CONCLUSION ON PESTICIDE PEER REVIEW

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

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Triflumizole is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. In accordance with Article 10(1) of the Regulation, The Netherlands, being the designated rapporteur Member State (RMS), provided an initial evaluation of triflumizole in the format of a Draft Assessment Report (DAR), which was received by the EFSA on 4 January 2006. The Commission of the European Communities (hereafter referred to as 'the Commission') examined triflumizole in accordance with Article 11a of the Regulation and it was concluded that there were clear indications of harmful effects, leading to the adoption of a decision on non-inclusion in Annex I to Council Directive 91/414/EEC, in accordance with Articles 11f and 12 of the Regulation.

Following the Commission Decision of 20 September 2008 (2008/748/EC)[5] concerning the non-inclusion of triflumizole in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Certis made a resubmission application for the inclusion of triflumizole in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/1061/08 – rev.0).

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, The Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 6 March 2009.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant(s) for comments on 10 March 2009. The EFSA collated and forwarded all comments received to the Commission on 14 April 2009.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to arrange a peer review in the area of Mammalian Toxicology and to deliver its conclusions on triflumizole.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of triflumizole as a fungicide on fruiting vegetables and ornamentals, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

No areas of concern were identified in the physical and chemical properties section.

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1 On request from the European Commission, Question No EFSA-Q-2009-00610, issued on 4 December 2009.

2 Correspondence: praper@efsa.europa.eu

3 OJ L224, 21.08.2002, p.25

4 OJ L 246, 21.9.2007, p. 19

5 OJ L 252, 20.09.2008, p.37

6 OJ L 15, 18.01.2008, p.5

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No areas of concern were identified in the mammalian toxicology section.

In the residues area for the specific uses on fruiting vegetables the plant metabolism data are acceptable. The only outstanding issue is that the storage stability study shows that the residue is only stable for 1 month and residue trials have been stored for up to 3 months. This has implications for the risk assessment but it is not a critical area of concern.

The data available on fate and behaviour in the environment are sufficient to carry out the required environmental exposure assessments at the EU level for the applied for intended uses. The assessments are based on there being no soil exposure from these uses.

The ecotoxicology risk assessment indicated no critical areas of concern and the risk to all non-target organisms was addressed.

KEY WORDS

triflumizole, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

Legislative framework

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

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

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

Triflumizole is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007.

In accordance with Article 10(1) of the Regulation, The Netherlands, being the designated rapporteur Member State (RMS), provided an initial evaluation of triflumizole in the format of a DAR (The Netherlands, 2006), which was received by the EFSA on 4 January 2006. In accordance with Article 11 of the Regulation, the EFSA dispatched the DAR to the Member States and the applicant Certis on 24 May 2006 for consultation and comments.

In accordance with the provisions of Article 11a of the Regulation the Commission examined triflumizole, following which it was concluded that there were clear indications of harmful effects, leading to the adoption of a decision on non-inclusion in Annex I to Council Directive 91/414/EEC, in accordance with Articles 11f and 12 of the Regulation.

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

Following the Commission Decision of 20 September 2008 (2008/748/EC)[10] concerning the non-inclusion of triflumizole in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Certis made a resubmission application for the inclusion of triflumizole in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/1061/08 – rev.0), as follows: the operator and worker exposure, the acute toxicity to birds, the acute toxicity to fish, the risk to mammals, the risk to non-target arthropods.

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 252, 20.09.2008, p.37

In accordance with Article 18, The Netherlands, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (The Netherlands, 2009a). The Additional Report was received by the EFSA on 6 March 2009.

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 10 March 2009. In addition, the EFSA conducted a public consultation on the Additional Report. The EFSA collated and forwarded all comments received to the Commission on 14 April 2009. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 20 May 2009, the Commission requested the EFSA to arrange a peer review in the area of Mammalian Toxicology and to deliver its conclusions on triflumizole within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 25 May 2009; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that further information should be requested from the applicant in the areas of the plant metabolism and the residue definition set in the residue trials.

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

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in October - November 2009.

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 fungicide on fruiting vegetables and ornamentals, 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, 2009) comprises the following documents:

- the comments received on the DAR and the Additional Report
- the Reporting Table (revision 1-1; 26 May 2009),

- the Evaluation Table (2 December 2009),
- the report(s) of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of October 2009 containing all individually submitted addenda) (The Netherlands, 2009b) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Triflumizole is the ISO common name for (*E*)-4-chloro-α,α,α-trifluoro-*N*-(1-imidazol-1-yl-2-propoxyethylidene)-*o*-toluidine (IUPAC).

The representative formulated product for the evaluation was 'Rocket EC', an emulsifiable concentrate (EC) containing 150 g/L triflumizole, registered under different trade names in Europe.

The representative uses evaluated comprise indoor foliar spraying against powdery mildew in cucumber, courgette, gherkin, tomato and ornamentals growing on artificial substrate. 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

Toluene was considered as a relevant impurity but, based on its hazard and the level proposed in the technical specification, does not give rise to significant toxicological concern. The batches tested in toxicological and ecotoxicological studies have been considered as representative to the proposed specification.

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

The compounds in the residue definition for plants can be determined with a multi-residue method (DFG S19). Analytical methods for food of animal origin are not required as there is no intake by livestock. LC-MS/MS methods are available to monitor the compounds in the residue definition for water. Adequate analytical methods are available to monitor triflumizole residues in soil and air.

