European Food Safety Authority

EFSA Journal 2014;12(7):3742

CONCLUSION ON PESTICIDE PEER REVIEW

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

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State France, for the pesticide active substance amitrole are reported. The context of the peer review was that required by Commission Regulation (EU) No 1141/2010 as amended by Commission Implementing Regulation (EU) No 380/2013. The conclusions were reached on the basis of the evaluation of the representative uses of amitrole as a herbicide in orchards, grapes, olives and non-crop uses. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

© European Food Safety Authority, 2014

KEY WORDS

amitrole, peer review, risk assessment, pesticide, herbicide

[1] On request from the European Commission, Question No EFSA-Q-2013-00807, approved on 19 June 2014.

[2] Correspondence: pesticides.peerreview@efsa.europa.eu

Suggested citation: EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance amitrole. EFSA Journal 2014;12(7):3742, 84 pp. doi:10.2903/j.efsa.2014.3742

Available online: www.efsa.europa.eu/efsajournal

© European Food Safety Authority, 2014

SUMMARY

Commission Regulation (EU) No 1141/2010, as amended by Commission Implementing Regulation (EU) No 380/2013, (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the approval of a second group of active substances in Annex I to Council Directive 91/414/EEC and establishes the list of those substances. Amitrole is one of the active substances listed in the Regulation.
The RMS provided its initial evaluation of the dossier on amitrole in the Renewal Assessment Report (RAR), which was received by the EFSA on 2 April 2013. The peer review was initiated on 17 April 2013 by dispatching the RAR for consultation of the Member States and the applicant Nufarm SAS.

Following consideration of the comments received on the RAR, it was concluded that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology and EFSA should adopt a conclusion on whether amitrole can be expected to meet the conditions provided for in Article 4 of Regulation (EC) No 1107/2009 of the European Parliament and the Council.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of amitrole as a herbicide on orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts), grapes, olives and non-crop uses, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

In the area of identity, physical/chemical/technical properties and methods of analysis data gaps were identified for some physchem properties of the active substance, information on relevant impurities, validation of the plant method for dry commodities and a suitable method of analysis for air.

In the area of mammalian toxicology, two data gaps and four critical areas of concern were identified. The data gaps are related to the toxicological relevance of impurities in the technical specification, and to the toxicological assessment of the metabolite aminotriazolylalanine. The areas of concern are raised by exposure estimates exceeding the AOEL, by the classification as Repr. Cat. 1B proposed by the EFSA Peer Review, by the potential endocrine disruption of amitrole, and by the non representativeness of the batches used in toxicity studies with regard to the technical specification.

The consumer risk assessment for the representative uses on crops, according to the residue definition for risk assessment established by the peer review is not finalised, and data gaps were identified for storage stability data in crops with high water content and sufficient residue trials for the representative crop uses.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at EU level, with the notable exception that satisfactory information on anaerobic route and rate of degradation in soil is not available that may be important for some uses (e.g. pome fruit orchards in some territories). Exposure assessments were provided for uses on crops where one third of the ground surface area is treated and the total annual dose is applied at the same time and additionally in the case of olives only one of the possible two applications originally requested was assumed. It should be noted that for the crop uses assessed, it is normal practice that up to one half of the ground surface area is treated and that splitting the annual dose is indicated as appropriate practice. In addition satisfactory surface water and sediment exposure assessments for parent amitrole are not available for geoclimatic situations where drainage will be a route of exposure to surface water. Data gaps are identified for these missing assessments. For the representative non-crop uses an environmental exposure assessment is available that was designed to cover the climatic and civil engineering situation in the UK. It is uncertain how applicable the available non-crop use assessment might be to other territories. The available crop use assessments where one third of the ground surface area is treated and the total annual dose is applied at the same time indicate a high potential for groundwater exposure above the parametric drinking water limit of

0.1 µg/L for the relevant metabolite 1,2,4-triazole at all nine of the pertinent FOCUS groundwater scenarios.

In the area of ecotoxicology, a number of data gaps and two critical area of concern were identified as a high risk for soil non-target macro- and microorganisms could not be excluded for the soil metabolite 1,2,4-triazole and on the potential endocrine disruption of amitrole.

TABLE OF CONTENTS

Abstract 1
Summary 2
Table of contents 4
Background 5
The active substance and the formulated product 7
Conclusions of the evaluation 7
1. Identity, physical/chemical/technical properties and methods of analysis 7
2. Mammalian toxicity 7
3. Residues 9
4. Environmental fate and behaviour 10
5. Ecotoxicology 12
6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments 14
6.1. Soil 14
6.2. Ground water 15
6.3. Surface water and sediment 15
6.4. Air 15
7. List of studies to be generated, still ongoing or available but not peer reviewed 16
8. Particular conditions proposed to be taken into account to manage the risk(s) identified 17
9. Concerns 18
9.1. Issues that could not be finalised 18
9.2. Critical areas of concern 18
9.3. Overview of the concerns identified for each representative use considered 20
References 22
Appendices 25
Abbreviations 81

BACKGROUND

Commission Regulation (EU) No 1141/2010[3], as amended by Commission Implementing Regulation (EU) No 380/2013[4] (hereinafter referred to as 'the Regulation') lays down the detailed rules for the procedure of the renewal of the approval of a second group of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant for comments on the initial evaluation in the Renewal Assessment Report (RAR) provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 16 of the Regulation, if mandated, EFSA is required to adopt a conclusion on whether the active substance is expected to meet the conditions provided for in Article 4 of Regulation (EC) No 1107/2009 within 6 months from the receipt of the mandate, subject to an extension of up to 9 months where additional information is required to be submitted by the applicant in accordance with Article 16(3).

In accordance with Article 9 of the Regulation, France (hereinafter referred to as the 'RMS') received an application from Nufarm SAS for the renewal of approval of the active substance amitrole. Complying with Article 11 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the Commission and the EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on amitrole in the RAR, which was received by the EFSA on 2 April 2013 (France, 2013). The peer review was initiated on 17 April 2013 by dispatching the RAR to Member States and the applicant Nufarm SAS for consultation and comments. In addition, the EFSA conducted a public consultation on the RAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation 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.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 16(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, and the European Commission on 3 September 2013. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that additional information should be requested from the applicant and EFSA should organise an expert consultation in the areas of mammalian toxicology, residues, environmental fate and behaviour and ecotoxicology. According to Art. 16(2) of the Regulation COM decided to consult the EFSA. The mandate was received on 23 September 2013.

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 an expert consultation, and the additional information to be submitted by the applicant, 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 consultation where this took place, were reported in the final column of the Evaluation Table.

[3] Commission Regulation (EU) No 1141/2010 of 7 December 2010 laying down the procedure for the renewal of the inclusion of a second group of active substances in Annex I to Council Directive 91/414/EEC and establishing the list of those substances. OJ L 322,8.12.2011, p. 10-19.

[4] Commission Implementing Regulation (EU) No 380/2013 of 25 April 2013 amending Regulation (EU) No 1141/2010 as regards the submission of the supplementary complete dossier to the Authority, the other Member States and the Commission. OJ L 116, 26.4.2013, p.4

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 May – June 2014.

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 in orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts), grapes, olives and non-crop uses, 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, 2014) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the RAR,
- the Reporting Table (16 September 2013),
- the Evaluation Table (18 June 2014),
- the reports of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the RAR including its addendum (compiled version of February 2014 containing all individually submitted addenda (France, 2014)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Amitrole is the ISO common name for 1-*H*-1,2,4-triazol-3-amine (IUPAC).

The representative formulated product for the evaluation was 'CA2735' a soluble concentrate (SL) containing 229 g/l amitrole.

The representative use evaluated is a ground spray in orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts), grapes, olives and non-crop uses for the control of weeds. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 - rev. 4 (European Commission, 2000), SANCO/10597/2003 - rev. 10.1 (European Commission, 2012), and SANCO/825/00 - rev. 8.1 (European Commission, 2010).

The minimum purity of the active substance as manufactured is 910 g/kg. The active substance contains 3 relevant impurities N-(1*H*-[1,2,4]-triazol-3-yl)-formamide max 13 g/kg, 4*H*-[1,2,4]-triazole-3,4-diamine max 12 g/kg and methanoic acid max 7 g/kg, for the other impurities the issue is open (see section 2). As these impurities are relevant an additional data gap was identified for methods of analysis of those impurities in the formulation, spectra and to address their possible increase during storage.

The main data regarding the identity of amitrole and its physical and chemical properties are given in Appendix A.

It should be noted that the physchem data in the RAR are either unacceptable or insufficient detail was given and for this reason a data gap is identified for a full physchem data package for the active substance apart from spectra (new study submitted), melting point, surface tension, autoflammability, explosivity, physical state, solubility in water and solubility in organic solvents. Some new data were given in the RAR and some data were also available in doc. 6840/VI/97 rev. 9 (France, 2014).

HPLC-UV methods were available for the determination of the active substance and impurities in the technical material and for the active substance in the formulated product.

Amitrole can not be analysed by current multi-residue methods. Products of plant origin are analysed by LC-MS/MS however validation data are missing for dry matrices. Soil and water are analysed by LC-LC-MS/MS and air is analysed by LC-MS/MS however, the LOQ of the method for air is not low enough and a data gap was identified. A method of analysis for products of animal origin is not required as no MRLs are proposed. The active substance is classified as a Health Hazard under GHS. A method for urine is available but a method for tissues is missing and therefore a data gap has been identified.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003) and SANCO/10597/2003 – rev. 10.1 (European Commission, 2012).

Amitrole was discussed at the Pesticides Peer Review meeting 109 on mammalian toxicology.

In the technical specification, the impurities N-(1*H*-[1,2,4]-triazol-3-yl)-formamide, 4*H*-[1,2,4]-triazole-3,4-diamine and methanoic acid are considered toxicologically relevant based on their existing

classification and structural alerts for mutagenicity and sensitisation. For the impurities 3 to 8 and 10, an evaluation of their hazardous properties is missing and a data gap was identified.

The batches tested in the main toxicological database were not demonstrated to be representative of the proposed specification (except for a new Ames test, a new chromosome aberration test in human lymphocytes and a new study on maternal toxicity in a developmental rabbit study). This was identified as a critical area of concern.

With a high oral absorption value, amitrole is mainly excreted unchanged in the urine. Of low acute toxicity, the main target organ after repeated exposure is the thyroid. Effects on the thyroid were observed in all tested species (rats, dogs, mice and rabbits) and the relevant short-term NOAEL is 0.1 mg/kg bw per day from the 90-day rat study. Based on these thyroid effects, amitrole is classified as STOT-RE 2 H373[5]. Considering the available data, amitrole is neither expected to be genotoxic nor carcinogenic in humans. Thyroid tumours in rats are of little relevance to humans but the mode of action (inhibition of peroxidase and of iodine uptake, causing the decrease of circulating thyroid hormones) is considered relevant to humans. The relevant long-term NOAEL is 0.5 mg/kg bw per day based on the 2-year rat study. In the rat multigeneration study, no specific adverse effects were observed on the reproductive parameters, and the parental NOAEL is 0.12 mg/kg bw per day based on increased activity of the thyroid (based on morphological changes). In two developmental toxicity studies in rabbits available in the DAR for the first approval, malformations of the head and limbs were observed. In a recent study focussing on maternotoxicity in rabbits, in which only external examination of the foetuses was performed, malformations of the head were observed. Considering the developmental effects in rabbits in presence of a limited maternal toxicity, and the lack of mechanistic data supporting the non-relevance to humans, the EFSA Peer Review proposed amitrole should be classified[6] as Repr. Cat. 1B, H360 May damage the unborn child (instead of Repr. Cat. 2 H361d[5] as agreed previously by ECB in 2004). A critical area of concern was identified with regard to Annex II, Point 3.6.4 of Regulation (EC) No 1107/2009.

Amitrole is currently classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and toxic effects were observed in endocrine organs. A critical area of concern was identified with regard to Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 interim provisions for active substances that may be considered to have endocrine disrupting properties, however it should be noted that EFSA is proposing a different classification.

For the plant metabolite aminotriazolylalanine, no toxicological assessment is available and a data gap was identified. For the plant metabolite triazolylalanine and the groundwater metabolite 1,2,4-triazole, no toxicological data were provided in the dossier. It is noted that 1,2,4-triazole is classified as Repr.Cat.2 H361d[5] and has to be considered as a relevant groundwater metabolite. Reference values have already been derived for both metabolites triazolylalanine and 1,2,4-triazole (EFSA, 2011), common metabolites to different triazole active substances.

The acceptable operator exposure level (**AOEL**) and acceptable daily intake (**ADI**) are 0.001 mg/kg bw per day, based on thyroid effects in the 90-day rat studies supported by the multigeneration study with rats, and applying an uncertainty factor (UF) of 100. The acute reference dose (**ARfD**) is 0.015 mg/kg bw, based on the recent rabbit teratogenicity study (study on maternotoxicity) and applying an UF of 200 due to the uncertainty related to the limited investigations of the developmental effects in the study (only external examinations). The dermal absorption value for the representative amitrole formulation is 25% (for both the concentrate and the dilution).

[5] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 OJ L 353, 31.12.2008, p. 1-1355.

[6] It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

The exposure estimates for operators, bystanders and workers are all exceeding the AOEL (critical area of concern). For the **operators** exposed to amitrole during crop uses (vineyards, orchards, olives), the exposure estimates with the German model and UK POEM are all above the AOEL, even considering a treated surface reduced by a factor of 2 or 3 to take into account an application under the row. In a valid field study, the exposure estimates by biomonitoring show an exceedence of the AOEL for 10 % of the operators (trained professional operators using PPE). For the non-crop uses (roads and railways), the exposure estimates provided by the applicant were performed with a dermal absorption value lower than 25%, therefore even for this scenario the estimated exposure is expected to exceed the AOEL (even with the use of PPE).

For the **bystanders** exposed during crop uses with application under the row, even when considering a reduction of the treated surface by a factor of 3, the exposure estimate is exceeding the AOEL. For the residents, the exposure estimates provided by the applicant are reported in the final addendum (France, 2014). It is noted that the exposure estimates did not take into account the revised dermal absorption value, nor the exposure to spray drift during application (dermal and inhalation), or during entry into treated crops (dermal exposure) and considered a distance of 10m from treated crops. For the non-crop uses, exposure estimates provided by the applicant for bystanders and residents have not been revised with the agreed parameters (including a higher dermal absorption value) and are expected to exceed the AOEL.

For the **workers** exposed during crop uses, with an application under the row, the exposure estimate is largely exceeding the AOEL. For the non-crop uses, considering the estimates provided by the applicant and the use of a dermal absorption value lower than 25%, the exposure of workers is likely to be above the AOEL even with the use of gloves.

3. Residues

The assessment in the residue section is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004, 2007).

Amitrole was discussed at the Pesticides Peer Review meeting 112 on residues.

