EbC_{50} ErC_{50}	**9.39 mm** **7.95 mm**
Microcosm or mesocosm tests: Not required				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.
2 in bold: values used in the TER calculations

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

FOCUS Step 2

Maize, 0.03 kg a.s./ha

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC max (µg/L)	TER[1]	Annex VI Trigger
metosulam	Fish	> 29300	Acute	2.693	> 10880	100
metosulam	Fish	4240	Chronic	2.693	1575	10
Metosulam SC 100	Invertebrate	6400	Acute	2.693	2377	100
Metosulam SC 100	Invertebrate	250	Chronic	2.693	93	10
Metosulam SC 100	Algae	45	Chronic	2.693	17	10
metosulam	Aquatic plant	0.789	Chronic	2.693	**0.29**	10
M01 (ATSA)	sediment dwellers	100000	Chronic	0.776	128866*	10
M01 (ATSA)	Algae	> 10000	Chronic	0.776	> 12887*	10
M01 (ATSA)	Aquatic plant	> 10000	Chronic	0.776	> 12887*	10
M02 (7-OH metosulam)	sediment dwellers	100000	Chronic	0.27	370370*	10

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC max (µg/L)	TER[1]	Annex VI Trigger
M02 (7-OH metosulam)	Algae	> 100000	Chronic	0.27	> 370370*	10
M02 (7-OH metosulam)	Aquatic plant	16000	Chronic	0.27	59259*	10
M04 (5,7-OH metosulam)	Algae	81000	Chronic	0.049	1653061	10
M04 (5,7-OH metosulam)	Aquatic plant	7950	Chronic	0.049	162245	10

[1] TER that are below the trigger value are in bold
*TERs for the metabolites M01 and M02 are based on indicative PECsw.

Cereals, 0.02 kg a.s./ha

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC max (µg/L)	TER[1]	Annex VI Trigger
metosulam	Fish	> 29300	Acute	1.690	> 17337	100
metosulam	Fish	4240	Chronic	1.690	2509	10
Metosulam SC 100	Invertebrate	6400	Acute	1.690	3787	100
Metosulam SC 100	Invertebrate	250	Chronic	1.690	148	10
Metosulam SC 100	Algae	45	Chronic	1.690	27	10
metosulam	Aquatic plant	0.789	Chronic	1.690	**0.47**	10
M01 (ATSA)	sediment dwellers	100000	Chronic	0.487	205339*	10
M01 (ATSA)	Algae	> 10000	Chronic	0.487	> 20533*	10
M01 (ATSA)	Aquatic plant	> 10000	Chronic	0.487	> 20533*	10
M02 (7-OH metosulam)	sediment dwellers	100000	Chronic	0.17	588235*	10
M02 (7-OH metosulam)	Algae	> 100000	Chronic	0.17	> 588235*	10
M02 (7-OH metosulam)	Aquatic plant	16000	Chronic	0.17	94118*	10
M04 (5,7-OH metosulam)	Algae	81000	Chronic	0.033	2454546	10

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC max (µg/L)	TER[1]	Annex VI Trigger
M04 (5,7-OH metosulam)	Aquatic plant	7950	Chronic	0.033	240909	10

[1] TER that are below the trigger value are in bold
*TERs for the metabolites M01 and M02 are based on indicative PECsw.

Refined aquatic risk assessment using higher tier FOCUS modelling

FOCUS Step 3

Maize, 0.03 kg a.s./ha

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
metosulam	D3	ditch	Aquatic plant	Chronic	0.789	0.157	**5.0**	10
metosulam	D4	pond	Aquatic plant	Chronic	0.789	0.006	132	10
metosulam	D4	stream	Aquatic plant	Chronic	0.789	0.133	**5.9**	10
metosulam	D5	pond	Aquatic plant	Chronic	0.789	0.006	132	10
metosulam	D5	stream	Aquatic plant	Chronic	0.789	0.134	**5.9**	10
metosulam	D6	ditch	Aquatic plant	Chronic	0.789	0.157	**5.0**	10
metosulam	R1	pond	Aquatic plant	Chronic	0.789	0.008	98.6	10
metosulam	R1	stream	Aquatic plant	Chronic	0.789	0.309	**2.6**	10
metosulam	R2	stream	Aquatic plant	Chronic	0.789	0.163	**4.8**	10
metosulam	R3	stream	Aquatic plant	Chronic	0.789	0.154	**5.1**	10
metosulam	R4	stream	Aquatic plant	Chronic	0.789	0.774	**1.0**	10

[1] TER that are below the trigger value are in bold

cereals, 0.02 kg a.s./ha

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
metosulam	D1	ditch	Aquatic	Chronic	0.789	0.595	**1.3**	10