2. Mammalian toxicity

Triflumizole is "Harmful if swallowed" (proposed to be labelled R22); it is not acutely toxic via the dermal and inhalation routes. It is not a skin or eye irritant, but it is a skin sensitiser (proposed R43 "May cause sensitization by skin contact"). In all short-term studies increased liver weights, altered liver histopathology and decreased body weight gain were observed. The relevant NOAEL is 4.1 mg/kg bw/day based on liver findings in a 13-wk study in rats. Triflumizole does not possess genotoxic and reproductive toxicity potential (the reproductive, parental and offspring NOAELs were likewise set at 4.8 mg/kg bw/day, whereas the maternal and developmental NOAELs were 10 mg/kg bw/day in rats and 100 mg/kg bw/day in rabbits). Triflumizole is not a carcinogen; the relevant NOAEL for long-term systemic effects in rats is 3.5 mg/kg bw/day based on liver effects; the long term toxicity NOAEL in mice is 16 mg/kg bw/day. Some indications of neurotoxicity potential of triflumizole were noted (e.g. in the 2 year rat study, convulsions only at high dose levels). The ADI and AOEL are 0.05 mg/kg bw/day, and the ARfD is 0.1 mg/kg bw. The operator and worker exposure in greenhouses is below the AOEL (with the use of PPE for the operator only). No bystander exposure is expected.

3. Residues

The residue definition for plants is based on a foliar applied grape metabolism study which is supported by a foliar applied cucumber metabolism study. Two other metabolism studies on apple and pear are not relied on. The grape metabolism study was only conducted at 1N for a single application whereas the representative uses have up to 6 applications. In this case it can be considered acceptable as the supported crops are continuously harvested and the accumulation of unidentified metabolites is

unlikely to occur. It is also for this reason that it can be accepted that there is no imidazole label in the metabolism studies. However, the metabolism data are only acceptable for fruiting vegetables and not for fruit crops in general. The main component of the residue was triflumizole and to a lesser extent metabolite FM-6-1. The residue definition for monitoring is therefore the sum of triflumizole and FM-6-1 expressed as triflumizole. For risk assessment it was concluded that a worst case conversion factor of 1.5 could be derived from the metabolism data and this then includes all identified metabolites containing the 4-chloro-2-(trifluoromethyl)phenyl moiety. It was accepted that this conversion factor could be used for tomato and cucumber.

Succeeding and rotational crops are not an issue as the crops are only to be grown on artificial substrate. Also it is not necessary to investigate the nature and magnitude of residues in livestock as the crops in question are not fed to animals. Sufficient residue trials on protected cucumber (extrapolate to cucurbits edible peel) and protected tomato have been provided. From these residue data MRLs of 0.1 mg/kg for cucurbits edible peel and 1 mg/kg for tomatoes have been proposed. A residue storage stability study was conducted that showed that triflumizole is only stable for 1 month and not 4 months as stated in the Additional Report (recovery 74 % at 33 days but <70 % at 125 days). The consequence of this is not known as it is stated in the Additional Report that trial samples were stored frozen for up to 3 months. From the stability study it can be seen that circa 40 % of the triflumizole residue is lost after 4 months and this should be taken into account for the risk assessment. As a consequence a data gap was identified. In the same stability study, residues of FM-6-1 appeared to be stable. However, it is not clear if the same samples were spiked with both triflumizole and FM-6-1 or if they were separate samples. If they were the same samples then, if triflumizole is breaking down to FM-6-1, any degradation of FM-6-1 could be masked. The risk assessment using the EFSA PRIMo model rev.2 is a maximum of 9.8 % of the ADI and 58 % of the ARfD for tomato and 7.7 % of the ARfD for cucumber (using proposed MRLs). But as mentioned above, this must be considered along with the instability seen in the storage study. Even taking this into account, it is highly unlikely that the reference doses will be exceeded for these crops.

4. Environmental fate and behaviour

The peer review concluded that acceptable data on the route and rate of degradation of triflumizole in soil were not available. The applicant's dossier did not include an assessment of the mobility of triflumizole in soil, though the water solubility of around 10 mg/L indicates that it might be expected to exhibit some mobility. As the applied for intended use is only for plants growing on artificial substrate, these data are not necessary to complete an environmental exposure assessment, which consequently has been based on the assumption that soil exposure will be negligible. If soil exposure is negligible, than the potential for groundwater exposure would also be expected to be negligible.

In laboratory incubations of triflumizole in aerobic natural sediment water systems triflumizole exhibited moderate to high persistence breaking down to the major metabolites (>10% applied radioactivity (AR)) FA-1-1 (persistence estimate not available) and imidazole (which exhibited moderate persistence). Triflumizole partitioned from the water to the sediment phase. The metabolites were relatively evenly distributed between the water and sediment phases of the test sediment water systems. Mineralisation of the phenyl and imidazole ring radiolabels accounted for less than 0.3 % AR and 20-39 % AR respectively after 95-101 days (study end). Residues not extracted from sediment by methanol including a Soxhlet extraction were also a sink for radioactivity representing 5.8-19 % AR at study end. The necessary surface water exposure assessments (for triflumizole, FA-1-1 and imidazole) were appropriately carried out using a FOCUS (2001) step 2 approach (version 1.1) that was then modified by post processing the spray drift input results (option no runoff or drainage was selected) to obtain a 0.1 % emission of triflumizole from glasshouses being re-deposited on adjacent surface water bodies. This approach has been accepted by Member State experts, as an assumption that can be used in EU level surface water exposure assessments for glasshouse uses. The PEC resulting from these calculations can be found in Appendix A. Note that risk to sediment dwellers was addressed by using a PECsw calculation that assumed no partitioning to sediment, consequently maximising the surface

water concentration calculated and (artificially) excluding dissipation by partitioning to sediment in this predicted concentration. This approach was combined with an ecotoxicology test where a water no effect concentration from a water spiked study design was selected for the risk assessment. This was considered acceptable in this case.