Primary crop metabolism was investigated in apples following spray application of ^{14}C-amitrole to the soil. In addition, metabolism was studied in model experiments with excised sprouts of apple trees and cell suspension cultures of apple fruits. In the study reflecting the representative use pattern, the parent amitrole was not detected in the mature fruits. More than 50% of the total radioactivity was incorporated into natural constituents. Metabolite triazolylalanine was the major component of the total residues in the mature apple fruit (22 to 24 % TRR) both under its free and conjugated forms. Aminotriazolylalanine was the major metabolite in the sprouts experiment and cell suspension culture experiment. Both metabolites triazolylalanine and aminotriazolylalanine belong to the class of triazole derivative metabolites (TDMs).

In the metabolism study and the representative residue trials in apples, parent amitrole itself was not detected in the fruits (<0.01 mg/kg). However, quantifiable residues of triazolylalanine (0.01 mg/kg) and aminotriazolylalanine (0.03 mg/kg) were recovered in apple fruit in field trials. Aminotriazolylalanine is considered a metabolite specific to amitrole.

It was therefore concluded that the residue definition for risk assessment for fruit crops should consist of two separate components, i.e. 1) parent amitrole (included by default) and 2) the TDMs. It is noted that the consideration of TDMs in the risk assessment is currently pending a decision on a common assessment approach for TDMs and triazole active substances. The residue definition for monitoring is proposed by default as parent amitrole.

A data gap was identified for sufficient residue trials complying with the current EC Guidance documents to support the representative uses, determining the residue levels of amitrole and the TDMs

(triazolylalanine and aminotriazolylalanine) according to the residue definition for risk assessment. In this context, the RMS was requested to reassess the available residue trials for compliance with the cGAP for the representative uses in orchard (last application at BBCH 79; for pome fruit, stone fruits, citrus, tree nuts) in the light of the residue definition for risk assessment including the TDMs, in order to identify the number of trials required to fulfil the current EU data requirements. According to the RMS, residue trial data are insufficient for citrus, stone fruits and tree nuts. It is noted by EFSA that for pome fruit only four trials determining residue levels of TDMs are available, and these residue data are not validated by sufficient storage stability data. Hence, a data gap was identified for sufficient storage stability data for TDMs in crops with high water content, such as pome fruit and stone fruit.

In addition, the toxicological profile of triazolylalanine and aminotriazolylalanine needs to be addressed in order to enable a consumer risk assessment. It is noted that triazolylalanine reference values have been set previously in the context of the assessment of another active substance (refer to section 2).

The investigation of the effect of industrial and/or household processing on the nature and the level of residues was not required according to current guidance. As a regular crop rotation is not applicable in orchards, the investigation of residues in rotational crops was not triggered for the representative uses according to current guidance.

As it concerns residues of amitrole alone, the estimated dietary burden for livestock does not trigger the requirement of data in food-producing animals as amitrole has never been detected in the crops. Therefore no further assessment was conducted and no studies investigating residues in food of animal origin were provided. However, the livestock dietary intake through fruit pomace has not been assessed for the residue definition for risk assessment including the TDMs, and a final estimate might be pending the submission of sufficient residue trial data in relevant fruit crops determining the levels of TDMs in those commodities.

With regard to residues of amitrole (<0.01 mg/kg) the consumer risk assessment was conducted by calculation of the TMDI and the IESTI with the EFSA PRIMo rev. 2. Consumer exposure from the representative uses did not exceed 14% of the ADI (German child) and 7% of the ARfD (apple, UK infant). As for the TDMs, no studies were provided to address the toxicological profile of the amitrole metabolites triazolylalanine and aminotriazolylalanine, however for triazolylalanine reference values have been set previously in the context of the assessment of another active substance (refer to section 2). Because of the lack of sufficient data regarding the TDMs the consumer risk assessment for the representative crop uses, according to the residue definition for risk assessment established by the peer review is not finalised.

4. Environmental fate and behaviour

Amitrole was discussed at the Pesticides Peer Review meeting 110 on environmental fate and behaviour.

In soil laboratory incubations under aerobic conditions in the dark, amitrole exhibited low to moderate persistence. Transformation products accounting for > 5% applied radioactivity (AR) were not formed. Mineralisation of the 3- ^{14}C radiolabel to carbon dioxide accounted for 44 % AR after 91 days. The formation of unextractable residues (not extracted by acidified ethanol / water followed by acidified methanol / acetone / water) for this radiolabel accounted for 41 % AR after 91 days. Reliable anaerobic soil incubations were not available, this is identified as a data gap for the representative uses in territories where these soil conditions occur. In a laboratory photolysis study the transformation product 1,2,4-triazole accounted for 9.9% AR. This metabolite exhibited moderate to high persistence in soil exhibiting a biphasic pattern of decline[7]. Amitrole exhibited high to medium mobility in soil. The photolysis transformation product 1,2,4-triazole exhibited very high to high soil mobility[7]. It was concluded that the adsorption of amitrole and 1,2,4-triazole was not pH dependent. In satisfactory field

[7] Agreed 1,2,4-triazole endpoints originating from the peer review of ipconazole, EFSA (2013) and UK (2013)

dissipation studies carried out at 2 sites in the USA and 1 in the UK amitrole exhibited low to moderate persistence. In European field dissipation studies at 4 sites where 1,2,4-triazole was dosed, this metabolite exhibited a biphasic pattern of decline having moderate to high persistence.[7]

In laboratory incubations in dark aerobic natural sediment water systems, amitrole exhibited medium persistence, forming no major (>10% AR) transformation products. The unextractable sediment fraction (not extracted by methanol) was the major sink for 3- 14C radiolabel, accounting for 26 – 40 % AR at study end (91 days). Mineralisation to carbon dioxide of this radiolabel accounted for 10 – 18 % AR at the end of the study. Amitrole was stable in a laboratory sterile aqueous photolysis experiment.

The surface water and sediment exposure assessments (Predicted environmental concentrations (PEC) calculations) were carried out for the identified soil photolysis metabolite 1,2,4-triazole, using the FOCUS (FOCUS, 2001) step 1 approach (version 1.1 of the Steps 1-2 in FOCUS calculator). For the active substance amitrole, step 3 (FOCUS, 2001) and step 4 calculations were available for the FOCUS runoff scenarios[8] for situations where a single application was made and one third of the surface area of orchards or vineyards were treated. This was considered by the RMS and experts from Member State competent authorities to represent a best case, as surveys of practice of non-selective herbicide use in orchards and vineyards in France indicated that between half and one third of the surface areas are usually treated. For drainage scenarios at step 3 and 4 the available simulations erroneously included crop interception being estimated by MACRO. For this herbicide application where downward application is made to weeds / the soil this is not appropriate. The step 4 calculations for the runoff scenarios appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray buffer zones up to 40 m for streams (94.8 % spray drift reduction) and 100 m for ponds (86% spray drift reduction) being combined with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80 % and erosion runoff by 95 %) being implemented. The SWAN tool (version 3.0.0) was appropriately used to implement these mitigation measures in the simulations. However, risk managers and others may wish to note 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. amitrole), 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. Data gaps are identified for surface water exposure assessments for FOCUS drainage scenarios and multiple (including split) application pattern GAPs as well as for situations where half the surface area of an orchard or vineyard are treated. For the representative use on impermeable surfaces (roads) and permeable surfaces (railways), PEC were calculated using the model HardSPEC 1.4.2 (Hollis et al, 2003). This model was developed for UK climatic conditions and reflects UK civil engineering specifications. Its applicability to other territories in the EU is not known.

Groundwater exposure assessments were carried out using FOCUS (FOCUS, 2009) scenarios and the model PELMO 4.4.3[8] for the active substance amitrole and its soil photolysis metabolite 1,2,4 triazole for the represented uses on crops. The simulations for 1,2,4-triazole followed FOCUS (FOCUS, 2006) kinetics guidance for implementing biphasic patterns of decline in FOCUS exposure modelling. This modelling assumed that one third of the surface area of orchards or vineyards were treated. Again this was considered by the RMS and experts from Member State competent authorities to represent a best case, for the same reasons already indicated above. The potential for groundwater exposure from these uses by amitrole 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 metabolite 1,2,4 triazole this modelling indicated that this relevant metabolite will exceed the parametric drinking water limit of 0.1 µg/L in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. The 80th percentile annual average recharge concentrations of 1,2,4-triazole leaving the top 1m soil layer in the available simulations were predicted to be 0.14 - 0.89 µg/L for the representative

[8] Simulations correctly utilised the agreed Q_{10} of 2.58 (following EFSA PPR Panel, 2007) and Walker equation coefficient of 0.7. Note the vapour pressure and water solubility used as input in simulations were assessed as not reliable by the peer review (see section 1).

uses assessed in cropping systems. Of course in situations when half the surface area of orchards or vineyards are treated the potential concentrations of 1,2,4-triazole in groundwater would be higher than 0.89 µg/L. A data gap is identified for groundwater exposure assessments for multiple application pattern GAPs as well as for situations where at least half the surface area of an orchard or vineyard are treated. In respect of just the parent amitrole it might be reasonably expected that when such an assessment is provided, concentrations would be indicated to be below 0.1 µg/L. For the representative use on permeable surfaces (railways), PEC were calculated using the model HardSPEC 1.4.2 (Hollis et al, 2003). This model was developed for UK geoclimatic conditions and reflects UK civil engineering specifications. Its applicability to other territories in the EU is not known. Using this UK model concentrations were calculated to be below the parametric drinking water limit of 0.1 µg/L for both amitrole and 1,2,4-triazole.

The available reliable PEC in soil, surface water, sediment, and groundwater covering a portion of the representative uses assessed can be found in Appendix A of this conclusion. Note data gaps are identified for some PEC as discussed above (see also section 7).

5. Ecotoxicology

The following documents were considered in the risk assessments: European Commission 2002a and 2002b; SETAC, 2001 and EFSA, 2009b.

Effects on endocrine organs have been observed in mammalian studies (see section 2). For the ecotoxicological assessments, a two generation bird and a two generation fish reproductive study, which are included in level 5 of the OECD Conceptual Framework (OECD, 2012), were available to address the **potential endocrine activity** of amitrole. The bird study indicated effects on the thyroid gland (enlarged gland size) throughout the generations in all tested concentrations. A NOEC value which includes also potential effects on thyroid glands of the birds could not be derived from this study. The relevance of the observed increase of thyroid size to bird populations was assessed in a position paper by the applicant. In these assessments a NOEC value was calculated by modelling. These assessments were discussed in an expert meeting (Pesticides Peer Review Meeting 111). The experts at the meeting agreed that a robust endpoint could not be derived from these assessments and thus no long-term risk assessments for birds could be conducted, which would include considerations of potential effects on thyroid glands. A data gap was identified to address the concern of effects of amitrole on the thyroid glands of birds. In the multi-generation fish study, there were also some indications for treatment related effects. However, due to some short comings of this study (low performance of the control, fungus infection of F2 generation) no firm conclusion could be reached. Additionally, a study on fish was available from the open literature (non-GLP). In this study fish were continuously exposed for 28 days to low concentrations of amitrole. Some alterations of thyroid hormones-related gene expressions in liver and brain of fish were noted. This study was considered only as supplementary information (the aim of the study was to investigate whether the activity of thyroid hormones-related genes can serve as biomarker to screen the effects on thyroid system in fish) and a data gap was identified to address the concern for potential endocrine mediated effects in fish (the applicant indicated that a new experimental two generation fish study is on-going). Moreover, no firm conclusion can be drawn from the available information as these studies alone are not sufficient to investigate all the relevant mechanisms and they may not be sufficient to detect all adverse effects which could be caused by an endocrine mechanism.

Risk assessments for birds and mammals and fish were available considering endpoints for mortality and for reproductive parameters from standard studies (i.e. not considering potential endocrine mediated effects).

On the basis of the available data, a low acute risk to **birds and mammals** was concluded for the representative uses on pome fruit, grapes and olives. However, the Tier 1 long-term risk assessments did not allow concluding a low risk for these representative uses. Therefore higher tier data were provided including the identification of the focal species in orchards and vineyards and the

determination of compound specific residue unit dose (RUD) values. These refinement steps were discussed in an expert meeting. The experts at the meeting agreed with the choice of the focal species and the related ecological parameters (PT and PD values) for pome fruit and grapes. However the use of the specific RUD values and the extrapolation of the ecological data to olives were not agreed. When the agreed parameters were considered in a refined risk assessment, a low risk could still not be concluded for the majority of the scenarios. Therefore data gaps for further refinements for these scenarios were identified for the representative uses in orchards, grapes and olives (see section 7).

It should be noted that in the risk assessments discussed above, only one third of the applied dose was considered (i.e. 1/3 of the application rate indicated in the GAP table), taking into account that the product is applied only under the rows (strip application). Therefore the risk assessments for birds and mammals as discussed above are valid only if one third of the dose is considered. Consequently, the scenario that birds and mammals feed only on the applied strips sprayed with the full application rate, was not addressed. Therefore a data gap was identified for appropriate risk assessments for birds and mammals, which considers the full application rate.

As regards to the non-crop uses (i.e. roads, railways), no specific risk assessments were available and a data gap was agreed for these uses by the experts at the meeting.

With regard to the **aquatic organisms**, the necessary data for a risk assessment were available. However, it was noted that the available chronic endpoint for fish (from a fish prolonged toxicity test over a 21-day exposure) does not necessarily cover all potential effects on development and reproduction (considering available information on potential endocrine activity of the active substance). The risk assessments using the available data and exposure estimations (FOCUS step 3 PECsw values) resulted in a low risk for aquatic organisms for the representative uses on pome fruit, grapes and olives. However, a data gap was identified for further exposure estimations in section 4. Consequently a data gap was identified for further risk assessments for aquatic organisms for those situations where no reliable PECsw estimations were available. The available risk assessments for the non-crop uses (i.e. roads, railways) resulted in a high risk for several scenarios for aquatic invertebrates, algae and aquatic macrophytes. Therefore a data gap was identified to further address to risk to aquatic organisms for the non-crop uses.

A low risk to aquatic organisms was concluded for the metabolite 1,2,4-triazole.

Based on the acute laboratory studies, a low risk to **bees** was concluded. A number of laboratory and extended laboratory studies were available for **non-target arthropods**. Based on these data, a low in-field risk to non-target arthropods could not be concluded. However, a low off-field risk was calculated considering a no-spray buffer zone of 75 metres. Therefore, a low risk to non-target arthropods considering the re-colonisation potential from no-spray areas was concluded for the representative uses of amitrole provided that a risk mitigation measure with equivalent efficiency to a no-spray buffer zone of 75 metres is applied. A field study focussing on predatory mite populations in a vineyard was also available, however due to some limitations in the study, a firm conclusion could not be drawn.