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
			plant					
metosulam	D1	stream	Aquatic plant	Chronic	0.789	0.373	**2.1**	10
metosulam	D2	ditch	Aquatic plant	Chronic	0.789	0.329	**2.4**	10
metosulam	D2	stream	Aquatic plant	Chronic	0.789	0.207	**3.8**	10
metosulam	D3	ditch	Aquatic plant	Chronic	0.789	0.126	**6.3**	10
metosulam	D4	pond	Aquatic plant	Chronic	0.789	0.004	197	10
metosulam	D4	stream	Aquatic plant	Chronic	0.789	0.102	**7.7**	10
metosulam	D5	pond	Aquatic plant	Chronic	0.789	0.004	197	10
metosulam	D5	stream	Aquatic plant	Chronic	0.789	0.092	**8.6**	10
metosulam	D6	ditch	Aquatic plant	Chronic	0.789	0.126	**6.3**	10
metosulam	R1	pond	Aquatic plant	Chronic	0.789	0.006	132	10
metosulam	R1	stream	Aquatic plant	Chronic	0.789	0.362	**2.2**	10
metosulam	R3	stream	Aquatic plant	Chronic	0.789	0.402	**2.0**	10
metosulam	R4	stream	Aquatic plant	Chronic	0.789	0.109	**7.2**	10

[1] TER that are below the trigger value are in bold

FOCUS Step 4

Maize, 0.03 kg a.s./ha with 10m buffer / vegetated filter strip (VFS) or 20m where indicated.

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
metosulam	D3	ditch	Aquatic plant	Chronic	0.789	0.027	29	10
metosulam	D4	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	D4	stream	Aquatic plant	Chronic	0.789	0.030	26	10

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
metosulam	D5	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	D5	stream	Aquatic plant	Chronic	0.789	0.030	26	10
metosulam	D6	ditch	Aquatic plant	Chronic	0.789	0.028	28	10
metosulam	R1	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	R1	stream	Aquatic plant	Chronic	0.789	0.131 20m0.067	**6.0** 11.8	10
metosulam	R2	stream	Aquatic plant	Chronic	0.789	0.073	11	10
metosulam	R3	stream	Aquatic plant	Chronic	0.789	0.034	23	10
metosulam	R4	stream	Aquatic plant	Chronic	0.789	0.352 **20m0.185**	**2.2** **4.3**	10

[1] TER that are below the trigger value are in bold

cereals, 0.02 kg a.s./ha with 10m buffer / vegetated filter strip (VFS) and 20m no spray zone at D1 and D2 or 20m joint buffer where indicated

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
metosulam	D1	ditch	Aquatic plant	Chronic	0.789	0.595	**1.3**	10
metosulam	D1	stream	Aquatic plant	Chronic	0.789	0.373	**2.1**	10
metosulam	D2	ditch	Aquatic plant	Chronic	0.789	0.329	**2.4**	10
metosulam	D2	stream	Aquatic plant	Chronic	0.789	0.207	**3.8**	10
metosulam	D3	ditch	Aquatic plant	Chronic	0.789	0.018	44	10
metosulam	D4	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	D4	stream	Aquatic plant	Chronic	0.789	0.020	40	10
metosulam	D5	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	D5	stream	Aquatic	Chronic	0.789	0.018	44	10

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (µg/L)	PECsw (µg/L)	TER [1]	Annex VI trigger
			plant					
metosulam	D6	ditch	Aquatic plant	Chronic	0.789	0.019	42	10
metosulam	R1	pond	Aquatic plant	Chronic	0.789	*safe use demonstrated at STEP 3*		10
metosulam	R1	stream	Aquatic plant	Chronic	0.789	0.159 20m0.082	**5.0** **9.6**	10
metosulam	R3	stream	Aquatic plant	Chronic	0.789	0.178 20m0.092	**4.4** **8.6**	10
metosulam	R4	stream	Aquatic plant	Chronic	0.789	0.050	16	10

[1] TER that are below the trigger value are in bold

Bioconcentration				
	Active substance	Metabolite1	Metabolite2	Metabolite3
$logP_{O/W}$	0.2 (pH 7)			
Bioconcentration factor (BCF)[1] ‡	Not required			
Annex VI Trigger for the bioconcentration factor				
Clearance time (days) (CT_{50})				
(CT_{90})				
Level and nature of residues (%) in organisms after the 14 day depuration phase				

[1] only required if log $P_{O/W}$ >3.