5. Ecotoxicology

The environmental risk assessment of triflumizole was conducted according to the guidance documents (see References). Toxicity studies with triflumizole indicated a low acute toxicity of triflumizole to birds and mammals. An assessment of the risk from exposure to contaminated surface water and an assessment of the risk for fish-eating birds and mammals were performed as drift from the glasshouse uses was expected. The risk from the intended uses was assessed as low.

Based on the available data, triflumizole and the formulation were considered to be very toxic to aquatic organisms. The metabolite FA-1-1 was found to be of less toxicity than the parent substance. The triflumizole toxicity to *Pimephales promelas* was driving the risk assessment and a low risk was found for the aquatic organisms. The risk for the metabolite imidazole was assessed as low. The bioconcentration factor was 1417. Triflumizole belongs to the azoles family, and due to the mode of action, the potential for endocrine disruption in fish was assessed. The potential for endocrine disruption was assessed based on the use of the most sensitive end point from an early-life stage test with an additional uncertainty safety factor of 5 (35 days NOEC = 44 µg a.s/L / 5 = 8.8 µg a.s./L).

HQ calculations based on acute oral and contact toxicity of triflumizole indicated a low risk to bees. Since triflumizole is applied to artificial substrate in the greenhouse, exposure to non-target arthropods is unlikely to occur. However, the intended uses of triflumizole could involve the use of integrated pest management (IPM) programmes. Laboratory studies on non-target arthropods were provided with the two standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi.* Additional tier I and aged residues studies with the parasitic wasp *Encarsia formosa* and the predatory mite *Phytoseiulus persimilis* were provided. Based on the available data it could be concluded that triflumizole should only be used in IPM programmes if a waiting period of a minimum of 3 days after the last application is introduced.

Since the intended uses of triflumizole involve only indoor treatment, the risk of triflumizole to soil non-target organisms (earthworms, other non-target macro-organisms and soil micro-organisms) and non-target plants are considered not relevant.

No significant adverse effects on sewage treatment were expected.

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

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
None due to the intended use	-	-

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
None due to the intended use	-	-	-	-	-

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
triflumizole	Triflumizole is very toxic to aquatic organisms. The risk to aquatic organisms from triflumizole was assessed as low.
FA-1-1	The metabolite FA-1-1 is toxic to aquatic organisms. The risk to aquatic organisms from FA-1-1 was assessed as low.

imidazole	The metabolite imidazole exhibits comparable toxicity to metabolite FA-1-1 in chironomus testing. The risk to aquatic organisms from imidazole was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
triflumizole	Not acutely toxic by inhalation.

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

- The stability in freezer storage showed that the residue is only stable for 1 month. As this is the case and given the fact that the residue trials are stored for up to 3 months, brings into question at least some of the trials. This issue needs to be addressed. This might need to be addressed by additional trials after which the risk assessment and MRLs should be reconsidered (relevant for all representative uses evaluated, data gap identified by EFSA, date of submission unknown; refer to section 3).

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

- The use of PPE (gloves and coverall) is needed for the operator to reach an exposure level below the AOEL.

ISSUES THAT COULD NOT BE FINALISED

- The consumer risk assessment can not be finalised because of the issue of instability of the residue.

CRITICAL AREAS OF CONCERN

- None

REFERENCES

EFSA (European Food Safety Authority), 2009. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance triflumizole. EFSA Journal 2009: 7(12): 1415.

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The Netherlands, 2009a. Additional Report to the Draft Assessment Report on the active substance triflumizole prepared by the rapporteur Member State The Netherlands in the framework of Commission Regulation (EC) No 33/2008, March 2009.

The Netherlands, 2009b. Final Addendum to the Additional Report on triflumizole, compiled by EFSA, October 2009.

APPENDICES

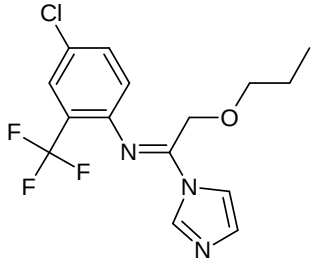
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	Triflumizole
Function (*e.g.* fungicide)	Fungicide