Based on the available laboratory data, a low risk to earthworms and to non-target macro- and microorganisms was concluded for amitrole. However, a high risk for soil non-target macro- and microorganisms could not be excluded for the soil metabolite 1,2,4-triazole. Therefore a data gap was identified for further assessments of **soil organisms** for the soil metabolite 1,2,4-triazole.

Based on the available data, a low risk to **non-target terrestrial plants** was concluded provided that a risk mitigation measure with equivalent efficiency to a no-spray buffer zone of 5 metres is applied.
A low risk was concluded for the organisms involved in **biological methods for sewage treatment** on the bases of the available data.

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

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
amitrole	Low to moderate persistence Single first-order DT_{50} 4.1-20.8 days (20ºC pF 2 or not reported soil moisture) Field dissipation studies single first-order DT_{50} 7.7-16.8 days	The risk to soil organisms was assessed as low.
1,2,4-triazole	Moderate to high persistence Biphasic decline DT_{50} 0.8-1.5 days (DT_{90} 20.6-248 days, 20ºC 40% maximum water holding capacity soil moisture) European field dissipation studies biphasic decline DT_{50} 6.8-28.1 days (DT_{90} 109-718 days)	Data gap. A high risk for soil non-target macro- and microorganisms could not be excluded.

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
amitrole	High to medium mobility K_{Foc} 20-202 mL/g	No	Yes	Yes	Data gaps were identified for further risk assessments for aquatic organisms.
1,2,4-triazole	Very high to high mobility K_{Foc} 43-120 mL/g	Yes for all crop uses assessed 0.14-0.89 µg/L	No	Yes, based on its classification as Repr.Cat.2 H361d	The risk to aquatic organisms was assessed as low.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Amitrole (water and sediment)	Data gap
1,2,4-triazole (water only)	The risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
amitrole	LC_{50} > 0.439 mg/L; NOEC 0.1 mg/L (28-day rat study)

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning information on potentially harmful effects).

- A full physchem package for the active substance apart from spectra (new study submitted) and melting point, surface tension, auto flammability, explosivity, physical state, solubility in water and solubility in organic solvents (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- For the relevant impurities method of analysis for the formulation, spectra and evidence that their content does not increase on storage (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- For the plant method validation data for dry matrices (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- Method of analysis for air (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- Method of analysis for tissues (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- Determination of the toxicological relevance of the impurities 3 to 8 and 10, taking into account their respective intrinsic hazardous properties (relevant for all representative uses evaluated; submission data proposed by the applicant: unknown; see section 2)

- Assessment of the toxicological properties of the plant metabolite aminotriazolylalanine (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2 and 3)

- Sufficient residue trials complying with the current EC Guidance documents and analysing for all compounds included in the residue definition for risk assessment (relevant for all representative crop uses evaluated; submission data proposed by the applicant: unknown; see section 3)

- Storage stability data in crops with high water content for the TDM analytes in the residue trials in accordance with the residue definition for risk assessment (relevant for the representative uses in pome fruit and stone fruit; submission data proposed by the applicant: unknown; see section 3)

- Anaerobic soil route and rate of degradation study (relevant for representative uses where anaerobic soil conditions cannot be excluded, this might apply to at least pome fruit in some territories; submission date proposed by the applicant: unknown; see section 4)

- A document summarising the main assumptions and process descriptions in the HardSPEC 1.4.2 model, currently only complete unabridged reports were provided (relevant for the representative uses evaluated on the non-crop uses for impermeable (roads) and permeable (railways) surfaces; submission date proposed by the applicant: unknown; see section 4)

- Groundwater exposure modelling for amitrole and 1,2,4-triazole covering the requested multiple applications per year (either split or 2 applications for olives) and situations for single and multiple applications per year where more than one third of the surface area might be treated were not available. It is normal practice to treat up to half of the surface area. (relevant for the

representative uses evaluated on orchards (citrus, pome, stone and other fruits, tree nuts, olives and grapes); submission date proposed by the applicant: unknown; see section 4)

- Surface water and sediment exposure assessments for parent amitrole covering the requested multiple applications per year (either split or 2 applications for olives) and situations for single and multiple applications per year where more than one third of the surface area might be treated were not available. It is normal practice to treat up to half of the surface area. (relevant for the representative uses evaluated on orchards (citrus, pome, stone and other fruits, tree nuts, olives and grapes); submission date proposed by the applicant: unknown; see section 4)

- Surface water and sediment exposure assessments for parent amitrole were not available to cover geoclimatic situations where the drainage route of exposure is predominant (relevant for the representative uses evaluated on orchards (citrus, pome, stone and other fruits, tree nuts, olives and grapes); submission date proposed by the applicant: unknown; see section 4)

- To address the concern of effects of amitrole on the thyroid glands of birds (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

- To address the concerns for potential endocrine mediated effects in fish (relevant for all representative uses evaluated; submission date proposed by the applicant: a two generation fish study is on-going; see section 5)

- Further refinements for omnivorous, insectivorous and granivorous birds and omnivorous, insectivorous and herbivorous mammals for grapes; insectivorous and granivorous birds and omnivorous, insectivorous and herbivorous mammals for orchards; granivorous birds and omnivorous, insectivorous and herbivorous mammals for olives (relevant for the representative uses in grapes, orchards and olives; submission date proposed by the applicant: unknown; see section 5)

- Appropriate risk assessments for birds and mammals, which considers the full application rate (relevant for the representative uses in grapes, orchards and olives; submission date proposed by the applicant: unknown; see section 5)

- Appropriate risk assessments for birds and mammals for the non-crop uses (relevant for the representative uses evaluated on the non-crop uses for impermeable (roads) and permeable (railways) surfaces; submission date proposed by the applicant: unknown; see section 5)

- Appropriate risk assessments for aquatic organisms for situations where no reliable PECsw estimations were available (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

- To address the risk for the non-crop uses for aquatic invertebrates, algae and aquatic macrophytes (relevant for the representative uses evaluated on the non-crop uses for impermeable (roads) and permeable (railways) surfaces; submission date proposed by the applicant: unknown; see section 5)

- To address the risk to soil organisms from the soil metabolite 1,2,4-triazole (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

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

- A low risk to non-target arthropods could only be concluded if a risk mitigation measure with equivalent efficiency to a no-spray buffer zone of 75 metres is considered (see section 5).

- A low risk to non-target terrestrial plants was concluded provided that a risk mitigation measure with equivalent efficiency to a no-spray buffer zone of 5 metres is applied (see section 5).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[9] and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

An issue is also listed as an issue that could not be finalised where the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

1. The consumer risk assessment for the representative uses on crops, according to the residue definition for risk assessment established by the peer review is not finalised.

2. The available reliable parent amitrole aquatic exposure assessment for the crop uses did not cover geoclimatic situations where drainage would be a route of exposure to surface water and in addition did not cover situations where more than one third of the ground surface area might be treated or for olives where two applications might be made. Consequently the aquatic risk assessment for parent amitrole could not be finalised for the crop uses.

3. The risk assessments for birds and mammals could not be finalised for all representative uses (both crop and non-crop uses).

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[9], and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

4. In accordance with the provisions of Regulation (EC) No 1272/2008, amitrole has been classified as Repr. Cat.2 H361d in 2004. However, the peer review proposed a classification as Repr. Cat.1B H360 for amitrole. According to this proposal a critical area of concern was identified with regard to Annex II, Point 3.6.4 of Regulation (EC) No 1107/2009.

5. Amitrole is classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and toxic effects were observed in endocrine organs. A critical

[9] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127-175.

area of concern was identified with regard to Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 interim provisions for active substances that may be considered to have endocrine disrupting properties, however, when assessing this concern, it should be noted that EFSA is proposing a different classification regarding toxicity to reproduction. The relevant mammalian NOAEL is based on thyroid effects. Endocrine disrupting properties can also be inferred from the observation of adverse effects on thyroid in birds.

6. For all representative uses (crop and non-crop uses), the exposure estimates for operators, workers and bystanders are expected to exceed the AOEL even with the use of PPE.

7. Insufficient information was available to compare whether the technical material specification proposed was comparable to the material used in the testing that was used to derive the toxicological reference values (except for a new Ames test, a new chromosome aberration test in human lymphocytes and a new study on maternal toxicity in a developmental rabbit study).

8. For all representative uses for which the risk assessment was finalised, a concern has been identified. For the crop uses a high potential for groundwater exposure by the relevant metabolite 1,2,4-triazole above the parametric drinking water limit of 0.1 µg/L was indicated. For the non-crop uses a risk was identified for aquatic organisms, consequent to their exposure to parent amitrole.

9. For all representative uses, a high risk for soil non-target macro- and microorganisms could not be excluded for the soil metabolite 1,2,4-triazole.

9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

All columns are grey as the technical material specification proposed was not comparable to the material used in the testing that was used to derive the toxicological reference values.

Representative use		Orchards (pome, citrus, stone & other fruits and tree nuts)	Grapes (table and wine)	Olives	Non-crop uses (impermeable (roads) and permeable surfaces (railways))
Operator risk	Risk identified	X[6]	X[6]	X[6]	X[6]
	Assessment not finalised				
Worker risk	Risk identified	X[6]	X[6]	X[6]	X[6]
	Assessment not finalised				
Bystander risk	Risk identified	X[6]	X[6]	X[6]	X[6]
	Assessment not finalised				
Consumer risk	Risk identified				
	Assessment not finalised	X[1]	X[1]	X[1]	
Risk to wild non target terrestrial vertebrates	Risk identified				
	Assessment not finalised	X[3]	X[3]	X[3]	X[3]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	X[9]	X[9]	X[9]	X[9]
	Assessment not finalised				
Risk to aquatic organisms	Risk identified				X
	Assessment not finalised	X[2]	X[2]	X[2]	
Groundwater exposure active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure metabolites	Legal parametric value breached	X	X	X	
	Parametric value of 10µg/L[(a)] breached				

	Assessment not finalised				
Comments/Remarks					

The superscript numbers in this table relate to the numbered points indicated in sections 9.1 and 9.2. Where there is no superscript number see sections 2 to 6 for further information.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003.

REFERENCES

EFSA(European Food Safety Authority),2009a. Scientific Opinion on Risk Assessment for a Selected Group of Pesticides from the Triazole Group to Test Possible Methodologies to Assess Cumulative Effects from Exposure through Food from these Pesticides on Human Health. EFSA Journal 2009;7(9);1167 187 pp. doi:10.2903/j.efsa.2009.1167.

EFSA (European Food Safety Authority), 2009b. Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. doi:10.2903/j.efsa.2009.1438

EFSA (European Food Safety Authority), 2011. Conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole. EFSA Journal 2011;9(1):1967. 71 pp. doi:10.2903/j.efsa.2011.1967

EFSA (European Food Safety Authority), 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2012;10(6):2763. 35 pp. doi:10.2903/j.efsa. 2012.2763

EFSA (European Food Safety Authority), 2013. Conclusion on the peer review of the pesticide risk assessment of the active substance ipconazole. EFSA Journal 2013;11(4):3181, 76 pp. doi:10.2903/j.efsa.2013.3181

EFSA (European Food Safety Authority), 2014. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance amitrole. Available at www.efsa.europa.eu

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2007. Opinion 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. EFSA Journal (2007) 622, 32pp. doi:10.2903/j.efsa.2008.622.

EPA (U.S. Environmental Protection Agency), 2006. 1,2,4-Triazole, triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds. Washington, DC. Available at www.epa.gov/opprd001/factsheets/tetraHHRA.pdf

European Commission, 1999. Guidelines for the generation of data concerning residues as provided in Annex II part A, section 6 and Annex III, part A, section 8 of Directive 91/414/EEC concerning the placing of plant protection products on the market, 1607/VI/97 rev.2, 10 June 1999.

European Commission, 2000. Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414. SANCO/3030/99 rev.4, 11 July 2000.

European Commission, 2001. Review report for the active substance amitrole. Finalised in the Standing Committee on Plant Health at its meeting on 12 December 2000 in view of the inclusion of amitrole in Annex I of Directive 91/414/EEC. SANCO/6839/VI/97-final, pp. 1-27.

European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002 rev.2 final, 17 October 2002.

European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001 rev 4 (final), 17 October 2002.

European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 - final, 25 February 2003.

European Commission, 2010. Guidance document on residue analytical methods. SANCO/825/00 rev. 8.1, 16 November 2010.

European Commission, 2012. Guidance Document on the Assessment of the Equivalence of Technical Materials of Substances Regulated under Council Directive 91/414/EEC. SANCO/10597/2003 – rev. 10.1, 13 July 2012.

FOCUS (Forum for the co-ordination of pesticide fate models and their use), 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., as updated by the Generic Guidance for FOCUS surface water scenarios, version 1.1 dated March 2012

FOCUS (Forum for the co-ordination of pesticide fate models and their use), 2006. Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp.

FOCUS (Forum for the co-ordination of pesticide fate models and their use), 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.

FOCUS (Forum for the co-ordination of pesticide fate models and their use), 2009. Assessing Potential for Movement of Active Substances and their Metabolites to Ground Water in the EU. Report of the FOCUS Workgroup, EC Document Reference SANCO/13144/2010-version.1. 604 pp, as outlined in Generic Guidance for Tier 1 FOCUS groundwater Assessment, version 2.0 dated January 2011.

France, 2013. Renewal Assessment Report (RAR) on the active substance amitrole prepared by the rapporteur Member State France in the framework of Commission Regulation (EU) No 1141/2010, April 2013. Available at www.efsa.europa.eu

France, 2014. Final Addendum to the Renewal Assessment Report on amitrole, compiled by EFSA, February 2014. Available at www.efsa.europa.eu

Hollis, J.M., Ramwell, C.T. and Holman, I.P. (2003). HardSPEC: A First-tier Model for Estimating Surface- and Ground-Water Exposure resulting from Herbicides applied to Hard Surfaces. NSRI research report No. SR3766E for DEFRA PL0531, 79 pp + 3 Appendices. Available at www.pesticides.gov.uk

JMPR (Joint Meeting on Pesticide Residues), 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 20–29 September 2004, Report 2004, 383 pp.

JMPR (Joint Meeting on Pesticide Residues), 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 18–27 September 2007, Report 2007, 164 pp.

JMPR (Joint Meeting on Pesticide Residues), 2008 - Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 9–18 September 2008 – Triazole fungicide metabolites p355-364.

OECD (Organisation for Economic Co-operation and Development), 2012. Guidance document on standardised test guidelines for evaluating chemicals for endocrine disruption, No. 150 ENV/JM/MONO(2012)22, 24 August 2012

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance Document on Regulatory Testing and Risk Assessment procedures for Plant Protection Products with Non-Target Arthropods. ESCORT 2.

United Kingdom, 2013. Final Addendum to Draft Assessment Report on ipconazole, compiled by EFSA, March 2013. Available at www.efsa.europa.eu.