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	> 106 µg a.s./bee	> 100 µg a.s./bee
Metosulam SC 100	> 270 µg product/bee	No valid study
Metabolite	Not required	Not required
Field or semi-field tests: Not required		

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

Maize, 0.03 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
Metosulam	Contact	< 0.3	50
Metosulam	oral	< 0.29	50
Metosulam SC 100	Contact		50
Metosulam SC 100	oral	< 1.18	50

Cereals, 0.02 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
Metosulam	Contact	< 0.2	50
Metosulam	oral	< 0.19	50
Metosulam SC 100	Contact		50
Metosulam SC 100	oral	< 0.79	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri ‡	Metosulam SC 100	Mortality	> 40 g a.s./ha
Aphidius rhopalosiphi ‡	Metosulam SC 100	Mortality	> 40 g a.s./ha

Maize, 0.03 kg a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
Metosulam SC 100	*Typhlodromus pyri*	> 40 g a.s./ha	< 0.75	<< 2	2
Metosulam SC 100	*Aphidius rhopalosiphi*	> 40 g a.s./ha	< 0.75	<< 2	2

Cereals, 0.02 kg a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
Metosulam SC 100	*Typhlodromus pyri*	> 40 g a.s./ha	< 0.5	<< 2	2
Metosulam SC 100	*Aphidius rhopalosiphi*	> 40 g a.s./ha	< 0.5	<< 2	2

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect[1]	Trigger value
C carnea	larvae	Metosulam SC 100	40 g a.s./ha	mortality reproduction	- 16.7 - 251	50 %
A bilineata	adults	Metosulam SC 100	40 g a.s./ha	mortality reproduction	0 15	50 %
P cupreus	adults	Metosulam SC 100	40 g a.s./ha	mortality predation	0 - 4	50 %
Pardosa sp	adults	Metosulam SC 100	40 g a.s./ha	mortality reproduction	0 - 21	50 %

[1] positive percentage relate to adverse effects

Field or semi-field tests: Not required

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

Test organism	Test substance	Time scale	End point
Earthworms			
E. fetida	Metosulam ‡	Acute 14 days	LC_{50} > 1000 mg a.s./kg soil
E. fetida	Metosulam SC 100	Acute	LC_{50} > 100 mg a.s./kg soil
E. fetida	M02 (7-OH metosulam)	Acute	LC_{50} > 1000 mg/kg soil
E. fetida	M01 (ATSA)	Chronic	NOEC = 316 mg/kg soil
Other soil macro-organisms			
Collembola			
	Metosulam ‡	Chronic	No data
F. candida	Metosulam SC 100	28 days	NOEC = 1000 mg a.s./kg soil
F. candida	M01 (ATSA)	28 days	NOEC = 1000 mg/kg soil
F. candida	M02 (7-OH metosulam)	28 days	NOEC = 1000 mg/kg soil
Soil micro-organisms			
Nitrogen mineralisation	metosulam ‡	28 days	Deviation < 25% compared to control at 150 mg a.s./kg soil

Test organism	Test substance	Time scale	End point
	M01	28 days	Deviation < 25% compared to control at 0.16 mg/kg soil
	M02	28 days	Deviation < 25% compared to control at 0.19 mg/kg soil
Carbon mineralisation	metosulam ‡	28 days	Deviation < 25% compared to control at 150 mg a.s./kg soil
	Metabolite	28 days	No data
Field studies: Not required			

Toxicity/exposure ratios for soil organisms

Maize, 0.03 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
E. fetida	Metosulam ‡	Acute	0.04	> 25000	10
E. fetida	Metosulam SC 100	Acute	0.04	> 2500	10
E. fetida	M02 (7-OH metosulam)	Acute	0.0084	> 119047	10
E. fetida	M01 (ATSA)	Chronic	0.0100	31600	5
Other soil macro-organisms					
F. candida	Metosulam SC 100	Chronic	0.04	25000	5
F. candida	M01(ATSA)	Chronic	0.0100	100000	5
F. candida	M02 (7-OH metosulam)	Chronic	0.0084	119048	5

Cereals, 0.02 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
E. fetida	Metosulam ‡	Acute	0.02	> 50000	10
E. fetida	Metosulam SC 100	Acute	0.02	> 5000	10
E. fetida	M02 (7-OH metosulam)	Acute	0.0042	> 238095	10
E. fetida	M01 (ATSA)	Chronic	0.0049	64490	5
Other soil macro-organisms					
F. candida	Metosulam SC 100	Chronic	0.02	50000	5
F. candida	M01(ATSA)	Chronic	0.0049	204082	5

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
F. candida	M02(7-OH metosulam)	Chronic	0.0042	238095	5

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

Preliminary screening data

Not required for herbicides as ER_{50} tests should be provided

Laboratory dose response tests

Maize, 0.03 kg a.s./ha

Most sensitive species	Test substance	ER_{50} (g a.s./ha) vegetative vigour	ER_{50} (g a.s./ha) emergence	Exposure[1] (g a.s./ha)	TER	Trigger
Rape	Metosulam SC 100	-	4.89 g a.s./ha	0.831 (1 m, 30 g a.s./ha)	5.89	5
Tomato	Metosulam SC 100	1.46 g a.s./ha	-	0.831(1 m, 30 g a.s./ha)	**1.76**	5
Tomato	Metosulam SC 100	1.46 g a.s./ha	-	0.171 (5 m, 30 g a.s./ha)	8.59	5