Rapporteur Member State	The Netherlands
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*E*)-4-chloro-α,α,α-trifluoro-*N*-(1-imidazol-1-yl-2-propoxyethylidene)-*o*-toluidine
Chemical name (CA) ‡	1-[(1*E*)-1-[[4-chloro-2-(trifluoromethyl)phenyl]imino]-2-propoxyethyl]-1*H*-imidazole
CIPAC No ‡	730
CAS No ‡	99387-89-0
EC No (EINECS or ELINCS) ‡	not available
FAO Specification (including year of publication) ‡	not available
Minimum purity of the active substance as manufactured ‡	980 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene Max. 1 g/kg
Molecular formula ‡	$C_{15}H_{15}ClF_3N_3O$
Molecular mass ‡	345.75 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	63 °C (99.3%)
Boiling point (state purity) ‡	not applicable, decomposition before boiling
Temperature of decomposition (state purity)	Exothermic decomposition above 150 °C (99.9%)
Appearance (state purity) ‡	white granulate material with a scentless odour (99.9%)
Vapour pressure (state temperature, state purity) ‡	1.91×10^{-4} Pa at 25 °C (99%)
Henry's law constant ‡	6.29×10^{-3} Pa.m^3.mol^{-1} (25 °C)
Solubility in water (state temperature, state purity and pH) ‡	in water and buffer solutions (pH 7 and pH 8): 10.5, 10.2 and 9.6 mg/L, respectively (20 °C) in water at 30 °C: 10.2 mg/L (99.9%) in buffer (pH 4): 21 mg/L (20°C) (99.7%)
Solubility in organic solvents ‡ (state temperature, state purity)	n-octanol 605 g/L at 25 °C acetonitrile 1187 g/L at 25 °C ethyl acetate 1486 g/L at 25 °C dichloromethane 3016 g/L at 25 °C n-hexane 17.6 g/L at 20 °C methanol 496 g/L at 20 °C xylene 639 g/L at 20 °C acetone 1440 g/L at 20 °C chloroform 2220 g/L at 20 °C 20°C: 98.6% pure; 25°C 98.7% pure
Surface tension ‡ (state concentration and temperature, state purity)	49.4 mN/m for a 90% saturated solution at 20 °C (99.2%)
Partition co-efficient ‡ (state temperature, pH and purity)	Calculated from the measured solubilities: $LogP_{ow}$ pH 4 = 4.46 $LogP_{ow}$ pH 7 = 4.77 $LogP_{ow}$ pH 8 = 4.80
Dissociation constant (state purity) ‡	pKa = 3.7 at 25 °C (98.6%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	maxima at (in methanol, purity 99.9%): 201.5 nm ($\varepsilon = 2.53 \times 10^4$ L.mol^{-1}.cm^{-1}) 236.0 nm ($\varepsilon = 2.64 \times 10^4$ L.mol^{-1}.cm^{-1}) and 301 nm ($\varepsilon_{301} = 4.91 \times 10^3$ L.mol^{-1}.cm^{-1})

Flammability ‡ (state purity)	not highly flammable (99.2%)
Explosive properties ‡ (state purity)	not explosive (statement)
Oxidising properties ‡ (state purity)	not oxidising (statement)

Summary of representative uses evaluated (triflumizole)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Cucumber	NL, BE	ROCKET EC	I	Powdery mildew	EC	150 g/L	spray ing	*	1-6[1]	7 days[1]	0.0156	500-1500	0.078-0.234	3	artificial substrates
Courgette	NL, BE	ROCKET EC	I	Powdery mildew	EC	150 g/L	spray ing	*	1-3	7 days	0.0156	500-1500	0.078-0.234	3	artificial substrates
Gherkin	BE	ROCKET EC	I	Powdery mildew	EC	150 g/L	spray ing	*	1-6[1]	7 days[1]	0.0104	500-1500	0.052-0.156	3	artificial substrates
Tomato	NL, BE	ROCKET EC	I	Powdery mildew	EC	150 g/L	spray ing	*	1-5 [2]	7 days[2]	0.0156	500-1500	0.078-0.234	3	artificial substrates
Ornamentals	NL, BE	ROCKET EC	I	Powdery mildew	EC	150 g/L	spray ing	all	1-6[1]	7 days[1]	0.0156	500-1500	0.078-0.234	-	only grown on artificial substrates

* Treatment during harvesting period (adult plants), not before May 1st or 4 weeks after planting (juvenile plants)

[1] The GAP involves up to 6 applications in 2 spray-programmes. 1 spray programme is 3 applications with a seven-day interval followed by a different fungicide. The minimum interval to the next spray-programme is 28 days.

[2] The GAP involves up to 5 applications in 2 spray-programmes. The first spray programme is 3 applications with a seven-day interval followed by at least two other different fungicides. The minimum interval to the second spray-programme of 2 applications is 49 days.

Remarks:

* Uses for which risk assessment could not been concluded due to lack of essential data are marked grey

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

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

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

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

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

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

(g) All abbreviations used must be explained

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

(i) g/kg or g/l

(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) The minimum and maximum number of application possible under practical conditions of use must be provided

(l) PHI - minimum pre-harvest interval

(m) Remarks may include: Extent of use/economic importance/restrictions

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC-UV
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Sum of triflumizole and FM-6-1 expressed as triflumizole
Food of animal origin		none (by current intended use)
Soil		none (by current intended use) but triflumizole in case of accident / misuse
Water	surface	triflumizole and FA-1-1. (Imidazole was excluded as it is a common residue that is not specific to triflumizole)
	drinking/ground	none (by current intended use) but triflumizole in case of accident / misuse
Air		triflumizole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS LOQ = 0.02 mg/kg for triflumizole and FM-6-1 in cucumber With ILV DFG-S19 (E1&LCMSMS): LOQ 0.01 mg/kg for triflumizole and FM-6-1
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	not required (no intake by livestock at the current intended use)
Soil (analytical technique and LOQ)	not required (intended use on substrate only) HPLC-MS/MS LOQ = 0.05 mg/kg for triflumizole
Water (analytical technique and LOQ)	LC-MS/MS LOQ = 0.1 µg/L for triflumizole and its metabolite FA-1-1