APPENDICES

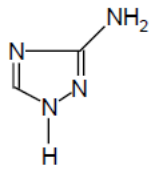
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Rapporteur Member State	France
Co-rapporteur Member State	Hungary

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	1-*H*-1,2,4-triazol-3-~~yl~~amine
Chemical name (CA)	1-*H*-1,2,4-triazol-3-amine
CIPAC No	90
CAS No	61-82-5
EC No (EINECS or ELINCS)	200-521-5
FAO Specification (including year of publication)	FAO Specifications 90/TC/S/P (1998)
Minimum purity of the active substance as manufactured	910 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	N-(1*H*-[1,2,4]-triazol-3-yl)-formamide max 13 g/kg, 4*H*-[1,2,4]-triazole-3,4-diamine max 12 g/kg and methanoic acid max 7 g/kg. Open for other impurities.
Molecular formula	$C_2H_4N_4$
Molecular mass	84.08 g/mol
Structural formula	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity)	155°C (99.7%)
Boiling point (state purity)	Open
Temperature of decomposition (state purity)	Open
Appearance (state purity)	Colourless crystals
Vapour pressure (state temperature, state purity)	Open
Henry's law constant	Open
Solubility in water (state temperature, state purity and pH)	A GLP study was performed on the pure a.s. (2 batches of 99.7 % and 98.6 %) ; solubility at 20°C : >1384 g/L at pH 4.0 (amitrole chlorhydr.) 264 g/L at pH 7.0 261 g/L at pH 10.0
Solubility in organic solvents (state temperature, state purity)	acetone: 2.9 – 3.3 g/L 1,2-dichloroethane: < 0.1 g/L ethyl acetate: 1 g/L n-heptane: << 0.1 g/L p-xylene: << 0.1 g/L methanol: 133-160 g/L (91.7%, 20°C)
Surface tension (state concentration and temperature, state purity)	– 73.3 mN/m (1g/L aqueous solution, 99.7%)
Partition co-efficient (state temperature, pH and purity)	Open
Dissociation constant (state purity)	Open
UV/VIS absorption (max.) incl. ε (state purity, pH)	UV_{max} 198 nm ; ε 4947 $L.mol^{-1}.cm^{-1}$
Flammability (state purity)	Open
Explosive properties (state purity)	Expert statement
Oxidising properties (state purity)	Open

Summary of representative uses evaluated (amitrole)

Crop and/or situation (a)	Member State	Product Name	F G 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 a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./hl min max (g/hl)	Water l/ha min max	Kg a.i./ha min max (*) (g/ha)		
Orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Application. after BBCH 94 (fruit senescence) till BBCH 75 (fruit above half final size or 50% fruits formed)	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	35	CA2735 is applied either once per year at 2977 g as/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 g as/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Grapes (table and wine)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	92-79	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	42	CA2735 is applied either once per year at 2977 g as/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 g as/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Olives	South EU MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Spring and autumn	1-2 (or several splitted applications)	2-3 months	0.18-0.5	300 to 500	0.9-1.375	35	CA2735 is applied either once or twice per year at 1375 g as/ha (ie 6 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 2750~~1375~~ ~~3000~~ g as/ha/year. A split application technique is possible at lower rates

															especially in case of mixture with foliar or residual herbicide according to the crop.
Non crop uses (impermeable and permeable surfaces: road, railways)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Not applicable	1 (or several splitted applications)	2-3 months	0.36-1	300 to 500	1.8-3	-	CA2735 is applied either once per year at 2977 g as/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 g as/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.

(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 (215 nm)
Impurities in technical as (analytical technique)	HPLC/UV (215 nm) and ion chromatography
Plant protection product (analytical technique)	HPLC/UV (215 nm) Open for relevant impurities.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Amitrole
Food of animal origin	Not relevant
Soil	Amitrole
Water surface	Amitrole
drinking/ground	Amitrole
Air	Amitrole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS LOQ = 0.01 mg/kg (grape, olive, apple) method required for dry commodities
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant
Soil (analytical technique and LOQ)	LC-LC-MS/MS LOQ = 0.01 mg/kg
Water (analytical technique and LOQ)	LC-LC-MS/MS LOQ = 0.05 µg/L (surface and drinking water)
Air (analytical technique and LOQ)	Open
Body fluids and tissues (analytical technique and LOQ)	LC-MS/MS LOQ = 5 µg/L (urine) Open for tissues

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

	RMS/peer review proposal
Active substance	-

Impact on Human and Animal Health

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

Rate and extent of oral absorption	Rapidly and almost completely absorbed
Distribution	Rapidly distributed to all tissues; highest level in liver
Potential for accumulation	No potential for accumulation
Rate and extent of excretion	Eliminated within 2 days; mainly in urine (70-95% within 24h)
Metabolism in animals	Limited metabolism (eg through glutathione-S-transferase). Minor metabolites including mercapturic acid derivatives and 1,2,4-triazole derivatives.
Toxicologically relevant compounds (animals and plants)	Amitrole
Toxicologically relevant compounds (environment)	Amitrole and 1,2,4-triazole

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	>5000 mg/kg bw	
Rat LD_{50} dermal	>2500 mg/kg bw	
Rat LC_{50} inhalation	>0.439 mg/L (highest attainable concentration, 4h exposure)	
Skin irritation	Not irritant	
Eye irritation	Slightly irritant	
Skin sensitisation	Not sensitiser (M & K)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Thyroid (rat, dog, monkey)	STOT-RE 2 H373
Relevant oral NOAEL	0.1 mg/kg bw per day (90-d rat) 0.3 mg/kg bw per day (1-y dog)	
Relevant dermal NOAEL	100 mg/kg bw per day (28-d rat)	
Relevant inhalation NOAEL	0.1 mg/L (NOEC) (28-d rat)	

Genotoxicity (Annex IIA, point 5.4)

No evidence of a genotoxic potential relevant to humans	

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

Target/critical effect	Thyroid effects (increased weight, dilated follicles, benign and malignant tumours), pituitary gland (hemorrhages and hyperaemia, benign tumours) (rat, mouse) Decreased body weight (hamster)	STOT-RE 2 H373
Relevant NOAEL	0.5 mg/kg bw per day (2-y rat) 1.5 mg/kg bw per day (18-mo mouse) 1 mg/kg bw per day (18-mo hamster)	
Carcinogenicity	Thyroid tumours (in rats, not relevant for humans)	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	Parental, offspring: thyroid, liver Reproductive parameters: lower mating and fertility indexes	STOT-RE 2 H373
Relevant parental NOAEL	0.12 mg/kg bw per day (2-generation rat)	
Relevant reproductive NOAEL	0.9 mg/kg bw per day (2-generation rat)	
Relevant offspring NOAEL	0.9 mg/kg bw per day (2-generation rat)	

Developmental toxicity

Developmental target / critical effect	Maternal: thyroid effects (rat, rabbit), liver (rabbit) Developmental: thyroid (rat, rabbit), malformations of the head and limbs (rabbit), visceral and skeletal variants (rabbit)	STOT-RE 2 H373, Repr 2 H361d Peer review proposal: Repr 1B H360
Relevant maternal NOAEL	3 mg/kg bw per day (rabbit maternotoxicity study) 100 mg/kg bw per day (rat)	
Relevant developmental NOAEL	3 mg/kg bw per day (rabbit maternotoxicity study) 100 mg/kg bw per day (rat)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	Not available – not required	
Repeated neurotoxicity	Not available – not required	
Delayed neurotoxicity	Not available – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	Amitrole acts via inhibition of peroxidase and of iodine uptake causing the decrease of circulating thyroid hormones.
Studies performed on metabolites or impurities	Not available

Medical data (Annex IIA, point 5.9)

The applicant reported two worker accidents in manufacturing plant. No major effects reported.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI	0.001 mg/kg bw per day	90-d rat studies, supported by rat multigeneration	100
AOEL	0.001 mg/kg bw per day	90-d rat studies, supported by rat multigeneration	100
ARfD	0.015 mg/kg bw	Rabbit maternotoxicity	200*

* increased UF due to the uncertainties related to the limited investigations of the developmental effects in the study

Dermal absorption (Annex IIIA, point 7.3)

Formulation (CA2735, 229 g/L SL)	Undiluted: 25% Spray dilutions: 25% *In vitro* study on human skin (with similar formulation)

Exposure scenarios (Annex IIIA, point 7.2)

Operators	Use on orchards, grapes, olives: estimated exposures (% AOEL)		
	Model	Without PPE	With PPE
	German	94550	3704*
	UK POEM	330228	35533**
	Field study	-	10 % of operators' exposures exceeded the AOEL
	For the non-crop uses (roads and railways), the exposure is expected to exceed the AOEL even with the use of PPE		
Workers	Orchards, grapes, olives: estimated exposure is 6206% of AOEL with use of long-sleeved shirt and trousers Non crop uses: the exposure is likely to be above the AOEL (even with the use of gloves)		

Bystanders	Orchards, grapes, olives: estimated exposure is 183% of AOEL Non crop uses: the exposure is expected to exceed the AOEL

* Personal Protective Equipment (PPE): gloves and coverall during mixing/loading (M/L) and application (A)
** PPE: gloves during M/L and A

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

Substance classified	Amitrole
Harmonised classification according to Regulation (EC) No 1272/2008 (CLP Regulation):	Repr.2, H361d Suspected of damaging the unborn child STOT RE 2, H373 May cause damage to organs through prolonged or repeated exposure
Peer review proposal*	STOT RE 2, H373 Repr. 1B (H360)

* It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

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

Plant groups covered	Apple, representative of fruits only
Rotational crops	Not relevant, applied on perennial crops
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable
Processed commodities	Not triggered
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Amitrole
Plant residue definition for risk assessment	Amitrole and TDMs, to be considered separately pending a decision on a common assessment approach for TDMs. Monitoring of TDMs is pending on a risk management decision
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	Not relevant for amitrole Assessment pending for TDMs, not finalised
Time needed to reach a plateau concentration in milk and eggs	Not applicable
Animal residue definition for monitoring	Not relevant for amitrole Assessment pending for TDMs, not finalised
Animal residue definition for risk assessment	Not relevant for amitrole Assessment pending for TDMs, not finalised
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	-
Fat soluble residue: (yes/no)	No

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

Not relevant

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

Crop	Characteristics of the crop group	Acceptable Maximum Storage duration
Apple	Crop with high water content	16 months for amitrole Data gap for TDMs
Grape	Crop with acid content	8 months for amitrole 6.5 months for triazolylalanine 6.5 months for aminotriazolylalanine

Olive	Crop with high lipid content	6.5 months for amitrole 6.5 months for triazolylalanine 6.5 months for aminotriazolylalanine
Animal Products		
Not relevant for amitrole Assessment pending for TDMs, not finalised		

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) Potential for accumulation (yes/no) Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Not relevant for amitrole Assessment pending for TDMs, not finalised		
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle Liver Kidney Fat Milk Eggs	Not relevant for amitrole Assessment pending for TDMs, not finalised		

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	EU zone	Trial results relevant to the representative usees			Recommendation / comments	MRL estimated from trials according to the representative use in mg/kg	HR	STMR
		Source	Residue definition for monitoring : **Amitrole**	Residue definition for risk assessment : **Amitrole and TDMs, to be considered separately pending a decision on a common assessment approach for TDMs**				
			Residue levels (mg/kg)					
Pome fruits	North	Overall trials	1-3 x 0.5-15 kg as/ha (BBCH 59-87), PHI 0-235days(d) Apple T: <0.01 x 8 ; <0.02 x 8 ; < 0.05 x 8 ; <0.1 x 7 Pear T: <0.02 x 4	1 x 3-3.3 kg as/ha (BBCH 81), PHI 0-35days(d) Apple T : <0.01 (0, 14, 21, 28) ; 2 x <0.01 (35d) Apple TA: <0.01 (0, 14, 21, 28) ; 2 x <0.01 (35d) Apple ATA: <0.01 (0, 14, 21, 28) ; 2 x <0.01 (35d)	Residue of TDMs observed => not a strict no residue situation with risk assessment definition Storage stability study not yet available for TDMs in matrix with high water content			
	South		1-4 x 3.3-19.2 kg as/ha (BBCH 74-87), PHI 0-111days(d) Apple T: <0.01 x 6 Pear T: <0.01	1 x 3.3-3.5 kg as/ha (BBCH 74-81), PHI 0-35days(d) Apple T : <0.01 (0, 14, 21, 28) ; 2 x <0.01 (35d) Apple TA: 2 x <0.01 (35d), 0.01 (0, 7,14, 21d) Apple ATA: <0.01 (0, 7, 14d); 2 x < 0.01 (35d); 0.03 (21d)				
	North	**Overall supporting data with GAP**	**1-2 x 1.2-3 kg as/ha (BBCH 94-75), PHI 35 days(d)** Apple T: <0.01 x 5 Pear T: <0.02	Apple T : <0.01 x 2 Apple TA : <0.01 x 2 Apple ATA : <0.01 x 2		0.01* F/I : in force EU MRL 0.01 Reg. (EC) No 149/2008 (pome fruit)	T : 0.01 TA : 0.01 ATA : 0.01	T : 0.01 TA : 0.01 ATA : 0.01
	South		Apple T : <0.01 x 2	Apple T : <0.01 x 2 Apple TA: <0.01 x 2 Apple ATA: <0.01 x 2				

Crop	EU zone	Trial results relevant to the representative usees			Recommendation / comments	MRL estimated from trials according to the representative use in mg/kg	HR	STMR
		Source	Residue definition for monitoring : **Amitrole**	Residue definition for risk assessment : **Amitrole and TDMs, to be considered separately pending a decision on a common assessment approach for TDMs**				
			Residue levels (mg/kg)					
Stone fruits	**North**	Overall trials	-	-	-			
	South		Peach : 1 x 6 kg as/ha (BBCH 75), PHI 37-105days(d) Peach T : <0.01 x 4	-				
	South	**Overall supporting data for GAP**	**1-2 x 1.2-3 kg as/ha (BBCH 94-75), PHI 35 days(d)** Peach T : <0.01 x 2 (1 x 6kg, 37 & 42 day PHI)	None available		0.01* /I : in force EU MRL 0.01 Reg. (EC) No 149/2008 (stone fruit)	T : 0.01 TA : n.a ATA : n.a	T : 0.01 TA : n.a ATA : n.a
Citrus fruits	-	Overall trials	-	-	-			
		Overall supporting data for GAP	**1-2 x 1.2-3 kg as/ha (BBCH 94-75), PHI 35 days(d)** None available	None available		-	-	-
Tree nuts	-	Overall trials	-	-	-			
		Overall supporting data for GAP	**1-2 x 1.2-3 kg as/ha (BBCH 94-75), PHI 35 days(d)** None available	None available		-	-	-
Grape	North	Overall trials	1-2 x 3-8 kg as/ha (BBCH 69-79), PHI 28-211 days(d)	1 x 3-3.3 kg as/ha (BBCH 71-79), PHI 91-100 days(d)	-			