[1]drift rates of 2.77 % at 1 m and 0.57 % at 5 m

Cereals, 0.02 kg a.s./ha

Most sensitive species	Test substance	ER_{50} (g a.s./ha) vegetative vigour	ER_{50} (g a.s./ha) emergence	Exposure[1] (g a.s./ha)	TER	Trigger
Rape	Metosulam SC 100	-	4.89 g a.s./ha	0.554 (1 m, 20 g a.s./ha)	8.9	5
Tomato	Metosulam SC 100	1.46 g a.s./ha	-	0.554 (1 m, 20 g a.s./ha)	**2.65**	5
Tomato	Metosulam SC 100	1.46 g a.s./ha	-	0.114 (5 m, 20 g a.s./ha)	13.3	5

[1]drift rates of 2.77 % at 1 m and 0.57 % at 5 m

Additional studies (e.g. semi-field or field studies)

No data

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

Test type/organism	end point
Activated sludge	EC_{50} > 1000 mg /L (test with metosulam technical, 3h)
Pseudomonas sp	Not required

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

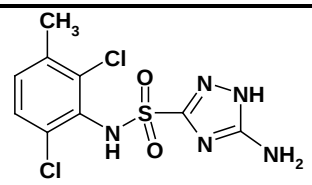
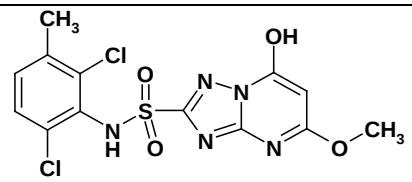
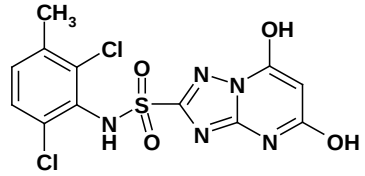
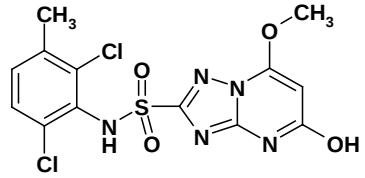
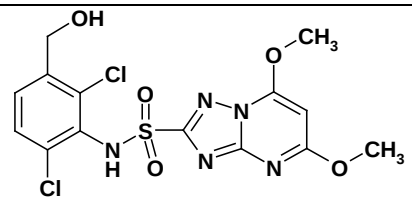
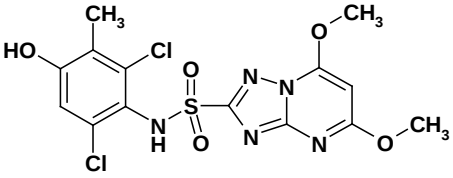
Compartment	
soil	Metosulam
water	Metosulam
sediment	None
groundwater	Metosulam

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

	RMS/peer review proposal
Active substance	N, R50/53

	RMS/peer review proposal
Preparation	N, R50/53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
ATSA (M01)	5-amino-N-(2,6-dichloro-3-methylphenyl)-1H-1,2,4-triazole-3-sulfonamide	
7-OH-metosulam (M02)	N-(2,6-dichloro-3-methylphenyl)-7-hydroxy-5-methoxy[1,2,4] triazolo[1,5-a]pyrimidine-2-sulfonamide	
5,7-OH-metosulam (M04)	N-(2,6-dichloro-3-methylphenyl)-5,7-dihydroxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide	
5-OH-metosulam (M03)	N-(2,6-dichloro-3-methylphenyl)-5-hydroxy-7-methoxy[1,2,4}triazolo[1,5-a]pyrimidine-2-sulfonamide	
3-OH-metosulam (M05)	N-[2,6-dichloro-3-(hydroxymethyl)phenyl]-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide	
4-OH-metosulam (M07)	N-(2,6-dichloro-4-hydroxy-3-methylphenyl)-5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide	

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	bioconcentration factor
BrDU	bromodeoxyuridine
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FOMC	first-order multi-compartment
g	gram

GAP	good agricultural practice
GC	gas chromatography
GC-ECD	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-DAD	high pressure liquid chromatography with diode array detector
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
HS	hockey stick
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M&K	Magnusson and Kligman test
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity

NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
POEM	Predictive Operator Exposure Model
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
Tmax	time to maximum plasma concentration
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
VFS	vegetated filter strip
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WG	water dispersible granule

WHO	World Health Organisation
wk	week
yr	year