Air (analytical technique and LOQ)	HPLC-MS/MS LOQ = 0.0045 mg/m^3 air (0.0045 µg/l air) for triflumizole
Body fluids and tissues (analytical technique and LOQ)	Not required [substance is not classified as toxic (T) or very toxic (T^+)]

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

	RMS/peer review proposal
Active substance	None (for transport: flammable liquid of class 3)

Impact on Human and Animal Health

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

Rate and extent of oral absorption	At least 72%, based on radiolabel recovered from urine, tissues and carcass 48 h after single and repeated administration (10 mg/kg bw). Taking also the similar pattern of metabolites in urine and feaces into account it is assumed that oral absorption is >80%. in the first 24 h at least 66%
Distribution	Highest concentration in liver, well-perfused organs higher concentrations than other organs, brain among top-3 highest concentrations
Potential for accumulation	No evidence for accumulation
Rate and extent of excretion	Ca. 95% within 48 h, mainly via urine (ca. 75%) Ca. 90% within the first 24 h
Metabolism in animals	Extensively metabolised: < 2% parent compound in urine and faeces 16 metabolites identified in urine and faeces (60-75% of radiolabel) Major metabolites in urine: Sulphate conjugates of n-(4-chloro-2-trifluoro-methylphenyl)-2-hydroxy-acetamidine and 2-amino-5-chloro-3-trifluoromethylphenol (each ca. 20% of urinary radiolabel)
Toxicologically relevant compounds (animals and plants)	Parent compound and metabolites containing the 4-chloro-2-(trifluoromethyl)phenyl group
Toxicologically relevant compounds (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	1057 mg/kg bw	**R22**
Rat LD_{50} dermal	>5000 mg/kg bw	
Rat LC_{50} inhalation	>3.6 mg/L (4 h, nose only)	
Skin irritation	Non-irritant	
Eye irritation	Non-irritant	
Skin sensitisation	Sensitizer (Maximisation test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Increased liver weight, liver histopathology	
Relevant oral NOAEL	13-w, neurotoxicity study rat: 70 ppm (4.1	

	mg/kg bw/d)	
Relevant dermal NOAEL	21-d, rat: 100 mg/kg bw/d	
Relevant inhalation NOAEL	No data – not required	

Genotoxicity (Annex IIA, point 5.4)

No genotoxic potential	

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

Target/critical effect	Increased liver weight, liver macroscopy and histopathology	
Relevant NOAEL	2-y, rat: 100 ppm (3.5 mg/kg bw/d)	
Carcinogenicity	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	mating/fertility parameters, male reproductive organs at parental toxic doses	
Relevant parental NOAEL	70 ppm (4.8 mg/kg bw/d)	
Relevant reproductive NOAEL	70 ppm (4.8 mg/kg bw/d)	
Relevant offspring NOAEL	70 ppm (4.8 mg/kg bw/d)	

Developmental toxicity

Developmental target / critical effect	reduced viability, body weight, increased resorptions, placental weight at maternal toxic doses. No teratogenic effects.	
Relevant maternal NOAEL	Rat: 10 mg/kg bw/d Rabbit: 100 mg/kg bw/d	
Relevant developmental NOAEL	Rat: 10 mg/kg bw/d Rabbit: 100 mg/kg bw/d	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	No specific neurotoxic effects observed. NOAEL rat: 25 mg/kg bw	
Repeated neurotoxicity	No specific neurotoxic effects observed. 13-w, rat: 70 ppm (4.1 mg/kg bw/d)	
Delayed neurotoxicity	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	No data-not required
Studies performed on metabolites or impurities	Acute oral toxicity studies with metabolites of triflumizole: Metabolite — LD_{50}(mg/kg/bw) FD-1-1 — 3405 FD-2-1 — >2000 FD-6-1 — >2000 FD-7-1 — 1000; R22 FM-2-1 — >2000 FM-5-1 — >2000 FM-6-1 — 2131 FM-8-1 — 1935; R22 FA-1-1 — 771; R22 FA-1-5 — >2000

Medical data (Annex IIA, point 5.9)

No effects in manufacturing, no cases of poisoning

Summary (Annex IIA, point 5.10)	**Value**	**Study**	**Safety factor**
ADI	0.05 mg/kg bw/d	rat, 2-generation toxicity study; supported by the 2-year and 13-week neurotox studies in rats and considering the dose spacing between these studies	100

AOEL (semi-chronic/chronic)	0.05 mg/kg bw/d	rat, 2-generation toxicity study; supported by the 2-year and 13-week neurotox studies in rats and considering the dose spacing between these studies	100
ARfD	0.1 mg/kg bw	rat, developmental study	100

Dermal absorption (Annex IIIA, point 7.3)

Formulation (Rocket EC)	4% for the concentrate (1.5 mg/cm^2) 11% for the dilution (1.5 µg/cm^2) Based on *in vitro* and *in vivo* studies with triflumizole formulated as Rocket EC