Crop	EU zone	Trial results relevant to the representative usees			Recommendation / comments	MRL estimated from trials according to the representative use in mg/kg	HR	STMR
		Source	Residue definition for monitoring : **Amitrole**	Residue definition for risk assessment : **Amitrole and TDMs, to be considered separately pending a decision on a common assessment approach for TDMs**				
			Residue levels (mg/kg)					
			T : <0.01 x 10; <0.02 x 11; <0.025	T: <0.01 x 2 TA: <0.01 x 2 ATA: <0.01 x2				
	South		1 x 2.9-4.8 kg as/ha (BBCH 0-83), PHI 15-203 days(d) T : <0.01 x 7; <0.02 x 4; <0.025 x 8	1 x 2.9-3.3 kg as/ha (BBCH 55-75), PHI 87-115 days(d) T: <0.01 x 2 TA: <0.01 x 2 ATA: <0.01 x2				
	North	Overall supporting data for GAP	**1-2 x 1.2-3 kg as/ha (BBCH 92-79), PHI 42 days(d)**		No residue data available for TDMs according to GAP	0.01* F/I : in force EU MRL **0.01** Reg. (EC) No 149/2008 (grapes)	T : 0.01 TA : n.a ATA : n.a	T : 0.01 TA : n.a ATA : n.a
			T : <0.01 x 5; <0.02 x 5	-				
	South		T : <0.01 x 5; <0.025 x 4	-				
Olive	South	Overall trials	1 x 1.9-2.1 kg as/ha (BBCH 75-89), PHI 6-35 days(d)	1 x 1.9-2.1 kg as/ha (BBCH 75-89), PHI 6-35 days(d)	-			

Crop	EU zone	Trial results relevant to the representative usees			Recommendation / comments	MRL estimated from trials according to the representative use in mg/kg	HR	STMR
		Source	Residue definition for monitoring : **Amitrole**	Residue definition for risk assessment : **Amitrole and TDMs, to be considered separately pending a decision on a common assessment approach for TDMs**				
			Residue levels (mg/kg)					
			T:<0.01 x 5	T:<0.01 x 5 TA: <0.01 x 5 (with all PHI) ATA: <0.01 x5 (with all PHI)				
		Overall supporting data for GAP	**1-2 x 1.2-3 kg as/ha (BBCH 94-75), PHI 35 days(d)**		No residue data available for TDMs according to GAP with BBCH 94-75	0.01* F/I : in force EU MRL **0.05** Reg. (EC) No 149/2008 (olives)	T : 0.01 TA : n.a ATA : n.a	T : 0.01 TA : n.a ATA : n.a
			T:<0.01 x 5	None available				

T : aminotriazole

TA : triazolylalanine

ATA : aminotriazolylalanine

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

ADI	0.001 mg/kg bw per day based on thyroid effects observed in the 90-day rat studies using a safety factor of 100 (Review Report 6839/VI/97 (European Commission, 2001)) and is comforted with multigeneration study on rat. (Pesticides Peer Review meeting 109) Concerning TDMs, According to Pesticides Peer Review meeting 112, information from EPA (2006), JMPR (2008) and EFSA (2009a) concerning triazoles cannot be used solely and according to Pesticides Peer Review meeting 109 concerning amitrole, no studies were provided by the applicant to address and derive toxicological references values for TDMs. In addition a decision on a common assessment approach for TDMs is currently not available at EU level. Consequently the toxicological relevance and resulting risk assessment with triazolylalanine and aminotriazolylalanine is not addressed.
TMDI (% ADI) according to WHO European diet	14% (pome fruits, grapes and olives) Note: Not included are the representative uses in citrus and tree nuts (no data)
NEDI (% ADI)	-
Factors included in IEDI and NEDI	-
ARfD	0.015 mg/kg bw based on rabbit maternotoxicity study, SF = 200b (EFSA Pesticides Peer Review meeting 109
IESTI (%ARfD)	7% (Apple) Note: Not included are the representative uses in citrus and tree nuts (no data) Concerning TDMs, see the previously comment about chronic assessment
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)
		Transfer factor	Yield factor	
Not relevant				

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

Pome fruits	0.01* mg/kg (currently 0.01 mg/kg under Reg. (EC) No 149/2008)

Stone fruits	0.01* mg/kg (currently 0.01 mg/kg under Reg. (EC) No 149/2008)
Grapes	0.01* mg/kg (currently 0.01 mg/kg under Reg. (EC) No 149/2008)
Olives (table and oil production)	0.01* mg/kg (currently 0.05 mg/kg under Reg. (EC) No 149/2008)

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

See EFSA reasoned opinion about the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of the Regulation (EC) No 396/2005 (EFSA, 2012).

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

Mineralization after 100 days ‡	44 % after 91 d, [3-^{14}C]-label (n= 1)
Non-extractable residues after 100 days ‡	41 % after 91 d, [3-^{14}C]-label (n= 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	None

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

Anaerobic degradation ‡

Mineralization after 100 days	Data gap
Non-extractable residues after 100 days	Data gap
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Data gap

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Conditions: Xenon lamp (300-800 nm, 500 W/m^2, 12h photoperiod) Amitrole: 66.4% AR after 30 days in irradiated samples, 88.7% AR in dark controls Metabolite 1,2,4-triazole: 9.9 % at *30* d (n= *1*) (minor non transient)

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	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Sand		6.2	22°C / 75% pF2	23.8/79.1	20.8	6.7	SFO
Standard 2.1		6.5	22°C / nr	3.4/11.2	4.1	17.6	SFO
Standard 2.2		6.1	22°C / nr	3.6/11.9	4.3	11.3	SFO
Standard 2.3		5.5	22°C / nr	6.8/22.5	8.2	4.3	SFO
Sand		6.2	7°C / 75% pF2	87.2/289.7	-	4.8	SFO
Geometric mean/median					7.4		

nr: not reported

Laboratory studies

1,2,4-triazole (applied as parent)	Aerobic conditions						
Soil type	X	pH	t. °C / % MWHC	DT_{50} fast phase/DT_{50} slow phase(d)/g	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.4	20 °C / 40 %	0.9/59.2/ 0.683			DFOP
Loamy sand		5.8	20 °C / 40 %	1.5/247.6/0.5 80			DFOP
Silt loam		6.7	20 °C / 40 %	0.8/20.6/ 0.443			DFOP
Geometric mean/median				1.0/67.1/ 0.569			DFOP

Field studies ‡

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. (χ^2)	DT_{50} (d) Norm.	Method of calculation
Loam (cropped)	Oregon (USA)		5.8	90	16.1	53.4	16.5	-	SFO
Loam (cropped)	Washington (USA)		6.8	90	7.7	25.4	26.0	-	SFO
Loam (bare)	Huntington (UK)		7.6	40	16.8	55.8	5.3	-	SFO
Geometric mean/median								-	

Field studies

1,2,4-triazole (applied as parent)	Aerobic conditions, kinetics calculated for **ambient conditions**. Bare soil with grass sown immediately after application (with exception of Spain site where no grass sown).							
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. (χ^2)	Method of calculation
Silt loam	Germany		6.4	0-30	7.8 α 0.4454	366.7 β 2.0966	15.2	FOMC
Silty clay loam	Italy		7.6	0-40	21.2 k1 0.3500	207.4 k2 0.0086 g 0.4000	10.7	DFOP
Sandy loam	UK		7.4	0-40	6.8 k1 0.4863	109.3 k2 0.0154 g 0.4633	17.8	DFOP
Loam	Spain		5.8	0-30	28.1 k1 0.0632	717.6 k2 0.0020 g 0.5732	13.3	DFOP
Geometric mean/median								

1,2,4-triazole (applied as parent)	Aerobic conditions, kinetics calculated timestep **normalised to 20ºC and pF2 moisture**. Bare soil with grass sown immediately after application (with exception of Spain site where no grass sown).								
Soil type	Location		pH	Depth (cm)	DT_{50} (d) Fast phase	DT_{50} (d) Slow phase	'g'	St. (χ2)	Method of calculation
Silt loam	Germany		6.4	0-30	2.5	70.7	0.655	18.8	DFOP
Silty clay loam	Italy		7.6	0-40	1.4	59.8	0.364	10.6	DFOP
Sandy loam	UK		7.4	0-40	0.5	25.1	0.458	18.1	DFOP
Loam	Spain		5.8	0-30	4.6	126.0	0.489	12.7	DFOP
Geometric mean ('g' value is arithmetic mean)					1.68	60.5	0.489		DFOP

pH dependence (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration	No accumulation expected for amitrole. A plateau concentration is calculated for 1,2,4-triazole (see PECsoil)

Laboratory studies

Parent	Anaerobic conditions Data gap

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
Sandy loam	1.74	6.1 (un)			3.52	202	0.65
Silt loam	3.42	6.8 (un)			3.79	111	0.77
Silty clay loam	2.9	7.0 (un)			1.57	54	0.86
Silty clay	0.64	7.4 ($CaCl_2$)			0.714	112	0.77
Sandy loam	0.75	6.8 ($CaCl_2$)			0.223	30	0.85
Sand	0.75	5.6 ($CaCl_2$)			0.152	20	0.87
Silt	1.8	5.3 ($CaCl_2$)			0.921	51	0.86
Clay	1.64	7.2 ($CaCl_2$)			1.9	114	0.81
Arithmetic mean						87	0.80
pH dependence, Yes or No			No				

(un): matrix of pH measurement unknown

Metabolite 1,2,4-triazole							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Silty clay	0.70	8.8			0.83	120	0.897
Clay loam	1.74	6.9			0.75	43	0.827
Silty clay loam	0.70	7.0			0.72	104	0.922
Sandy loam	0.81	6.9			0.72	89	1.016
Arithmetic mean/median					0.76	89	0.92
pH dependence (yes or no)			No				

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

Column leaching	Eluation (mm): 200 mm Time period (d): 2 d
	Leachate: 24-31 % AR in leachate, mainly Amitrole in standard soil 2.1 (6.8% silt + clay, 0.6% OC, pH6) 0.8 % AR in leachate in agricultural soil (32.4% silt + clay, 2.9% OC, pH5.5)
Aged residues leaching	No reliable data (ageing time too long), not required.
Lysimeter/ field leaching studies	No reliable data (LOD too high – 10 µg/L), not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Amitrole Method of calculation	DT_{50} (d): 28.6 days (the longest laboratory DT_{50} of 23.8 days measured at 22°C is normalized to 20°C using a Q_{10} of 2.58, resulting in a DT50 value of 28.6 days at 20°C) Kinetics: SFO Field or Lab: representative worst case from laboratory studies (at 20°C).
Application data	Crop: orchards, grapes, olives, non crop uses Depth of soil layer: 5cm Soil bulk density: 1.5g/cm^3 % plant interception: No interception Number of applications: 1 Interval (d): - Application rate(s): 2977 g as/ha

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		3.969		-	
Short term	24h	3.874	3.922	-	-
	2d	3.782	3.875	-	-
	4d	3.603	3.783	-	-
Long term	7d	3.350	3.651	-	-
	21 d	2.386	3.111		
	28d	2.014	2.882	-	-
	50d	1.182	2.301	-	-
	100d	0.352	1.493	-	-
Plateau concentration		No accumulation expected			

Metabolite 1,2,4-triazole Method of calculation	Molecular weight relative to the parent: 69.1/84.08 DT_{50} (d): 28.1 days Kinetics: DFOP (parameters: k_1 = 0.0632 day^{-1}, k_2 = 0.002 day^{-1}, g =0,573) Field or Lab: representative worst case from field studies.
Application data	Application rate assumed: 242 g as/ha (assumed 1,2,4-triazole is formed at a maximum of 9.9 % of the applied dose and molecular ratio of 69.1/84.08)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.323		-	
Short term	24h	0.311	0.317	-	-
	2d	0.300	0.311	-	-
	4d	0.280	0.301	-	-
Long term	7d	0.255	0.286	-	-
	21 d	0.181	0.237		
	28d	0.162	0.221	-	-
	50d	0.133	0.187	-	-
	100d	0.113	0.154	-	-
Plateau concentration		0.451 mg/kg after 8 yrs (in 5 cm)			

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

Hydrolytic degradation of the active substance and metabolites > 10 %	Stable at pH 5, 7, 9 and 25°C. Stable at pH 4, 7, 9 and 90°C.
Photolytic degradation of active substance and metabolites above 10 %	Stable at pH 5, 7, 9 and 25°C
Quantum yield of direct phototransformation in water at Σ > 290 nm	No light absorption above 290 nm.
Readily biodegradable (yes/no)	No

Degradation in water / sediment

Parent	Distribution (eg max in water 86.8-87.4 % after 0 d. Max. sed 5.9-14.0 % after 0-7 d)									
Water / sediment system	pH water phase	pH sed ($CaCl_2$)	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	$DissT_{50}$-$DissT_{90}$ water	St. (χ^2)	$DissT_{50}$-$DissT_{90}$ sed	St. (χ^2)	Method of calculation
Pond	8.6	6.9	20	88.7-294.5	3.0	87.6-291.1	3.1	116.8-388.2	1.6	SFO
Ditch	8.3	7.4	20	83.6-277.6	5.3	67.6-224.5	9.7	124.8-414.6	5.7	SFO
Geometric mean/median				86.1-285.9		77.0-255.6		120.7-401.2		

Metabolites	No major metabolite in water / sediment compartments

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Pond	8.6	6.9	18.7 % after 91 d	26.4 % after 91 d	26.4 % after 91 d
Ditch	8.3	7.4	10.3 % after 91 d	40.1 % after 91 d	40.1 % after 91 d

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

For agricultural uses

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: 1.1 Molecular weight (g/mol): 84.08 Water solubility (mg/L): 264 000 K_{OC}/K_{OM} (L/kg): 94 (mean) DT_{50} soil (d): 7.4 days (normalised geomean from lab) DT_{50} water/sediment system (d): 86.1 (geomean) DT_{50} water (d): 86.1 (geomean from total system) DT_{50} sediment (d): 86.1 (geomean from total system) Crop interception (%): No interception
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: SWASH 3.1, TOXSWA 3.3.1, MACRO 5.5.3 and PRZM 3.1.1 Vapour pressure: 3.3 10^{-5} (20°C) Kom/Koc: 111 (median)[10] 1/n: 0.81 (median)[7] DT_{50} water (d): 86.1 (geomean from total system) DT_{50} sediment (d): 1000 (conservative value) Plant uptake: 0.5
Application rate	Crop: Pome fruits, Vines, Citrus, Olives Crop interception: no interception (CAM 1 for R

[10] The correct agreed values to be used for further simulations are Kfoc = 87 mL/g with 1/n = 0.80 (mean values).

scenarios)

Number of applications: 1

Interval (d): -

Application rate(s): Amitrole is intended to be used as a banded application (1/3 of the surface area): 2977 g as/ha for drift entries, 992 g/ha for run-off/drainage entries for orchards, vines and citrus; 1375 g as/ha for drift entries, 458 g as/ha for run-off/drainage entries for olives

Drift was corrected for groundspray application

Application window:

For orchards (late) in autumn, olives and citrus in autumn: 01/10 - 31/10

For vines (early) and citrus in spring: 01/03-31/03

For orchards (early) in spring:

D3	01/04-01/05
D4	06/04-06/05
D5	18/03-17/04
R1	01/04-01/05
R2	01/03-31/03
R3	18/03-17/04
R4	01/03-31/03

No PECsw for Step 1-2 were provided. However since Step 3-4 are needed for Amitrole, no additional calculations in Step 1-2 are required.