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Manual spraying, use on roses, gherkins, courgette, tomato and cucumber in the greenhouse Dutch-90th: 154% of AOEL without PPE 15% of AOEL with PPE
Workers	Re-entry activities in roses in the greenhouse EUROPOEM II: 66% of AOEL without PPE 7% of AOEL with PPE Re-entry activities in gherkins, courgette, tomato and cucumber in the greenhouse EUROPOEM II: 60% of AOEL without PPE 6% of AOEL with PPE
Bystanders	Not applicable (greenhouse applications)

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

	RMS/peer review proposal
Substance classified (name)	**Xn** "Harmful" **R22** "Harmful if swallowed" **R43** "May cause sensitization by skin contact"

Residues

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

Plant groups covered	Fruiting vegetables only, artificial substrate only
Rotational crops	not investigated (substrate culture only)
Metabolism in rotational crops similar to metabolism in primary crops?	-
Processed commodities	-
Residue pattern in processed commodities similar to residue pattern in raw commodities?	-
Plant residue definition for monitoring	Sum of triflumizole and FM-6-1 expressed as triflumizole
Plant residue definition for risk assessment	Sum of triflumizole and metabolites containing the 4-chloro-2-(trifluoromethyl)phenyl group
Conversion factor (monitoring to risk assessment)	1.5

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

Animals covered	no significant residues (<0.01 mg/kg) are expected in feed
Time needed to reach a plateau concentration in milk and eggs	-
Animal residue definition for monitoring	-
Animal residue definition for risk assessment	-
Conversion factor (monitoring to risk assessment)	-
Metabolism in rat and ruminant similar (yes/no)	-
Fat soluble residue: (yes/no)	Not relevant

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

not investigated (substrate culture only)

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

Triflumizole and metabolite FM-6-1 are stable for only 1 month in watery matrices (cucumber)

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	no	no	no
Potential for accumulation (yes/no):			
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	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			

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Cucumber Substrate culture only (extrapolation to whole group of cucurbits edible peel)	Glasshouse	Triflumizole: 8x<0.02 FM-6-1: 8x<0.02	extrapolation to courgette, gherkin (whole group of cucurbits with edible peel)	0.1	0.04	0.04
Tomatoes Substrate culture only	Glasshouse	Triflumizole: 0.73, 0.18, 0.45, 0.46, 0.16, 0.19, 0.26, 0.12 FM-6-1: 2x<0.02, 3x0.02, 0.03 0.05, 0.08		1.0	0.78 (0.73 + 0.05)	0.27

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

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

ADI	0.05 mg/kg bw/d
TMDI (% ADI) (maximal value of PRIMo)	9.8% (WHO Cluster diet B)
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	
Factors included in IEDI and NEDI	
ARfD	0.1 mg/kg bw
IESTI (% ARfD)	-
NESTI (% ARfD) according to national (to be specified) large portion consumption data (maximal value of PRIMo)	58% (tomato, BE child) 7.7% (cucumber)
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	
No information provided and no information needed				

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

Cucumber, gherkin, courgette	0.10

.....

Tomatoes	1.0

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

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	No acceptable data submitted, not required for the intended use.
Non-extractable residues after 100 days ‡	No data submitted, not required for the intended use
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No acceptable data submitted, not required for the intended use.

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

Anaerobic degradation ‡

Mineralization after 100 days	No data submitted, not required for the intended use
Non-extractable residues after 100 days	-
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	-

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data submitted, not required for the intended use

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

Laboratory studies ‡

Parent	Aerobic conditions
No acceptable data submitted, not required for the intended use	

Met 1	Aerobic conditions
No acceptable data submitted, not required for the intended use	

Field studies ‡

Parent	Aerobic conditions
No data submitted, not required for the intended use	

pH dependence ‡ (yes / no) (if yes type of dependence)	-
Soil accumulation and plateau concentration ‡	No data submitted, not required for the intended use

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡
No data submitted, not required for the intended use

Metabolite FA-1-1 ‡
No data submitted, not required for the intended use

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

Column leaching ‡	-
Aged residues leaching ‡	-
Lysimeter/ field leaching studies ‡	-

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	PEC (soil) not required for the intended use
Application data	-

Metabolite FA-1-1 Method of calculation	PEC (soil) not required for the intended use
Application data	-

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 3: 18.5 hours at 20 °C (1st order, r^2=0.99) metabolites not quantified
	pH 5: 8.7 days at 25 °C (1st order, r^2=0.98) Met FD-1-1: 97.4 %AR (30 d)
	pH 6: 19.7-21.6 days at 20 °C (1st order, r^2=0.99) metabolites not quantified
	pH 7: 68.2 days at 25 °C (1st order, r^2=0.93) Met FD-1-1: 75.8 %AR (30 d)
	pH 9: 4.6-3.8 days at 20 °C (1st order, r^2=0.99) metabolites not quantified pH 9: 4 days at 25 °C (1st order, r^2=0.99) Met FD-1-1: 93.3 %AR (15 d)
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} : 5.9 days Calculated to natural sunlight at 40°N; DT_{50} 12.3 days (12 hour dark light cycle). FD-1-1: 11.2 %AR (6 d) FD-1-1: DT_{50} : 6 days Estimated DT_{50} at 40°N for FD-1-1 18.5 days (12 hour dark light cycle). Unidentified M1: 33.2% (15 d, end of study) FM-6-1: 25.9% (9 d)
Quantum yield of direct phototransformation in water at Σ > 290 nm	3.21 x 10^{-5}mol · Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	No data submitted, substance considered not ready biodegradable.

Degradation in water / sediment

Parent	Distribution (eg max in water 104.6 % after 0 d. Max. sed. 71.9% after 28d)									
Water / sediment system	pH water phase	pH sed [KCl]	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Sand[1]	5.7	5	20	48.7/162	0.70	1.9/6.4	0.995	105/348	0.91	SFO
Clay loam[1]	7.1	7.5	20	117/389	0.67	3.1/10.2	0.984	209/694	0.83	SFO
Sand[2]	5.7	5	20	64/212	0.88	2.6/8.5	0.971	114/379	0.92	SFO
Clay loam[2]	7.1	7.5	20	123/410	0.81	3.5/11.6	0.985	138/458	0.998	SFO
Geometric mean/~~median~~				81.3/272		2.7/9.0		155/398		

[1] [^{14}C-phenyl label]

[2] [^{14}C-imidazole label]

Metabolite FA-1-1	Distribution (eg max in water 10% after 31 d. Max. sed. 12.9 % after 59 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.[1]	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Sand	5.7	5	20	n.r.						SFO
Clay loam	7.1	7.5	20	n.r.						
Geometric mean/median										

[1] no reliable DT_{50} could be calculated for this metabolite

Metabolite imidazole	Distribution (eg max in water 14.6 after 28 d. Max. sed 10.1 % after 14d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Sand	5.7	5	20	13.2						SFO
Geometric mean/median										

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Sand[1]	5.7	5	0.17 (101 d)	10.1 after 59 d	9.2 at 101 days

Clay loam[1]	7.1	7.5	0.29 (101 d)	19 after 101 d	19 at 101 days
Sand[2]	5.7	5	39.5 (95 d)	16.2 after 28 d	5.8 after 95 days
Clay loam[2]	7.1	7.5	19.8 (94 d)	18.5 after 94 d	18.5 after 94 days

[1] [^{14}C-phenyl label]

[2] [^{14}C-imidazole label]

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: Step 1-2 version 1.1 Molecular weight (g/mol): 345.8 Water solubility (mg/L): 10.5 mg/L K_{OC}/K_{OM} (L/kg): 0 L/kg (conservative for aquatic phase) DT_{50} soil (d): parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input DT_{50} water/sediment system (d): 81.3 d (geomean, n=4) DT_{50} water (d): 1000[1] DT_{50} sediment (d): value total system[1] Crop interception (%): parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input No runoff and drainage for glasshouse use
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Crop: cucumber, ornamentals, worst case GAP Crop interception: 50% Number of applications: 6 Interval (d): 7 Application rate(s): 234 g as/ha Application window: no runoff, no drainage
Main routes of entry	Spray drift (0.1% of the dose rate as overall exposure estimation for greenhouse use, 'Dutch' approach).

[1] according to FOCUS Kinetics the $DT_{50,syst}$ was used as $DT_{50,water}$ and 1000 d for $DT_{50,sed}$ and vice versa. Highest PECsw values presented and used for RA

FOCUS STEP	Day after	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)

2 Scenario	overall maximum	Actual	TWA	Actual	TWA
Glasshouse	0 h	0.463		The assumption of a Koc of 0 L/kg assumes no partitioning to the sediment	
	24 h	0.462	0.462		
	2 d	0.462	0.462		
	4 d	0.461	0.462		
	7 d	0.460	0.462		
	14 d	0.458	0.460		
	21 d	0.456	0.459		
	28 d	0.454	0.458		
	42 d	0.449	0.456		

Metabolite FA-1-1 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 195.75 g/mol Water solubility (mg/L): 10.5 (parent value) Soil or water metabolite: soil and water (soil not relevant for the intended use) Koc/Kom (L/kg): 0 L/kg (conservative for aquatic phase) DT_{50} soil (d): parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input DT_{50} water/sediment system (d): 1000 d (default worst- case DT_{50} water (d): 1000 d (default worst-case) DT_{50} sediment (d): 1000 (default worst-case) Crop interception (%):parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input Maximum occurrence observed Water: 21.76 % Sediment: 9.5 %
Parameters used in FOCUSsw step 3 (if performed)	-

Application rate	Crop: cucumber, ornamentals Number of applications: 6 Interval (d): 7 Application rate(s): 234 g as/ha (parent) Depth of water body: 30 cm Application window: no runoff, no drainage
Main routes of entry	Spray drift (0.1% of the dose rate as overall exposure estimation for greenhouse use, 'Dutch' approach).

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.0601		The assumption of a Koc of 0 L/kg assumes no partitioning to the sediment	
	24 h	0.060	0.060		
	2 d	0.060	0.060		
	4 d	0.060	0.060		
	7 d	0.060	0.060		
	14 d	0.060	0.060		
	21 d	0.059	0.060		
	28 d	0.059	0.060		
	42 d	0.058	0.059		

Metabolite imidazole Parameters used in FOCUSsw step 1 and 2	Molecular weight: 68.08 g/mol Water solubility (mg/L): 10.5 (parent value) Soil or water metabolite: water Koc/Kom (L/kg): 0 L/kg DT_{50} soil (d):parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input DT_{50} water/sediment system (d): 13.2 d (n=1) DT_{50} water (d): 1000 d (default worst-case)[1] DT_{50} sediment (d): system value[1] Crop interception (%):parameter not utilised by the calculator as the no runoff or drainage option was selected, any value can be input Maximum occurrence observed Water: 22.3 % Sediment: 10.1 %
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Crop: cucumber, ornamentals Number of applications: 6 Interval (d): 7 Application rate(s): 234 g as/ha (parent) Depth of water body: 30 cm Application window: no runoff, no drainage
Main routes of entry	Spray drift (0.1% of the dose rate as overall exposure estimation for greenhouse use, 'Dutch' approach).