Step 3 and 4 calculations are presented below. Only values for R scenarios were validated (crop interception of the fruit crops was considered in D scenarios), whereas for this herbicide use no canopy interception is appropriate, values for D scenarios are therefore not reported.

FOCUS Step 3

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	Orchards, spring		Orchards, autumn	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.651	1.618	0.651	1.763
R1	Stream	0 h	12.390	1.218	12.490	1.441
R2	Stream	0 h	15.760	0.576	16.220	0.753
R3	Stream	0 h	17.130	1.609	17.600	2.840
R4	Stream	0 h	12.390	1.224	11.210	0.330

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	Vines		Olives	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.651	1.715	-	-
R1	Stream	0 h	12.470	1.409	-	-
R2	Stream	0 h	15.710	0.561	-	-
R3	Stream	0 h	17.060	1.491	-	-
R4	Stream	0 h	12.360	1.167	5.216	0.293

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	Citrus, spring		Citrus, autumn	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R4	Stream	0 h	12.360	1.156	11.270	0.346

Step 4, orchards spring

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	20 m no spray buffer zone + 20 m vegetative filter strip		30 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.270	0.722	0.206	0.563
R1	Stream	0 h	1.247	0.133	0.845	0.091
R2	Stream	0 h	1.652	0.092	1.120	0.063
R3	Stream	0 h	1.755	0.414	1.190	0.404
R4	Stream	0 h	1.247	0.134	0.845	0.092

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	35 m no spray buffer zone + 20 m vegetative filter strip		40 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.184	0.509	0.167	0.465
R1	Stream	0 h	0.729	0.079	0.640	0.070
R2	Stream	0 h	0.965	0.055	0.848	0.048
R3	Stream	0 h	1.026	0.401	0.943	0.399
R4	Stream	0 h	0.729	0.080	0.641	0.070

Step 4, orchards autumn

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	20 m no spray buffer zone + 20 m vegetative filter strip		30 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.270	0.789	0.206	0.615
R1	Stream	0 h	1.256	0.160	0.852	0.110
R2	Stream	0 h	1.668	0.441	1.131	0.435
R3	Stream	0 h	2.122	0.690	2.122	0.671
R4	Stream	0 h	1.128	0.096	0.765	0.094

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	40 m no spray buffer zone + 20 m vegetative filter strip		100 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.167	0.507	0.080	0.257
R1	Stream	0 h	0.645	0.084		
R2	Stream	0 h	1.048	0.432		
R3	Stream	0 h	2.122	0.660		
R4	Stream	0 h	0.580	0.093		

Step 4, vines

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	20 m no spray buffer zone + 20 m vegetative filter strip		30 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.270	0.767	0.206	0.598
R1	Stream	0 h	1.255	0.156	0.851	0.107
R2	Stream	0 h	1.650	0.113	1.119	0.109
R3	Stream	0 h	1.753	0.252	1.188	0.174
R4	Stream	0 h	1.244	0.128	0.844	0.088

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	35 m no spray buffer zone + 20 m vegetative filter strip		40 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R1	Pond	0 h	0.184	0.540	0.167	0.494
R1	Stream	0 h	0.734	0.093	0.645	0.082

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	35 m no spray buffer zone + 20 m vegetative filter strip		40 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R2	Stream	0 h	0.964	0.107	0.848	0.106
R3	Stream	0 h	1.024	0.151	0.900	0.134
R4	Stream	0 h	0.727	0.076	0.639	0.067

Step 4, olives

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	10 m no spray buffer zone + 10 m vegetative filter strip		14 m no spray buffer zone + 10 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R4	Stream	0 h	1.010	0.132	0.737	0.131

Step 4, citrus spring

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	20 m no spray buffer zone + 20 m vegetative filter strip		25 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R4	Stream	0 h	1.244	0.127	1.005	0.103

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	30 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual
R4	Stream	0 h	0.843	0.087

Step 4, citrus autumn

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	20 m no spray buffer zone + 20 m vegetative filter strip		25 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual	Actual	Actual
R4	Stream	0 h	1.134	0.116	0.916	0.115

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	30 m no spray buffer zone + 20 m vegetative filter strip	
			PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual
R4	Stream	0 h	0.769	0.114

Metabolite 1,2,4-triazole Parameters used in FOCUSsw step 1 and 2	Molecular weight: 69.1 Water solubility (mg/L): 730 000 Soil or water metabolite: Soil Koc/Kom (L/kg): 89 DT_{50} soil (d): 60.5 (Step 1 only) DT_{50} water/sediment system (d): 1000 (conservative value) DT_{50} water (d): not needed (Step 1 only) DT_{50} sediment (d): not needed (Step 1 only) Crop interception (%): No interception
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	Crop: pome/stone fruits (early & late), citrus, vines (early), olives Number of applications: 1 Interval (d): - Application rate(s): 121 g as/ha (2977 g/ha corrected by ½ for banded application, by maximum occurrence in soil of 9.9% and by molecular ratio of 69.1/84.08) Application window: not needed (Step 1 only)
Main routes of entry	Run-off / drainage (option no drift selected)

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	36.09		32.12	

For non crop uses, impermeable (road) /permeable (railway) surfaces

Method of calculation	Model(s) used: HardSPEC 1.4.2 Crop: non crop uses, impermeable surfaces (roads), permeable surfaces (railways)
	Parent: Water solubility : 264 g/L (20°C) Specific gravity: 1.138 Soil DT_{50lab} 7.4 d (geomean) K_{OC}: median 111 mL/g DT_{50} water (d): 86.2 (geomean from total system) DT_{50} sediment (d): 86.2 (geomean from total system)
	Metabolite 1,2,4-triazole: simulated with a pseudo-application Water solubility : 730 g/L (20°C) Specific gravity: 1.138 (same as parent) Geometric mean $DT_{50field}$ 60.5 d (geomean from DFOP slow phase) K_{OC}: mean 89 mL/g DT_{50} water (d): 1000 (conservative value) DT_{50} sediment (d): 1000 (conservative value)
Application rate	Application rate for parent: 2977 g/ha Application rate for metabolite (pseudo-application): 242 g/ha (2977 g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08) No. of applications: 1

Amitrole

	Acute (24 hrs) concentration		
	Water phase (µg / L)	Sediment phase (µg / kg)	Application day PECsw from spray drift (mg l^{-1})
Urban stream	453.782	503.335	27.309
Urban pond	42.733	47.350	0.172
Major road stream	233.210	258.863	19.399
Domestic stream	76.356	84.755	0.000
Railway ditch leaching	7.821	0.877	7.821
Railway ditch runoff	7.821	3.616	7.821

1,2,4-triazole

	Acute (24 hrs) concentration	
	Water phase (µg / L)	Sediment phase (µg / kg)
Urban stream	37.615	33.454
Urban pond	3.589	3.202
Major road stream	19.570	17.417
Domestic stream	8.922	7.940
Railway ditch leaching	0.636	0.128
Railway ditch runoff	0.636	0.454

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

For agricultural uses

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PELMO 4.4.3 Scenarios (list of names): all relevant scenarios Crop: apples, vines, citrus
	Parent: Vapour pressure: 3.3 10^{-5} Pa (20°C), 1.32 10^{-4} Pa (30°C) Water solubility : 264 g/L (20°C), 528 g/L (30°C) Geometric mean DT_{50lab} 7.4 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). K_{OC}: median 111[11] mL/g, $^1/_n$= 0.81[8]. Plant uptake: 0.5
	Metabolite 1,2,4-triazole: simulated with a pseudo-application Vapour pressure: 10^{-10} Pa (20°C), 4 10^{-10} Pa (30°C) (conservative values) Water solubility : 730 g/L (20°C), 1460 g/L (30°C) Geometric mean $DT_{50field}$ DFOP kinetics 1.68 d for fast phase, 60.5 d for slow phase, g= 0.489 (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). K_{OC}: mean 89 mL/g, $^1/_n$= 0.92. Plant uptake: 0
Application rate	Application rate for parent: 992 g/ha (2977 g/ha corrected by 1/3 for banded application). Application rate for metabolite (pseudo-application): 80.7 g/ha (992g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08)[12]

[11] The correct agreed values to be used for further simulations are Kfoc = 87 mL/g with 1/n = 0.80 (mean values). It was not considered necessary to perform again the simulations with the correct values considering the high safety margins.
[12] Recommendations of the FOCUS kinetic guidance document were followed to implement the DFOP kinetic of metabolite 1,2,4-triazole. 2 simulations were conducted: the first for the fast-phase, with an application rate corrected by g, the 2nd for the slow phase, with an application

No. of applications: 1 Time of application (month or season): 15 March and 15 October

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

PELMO 4.4.3 / Apples	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
	Chateaudun	<0.001	0.622	<0.001	0.624
	Hamburg	<0.001	0.503	<0.001	0.813
	Jokioinen	<0.001	0.255	<0.001	0.375
	Kremsmunster	<0.001	0.444	<0.001	0.549
	Okehampton	<0.001	0.606	<0.001	0.889
	Piacenza	<0.001	0.522	<0.001	0.699
	Porto	<0.001	0.301	<0.001	0.633
	Sevilla	<0.001	0.361	<0.001	0.335
	Thiva	<0.001	0.358	<0.001	0.530

PELMO 4.4.3 / Vines	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
	Chateaudun	<0.001	0.463	<0.001	0.517
	Hamburg	<0.001	0.429	<0.001	0.671
	Kremsmunster	<0.001	0.391	<0.001	0.474
	Piacenza	<0.001	0.419	<0.001	0.619
	Porto	<0.001	0.262	<0.001	0.614
	Sevilla	<0.001	0.169	<0.001	0.168
	Thiva	<0.001	0.184	<0.001	0.403

rate corrected by (1-g). The concentrations were then summed to get the final concentrations. Since 1/n of 1,2,4-triazole differs from 1, the application rate was doubled, and the final concentrations were divided by 2.

	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
PELMO 4.4.3 / Citrus	Piacenza	<0.001	0.355	<0.001	0.608
	Porto	<0.001	0.222	<0.001	0.555
	Sevilla	<0.001	0.142	<0.001	0.324
	Thiva	<0.001	0.172	<0.001	0.547

For non-crop uses, permeable surfaces

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using HardSPEC. Model(s) used: HardSPEC 1.4.2 Crop: non crop, railway
	Parent: Water solubility : 264 g/L (20°C) Specific gravity: 1.138 Soil DT_{50lab} 23 d (median)[13] K_{OC}: median 114 mL/g[14]
	Metabolite 1,2,4-triazole: simulated with a pseudo-application Water solubility : 730 g/L (20°C) Specific gravity: 1.138 (same as parent) Geometric mean $DT_{50field}$ 60.5 d (geomean from DFOP slow phase) K_{OC}: mean 89 mL/g
Application rate	Application rate for parent: 2977 g/ha Application rate for metabolite (pseudo-application): 242 g/ha (2977 g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08) No. of applications: 1

Amitrole - Railway over Groundwater			
Average annual concentration at the base of the railway formation (mg / L)			0.64
Exposure at the abstraction well-head	Chalk	Limestone	Sandstone
Maximum concentration in well (µg / L)	0.0835	0.0038	0.0042
Period when plume > 0.1 ug / L in well (days)	0.0	0.0	0.0

[13] It is noted that the correct value to be used is 7.4 days. However, calculations performed are conservative and so were not performed again.
[14] It is noted that the correct value to be used is 111 mL/g.

1,2,4-triazole - Railway over Groundwater			
Average annual concentration at the base of the railway formation (mg / L)			0.08
Exposure at the abstraction well-head	Chalk	Limestone	Sandstone
Maximum concentration in well (µg / L)	0.0657	0.0263	0.0257
Period when plume > 0.1 ug / L in well (days)	0.0	0.0	0.0

Groundwater exposure is not considered as likely to occur from impermeable surface non crop uses in the HardSPEC framework

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

Direct photolysis in air	No data, not required.
Quantum yield of direct phototransformation	No data, not required.
Photochemical oxidative degradation in air	DT_{50} of 4.8 hours derived by the Atkinson model. OH (24 h) concentration assumed = $5x10^5$ cm^{-3}
Volatilisation	from plant surfaces (BBA guideline): 11 % after 24 hours
	from soil surfaces (BBA guideline): negligible after 24 hours

PEC (air)

Method of calculation	Expert judgement, (though validated reliable vapour pressure and water solubility measurements are not available) and information on volatilisation from plants and soil.

PEC(a)

Maximum concentration	Negligible from soil, 11% volatilisation of amitrole measured from plant surfaces in the first 24 hours.

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: Amitrole, 1,2,4-triazole Surface Water: Amitrole, 1,2,4-triazole Sediment: Amitrole Ground water: Amitrole, 1,2,4-triazole Air: Amitrole

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)	Provided data are difficult to interpret. No conclusion can be delivered.
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

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)
Bird				
Bobwhite quail	a.s.	Acute	LD_{50} > 2150 mg/kg bw	-
Mallard duck	a.s.	Short-term (5d)	LC_{50} > 829 mg a.s./kg bw	> 5000 ppm a.s.
Mallard duck	a.s.	Long-term_1 generation (22 weeks)*	NOEC = 12.1 mg a.s./kg bw per day	NOEC = 100 ppm a.s.
Mallard duck	a.s.	Long-term_2 generations (15 months)	NOEC reproductive = 16 mg a.s./kg bw per day At all necropsy intervals, impacts upon thyroid size were noted at all concentrations. Overall LOEC = 16 mg a.s./kg bw per day Overall NOEC: none	NOEC reproductive = 95 ppm a.s. At all necropsy intervals, impacts upon thyroid size were noted at all concentrations. Overall LOEC = 95 ppm a.s. Overall NOEC: none
Mammals				
rat	a.s.	Acute	LC_{50} = 5000 mg a.s./kg bw	-
rat	a.s.	Long-term_2 generations	NOAEL = 0.9 mg a.s/kg bw per day	-
Additional higher tier studies				
-				

* Toxicity data not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties of the active substance

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

Long term DDD and TER for birds were calculated by the applicant based on the one-generation NOEL of 12.1 mg/kg b.w./day but as no overall NOEC could be established from the two-generation bird study, long term risk assessment for birds couldn't be finalized.

Vineyard: 1 × 0.993 kg Amitrole/ha (1/3 of the full dose rate due to the application made under the row)

Indicator species	Time scale	DDD	TER	Trigger
BIRDS				
Screening step				
Small omnivorous bird	Acute	94.63	22.7	10
	Long-term (overall NOEC)	-	-	5
	Long-term (reproductive NOEC)	20.47	**0.6**	
Tier 1 (Birds)				
Small insectivorous species: "Redstart"	Long-term (reproductive NOEC)	6.05	**2.0**	5
Small granivorous bird "Finch"		3.63	**3.3**	
Small omnivorous bird "lark"		3.42	**3.5**	
Higher tier refinement (Birds)_based on focal species and corresponding refined PD and PT values				
Medium Omnivorous Bird (Cirl bunting)	Long-term (reproductive NOEC)	4.53	**2.7**	5
Small Insectivorous Bird (Great tit)		5.63	**2.1**	
Small Granivorous Bird (Linnet)		6.14	**2.0**	
Medium Omnivorous Bird (Woodlark)		7.07	**1.7**	
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	135.45	36.9	10
	Long-term	38.05	**0.02**	5
Tier 1 (Mammals)				
Large herbivorous mammal "lagomorph"	Long-term	5.8	**0.2**	5
Small herbivorous mammal "vole		38.1	**0.02**	
Small insectivorous mammal "shrew"		2.2	**0.4**	
Wood mouse (*Apodemus sylvaticus*): 25% weeds / 50% weed seeds / 25% ground arthropods		4.11	**0.2**	
Higher tier refinement (Mammals)_based on focal species and refined PT values				
Large herbivorous mammal	Long-term	5.89	**0.2**	5

"lagomorph"				
Small herbivorous mammal "vole		37.94	**0.02**	
Small insectivorous mammal "shrew"		2.19	**0.4**	
Wood mouse (*Apodemus sylvaticus*)_focal species		1.7	**0.5**	

Orchards: 1 × 0.993 kg Amitrole/ha (1/3 of the full dose rate due to the application made under the row)

Indicator species	Time scale	DDD	TER	Trigger
BIRDS				
Screening step				
Small insectivorous bird	Acute	46.47	46.3	10
	Long-term (overall NOEC)	-	-	5
	Long-term (reproductive NOEC)	8.58	**1.4**	
Tier 1 (Birds)				
Small insectivorous/worm feeding species: "thrush"	Long-term (reproductive NOEC)	1.424	8.5	5
Small granivorous bird: "finch"		6.63	**1.8**	
Higher tier refinement (Birds)_based on focal species and corresponding refined PD and PT values				
Medium Omnivorous Bird (Blackbird)	Long-term (reproductive NOEC)	0.5	24.3	5
Small Omnivorous Bird (Chaffinch)		1.06	11.4	
Small Granivorous Bird (Linnet)		4.87	**2.5**	
Small Granivorous Bird (Serin)		4.25	**2.8**	
insectivorous Bird (Great tit)		5.83	**2.1**	
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	135.45	36.9	10
	Long-term	38.05	**0.02**	5
Tier 1 (Mammals)				
Small insectivorous mammal "shrew"	Long-term	1	**0.9**	5
Small herbivorous mammal "vole		38.1	**0.02**	
Large herbivorous mammal "lagomorph"		7.5	**0.1**	

Wood mouse (*Apodemus sylvaticus*): 25% weeds / 50% weed seeds / 25% ground arthropods		4.1	**0.2**	

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)

Olive: 1 × 0.459 kg Amitrole/ha (1/3 of the full dose rate due to the application made under the row)

Indicator species	Time scale	DDD	TER	Trigger
BIRDS				
Screening step				
Small insectivorous bird	Acute	21.48	100.1	10
	Long-term (overall NOEC)	-	-	5
	Long-term (reproductive NOEC)	4.43	**2.7**	
Tier 1 (Birds)				
Small insectivorous/worm feeding species: "thrush"	Long-term (reproductive NOEC)	0.66	18.4	5
Small granivorous bird: "finch"		3.07	**4.0**	
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	62.61	79.9	10
	Long-term	17.59	**0.05**	5
Tier 1 (Mammals)				
Small insectivorous mammal "shrew"	Long-term	0.46	1.9	5
Small herbivorous mammal "vole		17.6	0.05	
Large herbivorous mammal "lagomorph"		3.5	0.3	
Wood mouse (*Apodemus sylvaticus*): 25% weeds / 50% weed seeds / 25% ground arthropods		1.9	0.5	

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

Group (species)	Test substance	Time scale	Endpoint	Value (mg a.s./L)	Expressed as *
Fish					

Fish (*O. mykiss*)	a.s.	Acute 96H (static)	LC_{50}	>1000	Nominal
Fish (*O. mykiss*)	a.s.	Chronic 21d (static) [1]	NOEC	100	Nominal
Fish (*O. mykiss*)	preparation (Weedazol TL)	Acute 96H (static)	LC_{50}	>100 mg preparation/L (>22.15 mg a.s/L)	Nominal
Fish (*O. mykiss*)	1,2,4-triazole	Acute 96H (static)	LC_{50}	498	Nominal
Fish (*O. mykiss*)	1,2,4-triazole	Chronic 28d (semi-static)	NOEC	>100 (mortality) 3.2 (sub lethal effects)	Nominal
Aquatic invertebrate					
Invertebrate (*D. magna*)	CA1678 (SG formulation containing 86% a.s.)	Acute 48H (static)	EC_{50}	7.1 mg preparation/L 6.1 mg a.s/L	Nominal
Invertebrate (*Mysidopsis bahia*)	a.s.	Acute 96H (static)	EC_{50}	2.8	Mean measured
Invertebrate (*D. magna*)	a.s.	Chronic 21d (static)	NOEC	0.32	Nominal
Invertebrate (*D. magna*)	preparation (Weedazol TL)	Acute 48H (static)	EC_{50}	12 mg preparation/L (2.66 mg a.s/L)	Nominal
Invertebrate (*D. magna*)	1,2,4-triazole	Acute 48H (static)	EC_{50}	>100	Nominal
Aquatic molluscs					
Aquatic molluscs (*Crassostrea virginica)*	a.s.	Acute 96 h	EC_{50}	>110	Mean measured
Algae					
Algae (*Scenedesmus subspicatus*)	a.s.	72H growth test	EC_{50}	2.3	Nominal
Algae (*Anabaena flos-aquae*)	a.s.	120H growth test (static)	E_bC_{50} EC_{r50}	3.9 >4.8	Nominal
Algae (*Selenastrum capricornutum)*	a.s.	72h growth test	EC_{b50} EC_{r50}	1.6 >5.1	Mean measured
Algae (*Selenastrum capricornutum)*	a.s.	8d growth test	EC_{b50}/EC_{r50} NOEC	> 6 6	Nominal
Algae (*Skeletonema costatum*)	a.s.	72h growth test	EC_{b50} EC_{r50}	1.3 >5.1	Mean measured
Algae (*Navicula pelliculosa)*	a.s.	72h growth test	EC_{b50} EC_{r50}	1.5 >3.1	Mean measured

Algae (*Selenastrum capricornutum)*	preparation (Weedazol TL)	72H growth test	EC_{b50} EC_{r50}	126 mg preparation/L (27.91 mg a.s/L) >200 mg preparation/L (>44.3 mg a.s/L)	Nominal
Algae (*Selenastrum capricornutum)*	1,2,4-triazole	72H growth test	EC_{b50} EC_{r50}	13 >31	Nominal
Algae (*Selenastrum capricornutum)*	1,2,4-triazole	72H growth test	EC_{b50} EC_{r50}	8.2 22.5	Nominal
Aquatic plant					
Aquatic plant (*Lemna gibba*)	a.s.	14d growth test (static)	EC_{50}	2.5	Measured (initial concentration)

[1] Toxicity data not sufficient for assessing all potential effects on development and reproduction due to endocrine disrupting properties of the active substance. TER calculation based on this chronic endpoint on juvenile fish (Fish prolonged toxicity test of 21 d with a NOEC of 100 mg a.s/) relevant also only for part of potential effects on development and reproduction of the active substance (i.e. it covers only partly the long-term risk for fish)

*: endpoint expressed in term of mean measured concentration could be expressed in term of nominal concentration as amitrole was very stable during these tests

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

AGRICULTURAL USES (pome fruit, citrus, olives and vineyard)

AMITROLE_FOCUS STEP 3 PECSW

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
O. mykiss	LC_{50} > 1000000	**Agricultural uses (FOCUS Step 3 PECsw)**			100
		Orchard in spring			
		R1 pond	0.651	1536098.31	
		R1 stream	12.39	80710.25	
		R2 stream	15.76	63451.78	
		R3 stream	17.13	58377.12	
		R4 stream	12.39	80710.25	
		Orchard in autumn			
		R1 pond	0.651	1536098.31	
		R1 stream	12.49	80064.05	
		R2 stream	16.22	61652.28	
		R3 stream	17.6	56818.18	
		R4 stream	11.21	89206.07	
		Vine in spring			
		R1 pond	0.651	1536098.31	
		R1 stream	12.47	80192.46	
		R2 stream	15.71	63653.72	

		R3 stream	17.06	58616.65	
		R4 stream	12.36	80906.15	
		Olive in autumn			
		R4 stream	5.216	191717.79	
		Citrus in spring			
		R4 stream	12.36	80906.15	
		Citrus in autumn			
		R4 stream	11.27	88731.14	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
O. mykiss	NOEC **(**covering only partly the long-term risk for fish): 100000	**Agricultural uses (FOCUS Step 3 PECsw)**			10
		Orchard in spring			
		R1 pond	0.651	153609.83	
		R1 stream	12.39	8071.03	
		R2 stream	15.76	6345.18	
		R3 stream	17.13	5837.71	
		R4 stream	12.39	8071.03	
		Orchard in autumn			
		R1 pond	0.651	153609.83	
		R1 stream	12.49	8006.41	
		R2 stream	16.22	6165.23	
		R3 stream	17.6	5681.82	
		R4 stream	11.21	8920.61	
		Vine in spring			
		R1 pond	0.651	153609.83	
		R1 stream	12.47	8019.25	
		R2 stream	15.71	6365.37	
		R3 stream	17.06	5861.66	
		R4 stream	12.36	8090.61	
		Olive in autumn			
		R4 stream	5.216	19171.78	
		Citrus in spring			
		R4 stream	12.36	8090.61	
		Citrus in autumn			
		R4 stream	11.27	8873.11	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
D. magna	EC_{50} = 6100	**Agricultural uses (FOCUS Step 3 PECsw)**			100
		Orchard in spring			
		R1 pond	0.651	9370.20	
		R1 stream	12.39	492.33	
		R2 stream	15.76	387.06	
		R3 stream	17.13	356.10	
		R4 stream	12.39	492.33	
		Orchard in autumn			
		R1 pond	0.651	9370.20	
		R1 stream	12.49	488.39	
		R2 stream	16.22	376.08	
		R3 stream	17.6	346.59	
		R4 stream	11.21	544.16	
		Vine in spring			
		R1 pond	0.651	9370.20	
		R1 stream	12.47	489.17	
		R2 stream	15.71	388.29	
		R3 stream	17.06	357.56	
		R4 stream	12.36	493.53	
		Olive in autumn			
		R4 stream	5.216	1169.48	
		Citrus in spring			
		R4 stream	12.36	493.53	
		Citrus in autumn			
		R4 stream	11.27	541.26	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
D. magna	NOEC = 320	**Agricultural uses (FOCUS Step 3 PECsw)**			10
		Orchard in spring			
		R1 pond	0.651	491.55	
		R1 stream	12.39	25.83	
		R2 stream	15.76	20.30	
		R3 stream	17.13	18.68	
		R4 stream	12.39	25.83	
		Orchard in autumn			
		R1 pond	0.651	491.55	
		R1 stream	12.49	25.62	

		R2 stream	16.22	19.73	
		R3 stream	17.6	18.18	
		R4 stream	11.21	28.55	
		Vine in spring			
		R1 pond	0.651	491.55	
		R1 stream	12.47	25.66	
		R2 stream	15.71	20.37	
		R3 stream	17.06	18.76	
		R4 stream	12.36	25.89	
		Olive in autumn			
		R4 stream	5.216	61.35	
		Citrus in spring			
		R4 stream	12.36	25.89	
		Citrus in autumn			
		R4 stream	11.27	28.39	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
Mysidopsis bahia	EC_{50} = 2800	**Agricultural uses (FOCUS Step 3 PECsw)**			100
		Orchard in spring			
		R1 pond	0.651	4301.08	
		R1 stream	12.39	225.99	
		R2 stream	15.76	177.66	
		R3 stream	17.13	163.46	
		R4 stream	12.39	225.99	
		Orchard in autumn			
		R1 pond	0.651	4301.08	
		R1 stream	12.49	224.18	
		R2 stream	16.22	172.63	
		R3 stream	17.6	159.09	
		R4 stream	11.21	249.78	
		Vine in spring			
		R1 pond	0.651	4301.08	
		R1 stream	12.47	224.54	
		R2 stream	15.71	178.23	
		R3 stream	17.06	164.13	
		R4 stream	12.36	226.54	
		Olive in autumn			
		R4 stream	5.216	536.81	
		Citrus in spring			

		R4 stream	12.36	226.54	
		Citrus in autumn			
		R4 stream	11.27	248.45	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
Navicula pelliculosa	E_bC_{50} = 1300 (lowest EC_{50})	**Agricultural uses (FOCUS Step 3 PECsw)**			10
		Orchard in spring			
		R1 pond	0.651	1996.93	
		R1 stream	12.39	104.92	
		R2 stream	15.76	82.49	
		R3 stream	17.13	75.89	
		R4 stream	12.39	104.92	
		Orchard in autumn			
		R1 pond	0.651	1996.93	
		R1 stream	12.49	104.08	
		R2 stream	16.22	80.15	
		R3 stream	17.6	73.86	
		R4 stream	11.21	115.97	
		Vine in spring			
		R1 pond	0.651	1996.93	
		R1 stream	12.47	104.25	
		R2 stream	15.71	82.75	
		R3 stream	17.06	76.20	
		R4 stream	12.36	105.18	
		Olive in autumn			
		R4 stream	5.216	249.23	
		Citrus in spring			
		R4 stream	12.36	105.18	
		Citrus in autumn			
		R4 stream	11.27	115.35	

Organism	Toxicity end point (µg/L)	Scenario	PECSW [µg/L]	TER	Trigger value
Lemna gibba	E_bC_{50} = 2500	**Agricultural uses (FOCUS Step 3 PECsw)**			
		Orchard in spring			
		R1 pond	0.651	3840.25	
		R1 stream	12.39	201.78	
		R2 stream	15.76	158.63	

		R3 stream	17.13	145.94	
		R4 stream	12.39	201.78	
		Orchard in autumn			
		R1 pond	0.651	3840.25	
		R1 stream	12.49	200.16	
		R2 stream	16.22	154.13	
		R3 stream	17.6	142.05	
		R4 stream	11.21	223.02	
		Vine in spring			
		R1 pond	0.651	3840.25	
		R1 stream	12.47	200.48	
		R2 stream	15.71	159.13	
		R3 stream	17.06	146.54	
		R4 stream	12.36	202.27	
		Olive in autumn			
		R4 stream	5.216	479.29	
		Citrus in spring			
		R4 stream	12.36	202.27	
		Citrus in autumn			
		R4 stream	11.27	221.83	

METABOLITE 1,2,4 TRIAZOLE_FOCUS Step 1

Organism	Toxicity end point (µg/L)	Time scale	Worst case scenario	PEC	TER	Annex VI Trigger
Fish	LC_{50} = 498000	Acute	orchards	36	≥ 13833	100
Fish	NOEC = 3200	Chronic	orchards	36	≥ 89	10
Aquatic invertebrates	EC_{50} > 100000	Acute	orchards	36	> 2778	100
Algae	E_bC_{50} = 8200	Chronic	orchards	36	≥228	10

IMPERMEABLE NON CROP USES (ROADS) AND PERMEABLE NON-CROP AREAS (RAILWAYS)

AMITROLE AND METABOLITE 1,2,4 TRIAZOLE_HARDSPEC

Test substance	Organism	Toxicity end point (µg/L)	Time scale	Worst case scenario	PEC (µg/L)	TER	Trigger[1]
a.s.	Fish	LC_{50} > 1000000	Acute	Urban stream	454	>2202	100
				railway spray drift	7821	>127	100
a.s.	Fish	NOEC	Chronic	Urban stream	454	N.A	10

		(covering all potential effects on development and reproduction): N.A		railway spray drift	7821	N.A	10
		NOEC **(**covering only partly the long-term risk for fish): 100000	Chronic	Urban Stream	454	220	10
				railway spray drift	7821	12.7	
a.s.	Aquatic invertebrates (*D. magna*)	EC_{50} = 6100	Acute	Urban stream	454	**14**	100
				Urban pond	43	142	
				Major road stream	233	**26**	
				Domestic stream	77	**79**	
				Railway ditch leaching	8	763	
				Railway ditch runoff	8	763	
				railway spray drift	7821	**0.78**	
a.s.	Aquatic invertebrates (*D. magna*)	NOEC = 320	Chronic	Urban stream	454	**0.7**	10
				Urban pond	43	**7.5**	
				Major road stream	233	**1.4**	
				Domestic stream	77	**4.1**	
				Railway ditch leaching	8	40	
				Railway ditch runoff	8	40	
				railway spray drift	7821	**0.04**	
a.s.	Aquatic invertebrates *(Mysidopsis bahia)*	EC_{50} = 2800	Acute	Urban stream	454	**6**	100
				Urban pond	43	**65**	
				Major road stream	233	**12**	
				Domestic stream	77	**36**	
				Railway ditch leaching	8	350	
				Railway ditch runoff	8	350	
				railway spray drift	7821	**0.36**	

a.s	Aquatic molluscs (*Crassostrea virginica)*	EC_{50} > 100000	acute	Urban stream	454	>221	100
a.s.	Algae	E_bC_{50} = 1300 (lowest EC_{50})	Chronic	Urban stream	454	**2.9**	10
				Urban pond	43	30.2	
				Major road stream	233	**5.6**	
				Domestic stream	77	16.9	
				Railway ditch leaching	8	162.5	
				Railway ditch runoff	8	162.5	
				railway spray drift	7821	**0.17**	
a.s.	Higher plants	E_bC_{50} = 2500	Chronic	Urban stream	454	**6**	10
				Urban pond	43	58	
				Major road stream	233	11	
				Domestic stream	77	32	
				Railway ditch leaching	8	312	
				Railway ditch runoff	8	312	
				railway spray drift	7821	**0.32**	
1,2,4-triazole	Fish	LC_{50} = 498000	Acute	Urban stream	37.615	≥ 13239	100
1,2,4-triazole	Fish	NOEC = 3200	Chronic	Urban stream	37.615	≥ 85	10
1,2,4-triazole	Aquatic invertebrates	EC_{50} > 100000	Acute	Urban stream	37.615	> 2658	100
1,2,4-triazole	Algae	E_bC_{50} = 8200	Acute	Urban stream	37.615	> 217	10

	Active substance
$logP_{O/W}$	-0.969 (pH7;23°C)
Bioconcentration factor (BCF)[1] ‡	2.38 (whole fish)
Annex VI Trigger for the bioconcentration factor	-
Clearance time (days) (CT_{50})	Not available, not triggered

(CT_{90})	Not available, not triggered
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not available, not triggered

[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.	LD_{50} > 152 µg a.s./bee	LD_{50} > 100 µg a.s./bee
Preparation	LD_{50} > 200 µg preparation/bee (> 42 µg a.s./bee)	LD_{50} > 200 µg preparation/bee (> 42 µg a.s./bee)

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

Crop and application rate

Test substance	Route	Hazard quotient	Trigger
a.s.	Contact	<30	50
a.s.	oral	<20	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
Aphidius colemani (adults; lab. test)	4.72 kg as/ha; Amitrole SL 236 g a.s./L	Mortality	Effect (mortality): 80%
Typhlodromus pyri (protonymphs; lab. test)	4.72 kg as/ha; Amitrole SL 236 g a.s./L	Mortality	Effect (mortality): 100%
Orius insidiosus (nymphs, 2nd stage; lab. test)	4.72 kg as/ha; Amitrole SL 236 g a.s./L	Mortality	Effect (mortality): 100%
Poecilus cupreus (adults; lab. test)	4.72 kg as/ha; Amitrole SL 236 g a.s./L	Mortality	Effect (mortality): 3.7%
Poecilus cupreus (adults; lab. test)	14.6 kg a.s./ha; Amitrole WP 50% w/w a.s.)	Mortality Food consumption	Effect (mortality): 0% Effect (food consumption) = 1.18 (ratio treated/control)

Species	Test Substance	End point	Effect
Pardosa armentata (adults)	4.9 kg a.s./ha; Amitrole WP 50% w/w a.s.	Mortality	Effect (mortality): 100%
Aleochara bilineata (adults; lab. test)	5.0 kg a.s./ha; Amitrole WP 50% w/w a.s.	Mortality Reproduction	Effect (mortality): 0% Effect (reproduction) = 0.01 (ratio treated/control)
Aleochara bilineata (adults; lab. test)	5.0 kg a.s./ha; Amitrole WP 50% w/w a.s.	Mortality Fecundity	Effect (mortality): 11.7% Effect (fecundity) = 1.0 (ratio treated/control)

Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate	Dose (L preparation/ha)	End point	% effect	Trigger value
Aphidius rhopalosiphi	Adults	Amitrole SL 236 g a.s./L Test substrate: barley seedlings	20 L preparation/ha	Mortality Reproduction ability	Corrected mortality: 45.71% Reproduction ability: 0.1469	50 %
Aphidius rhopalosiphi	Adults	Amitrole SL 229 g a.s./L (CA2210) Test substrate: barley seedlings	up to 45 L preparation/ha	LR50 ER50	LR_{50}: > 45000 mL preparation/ha ER_{50}: > 45000 mL preparation /ha	50 %
Typhlodromus pyri	Proto-nymphs	Amitrole SL 229 g a.s./L (CA2210) Test substrate: vine plants	up to 0.015 L preparation/ha	LR50 ER50	LR_{50}: 3.6 mL preparation/ha ER_{50}: > 3.75 mL preparation/ha (highest tested dose in the reproduction phase)	50 %
Pardosa spp.	Adults	Amitrole SL 229 g a.s./L (CA2210) Test substrate: soil Lufa 2.1	15 L preparation/ha	Mortality Feeding capacity	Effect (mortality): 21.2% at 15000 mL/ha Effect (feeding capacity): none up to 15000 mL/ha	50 %

Species	Life stage	Test substance, substrate	Dose (L preparation/ha)	End point	% effect	Trigger value
Orius insidiosus	Nymphs	Amitrole SL 236 g a.s./L Test substrate: corn plants	20 L preparation/ha	Mortality	Effect (mortality): 100%	50 %
Chrysoperla carnea	Adults	Amitrole SL 229 g a.s./L (CA2210) Test substrate: vine plants	9 L preparation/ha	LR50 ER50	LR_{50}: > 9000 mL prod./ha ER_{50}: > 9000 mL prod./ha (2nd assessment)	50 %

Note: Compared to CA2210, one ingredient was removed in CA2735 and replaced by water. So that the toxicity data generated with CA2210 cover the toxicity of CA2735

Agricultural uses: 13 L preparation/ha

Test substance	Species	Effect (LR_{50} mL/ha)	Exposure in field (mL/ha)	Exposure off-field (mL/ha) taking into account VDF [1] and SCF [2]	Trigger
Amitrole SL 229 g a.s./L	*Typhlodromus pyri*	3.6	13000	1m: 180	50%
				50m: 3.9	
				75m: 2.6	
Amitrole SL 229 g a.s./L	*Aphidius rhopalosiphi*	> 45000	13000	Not necessary (risk acceptable in-field)	50%

[1] vegetation distribution factor of 10 was considered to be appropriate for 2D extended lab studies with *T.pyri*
[2] species safety factor of 5, covers differences in sensitivity between different species

Field or semi-field tests
A field study conducted in a vineyard carried out to investigate long term effects on the population development of leaf-dwelling phytoseiid mites (Acari: Phytoseiidae) was available. No effects on predatory mite populations (Acari: Phytoseiidae) were observed when CA2735 was applied in a vineyard by not crop-directed application in very early spring at grows stage BBCH 00.

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			
	a.s.	Acute 14 days	LC_{50} >448 mg a.s./kg d.w.soil

Test organism	Test substance	Time scale	End point
	Preparation	Acute	>1000 mg formulation/kg soil dry weight (equivalent to >221.5 mg a.s/ kg soil dry weight)
	1,2,4 triazole	Acute	>1000
	1,2,4 triazole	Chronic	1
Other soil macro-organisms			
Collembolan			
	1,2,4 triazole	Chronic	NOEC= 1.8 mg a.i./kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	a.s.		transient retardation of nitrification processes, recovery after 42 days (up to 20 mg a.s/kg soil)
	1,2,4 triazole		< 25% effects on nitrogen and carbon mineralisation after 28 days at up to 0.333 mg/kg soil (highest dose tested)
Carbon mineralisation	a.s.		No effect on carbon mineralisation up to 20 mg/kg soil.
	1,2,4 triazole		< 25% effects on nitrogen and carbon mineralisation after 28 days at up to 0.333 mg/kg soil (highest dose tested)
Field studies			
None available			

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s.	Acute	3.969[1]	>112.8	10
	1,2,4 triazole	Acute	0.451[2]	>2217	10
	1,2,4 triazole	Chronic	0.451[2]	2.2	5
Other soil macro-organisms					
Collembola	1,2,4 triazole		0.451[2]	3.99	5

[1] initial PEC soil was used
[2] plateau PEC soil was used (after 8 years)

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

Laboratory dose response tests

Most sensitive species	Test substance	EC_{50} (kg/ha) vegetative vigour	EC_{50} (kg/ha) emergence
Cabbage (for emergence) and sunflower (vegetative vigour)	Active substance	0.1345 kg a.s./ha	0.616 kg a.s./ha

Application rate (kg as/ha)	Crop	Test	Buffer distance (m)	TER	Trigger
Based on lowest EC_{50} = 0.1345 kg a.s./ha (Tier 1)					
1 x 2.977	Agricultural uses	Vegetative vigour	1 (default)	**1.63**	5
			5	7.9	5

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

Not necessary

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

Test type/organism	end point
Activated sludge	EC50 > 1000 mg/L

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

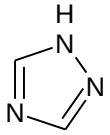
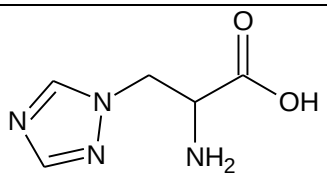
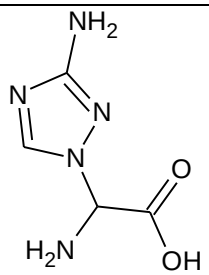
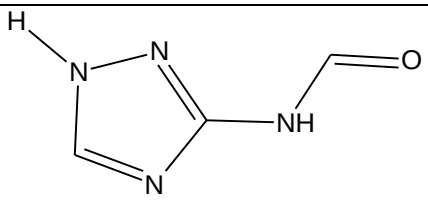
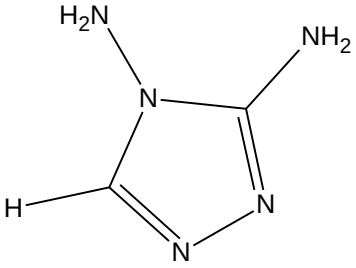
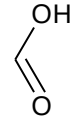
Compartment	
soil	Amitrole, 1,2,4 triazole
water	Amitrole, 1,2,4 triazole
sediment	Amitrole
groundwater	Amitrole, 1,2,4 triazole

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	**Classification acc. to Dir. 67/549/EEC:** Proposed Label: Symbol: N Indication of danger: Dangerous for the environment Risk phrases: R51/53 Safety phrases: S60, S61 **Classification acc. to Reg. 1272/2008:** Proposed Label: Symbol: Warning, GHS09 Indication of danger: Aquatic chronic 2 Risk phrases: H411 Safety phrases: P273, P391, P501

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name SMILES code	Structural formula
1,2,4-triazole	1H-1,2,4-triazole c1ncnn1	
triazolylalanine	3-(1,2,4-triazol-1-yl)-2-aminopropionic acid NC(Cn1cncn1)C(=O)O	
aminotriazolylalanine	3-(3-amino-1,2,4-triazol-1-yl)-2-aminopropionic acid Nc1ncn(n1)C(N)C(=O)O	
N-(1*H*-[1,2,4]-triazol-3-yl)-formamide	N-(1*H*-[1,2,4]-triazol-3-yl)-formamide O=CNc1ncnn1	
4*H*-[1,2,4]-triazole-3,4-diamine	4*H*-[1,2,4]-triazole-3,4-diamine Nc1nncn1N	
Methanoic acid	Methanoic acid O=CO	

* The metabolite name in bold is the name used in the conclusion.

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
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
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAM	setting in PRZM defining the method of application and distribution of soil incorporation
CAS	Chemical Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
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
ECB	European Chemicals Bureau
ECHA	European Chemicals 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
FID	flame ionisation detector
FIR	Food intake rate

FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GHS	globally harmonised system
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-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
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/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
mN	milli-newton
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
NPD	nitrogen phosphorous detector
OECD	Organisation for Economic Co-operation and Development
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
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
REACH	Registration, Evaluation, Authorisation of CHemicals
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
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell

WG	water dispersible granule
WHO	World Health Organization
wk	week
yr	year