[1] according to FOCUS Kinetics the $DT_{50,syst}$ was used as $DT_{50,water}$ and 1000 d for $DT_{50,sed}$ and vice versa. Highest PECsw values presented and used for RA

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	0.023		The assumption of a Koc of 0 L/kg assumes no partitioning to the sediment	
	24 h	0.023	0.023		
	2 d	0.023	0.023		
	4 d	0.023	0.023		
	7 d	0.022	0.023		
	14 d	0.022	0.022		

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	21 d	0.022	0.022		
	28 d	0.022	0.022		
	42 d	0.022	0.022		

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	No calculations; not required with regard to the intended use
Application rate	-

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	active substance: $\varepsilon = 2.53 \times 10^4$ (at 201.5 nm in methanol)
Photochemical oxidative degradation in air ‡	DT_{50} of 11.7 hours derived by the Atkinson model (version 2001). OH (24 h) concentration assumed = 1.5×10^6 molecules/cm^{-3}.
Volatilisation ‡	from plant surfaces (BBA guideline): -
	from soil surfaces (BBA guideline): -
Metabolites	FA-1-1 is proposed to be volatile

PEC (air)

Method of calculation	-

$PEC_{(a)}$

Maximum concentration	Based on low vP of the parent and the estimated DT_{50} of 11.7 hours no significant concentration in air is expected

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: none from the intended uses Surface Water: triflumizole, FA-1-1, imidazole Sediment: triflumizole, FA-1-1, imidazole Ground water: none from the intended uses

Air:	triflumizole by default

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

Soil (indicate location and type of study)	No data provided - none requested
Surface water (indicate location and type of study)	No data provided - none requested
Ground water (indicate location and type of study)	No data provided - none requested
Air (indicate location and type of study)	No data provided - none requested

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

Not readily biodegradable. Candidate for R53.

Effects on Non-target Species

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Colinus virginianus	a.s.	Acute	>2510	
Anas platyrhynchos	a.s.	Short-term	>1428	>5620
Colinus virginianus	a.s.	Long-term	≥97.2	≥1000
Mammals ‡				
Rat	a.s.	Acute	1057	
Rat	a.s.	Long-term	4.8	
Additional higher tier studies ‡				

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

Crop and application rate

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
	Acute		>1000	10
	Short-term		-	10
	Long-term	0.0005	194400	5
Tier 1 (Mammals)				
	Acute		>1000	10
	Long-term	0.0003	16000	5

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

[2] for cereals indicate if it is early or late crop stage

[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg a.s./L)
Laboratory tests ‡				
Fish				
Salmo gairdneri	NF-114 (purity 98.2%)	96 hr (static)	Mortality, LC_{50}	0.96
Pimephales promelas	a.s.	35 d (flow-through)	Growth NOEC	0.044
Cyprinus carpio	Rocket EC	96 hr (static)	Mortality, LC_{50}	1.28
Oncorhynchus mykiss	Metabolite FA-1-1	96 hr (semi-static)	Mortality, LC_{50}	5.3
Aquatic invertebrates				
Daphnia magna	a.s.	48 h (semi-static)	Mortality, EC_{50}	2.11
Daphnia magna	a.s.	21 d (semi-static)	Reproduction, NOEC	0.18
Daphnia magna	Rocket EC	48 h (static)	Mortality, EC_{50}	1.59
Daphnia magna	Metabolite FA-1-1	48 h (static)	Mortality, EC_{50}	1.64
Sediment dwelling organisms				
Chironomus riparius	Metabolite FA-1-1	28 d (static)	NOEC	10
Chironomus riparius	Metabolite imidazole	28 d(static)	NOEC	10
Algae				
Selenastrum capricornutum	a.s.	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.63 1.66
Selenastrum capricornutum	Rocket EC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.75 2.5 (nom)
Selenastrum capricornutum	Metabolite FA-1-1	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	11 24
Microcosm or mesocosm tests				
not required				

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

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

FOCUS Step 2

State crop, application rate and growth stage, Northern Europe or Southern Europe

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC[3]	TER	Annex VI Trigger[4]
a.s.		Fish	0.96	Acute	0.463	2073	100
a.s.		Fish	0.044	Chronic	0.463	19	10
a.s.		Aquatic invertebrates	1.59	Acute	0.463	3434	100
a.s.		Aquatic invertebrates	0.18	Chronic	0.463	389	10
a.s.		Algae	0.63	Chronic	0.463	1361	10
a.s.		Higher plants[5]	-	Chronic	-	-	10
a.s.		Sediment-dwelling organisms[6]	-	Chronic	-	-	10
FA-1-1		Fish	5.3	Acute	0.0601	88186	100
		Aquatic invertebrates	1.64	Acute	0.0601	27288	100
		Algae	11	Acute	0.0601	183028	10
		Sediment-dwelling organisms	10	Chronic	0.0601	166389	10
imidazole		Sediment-dwelling organisms	10	Chronic	0.023	434783	10
Product[7]		Fish	1.28	Acute	0.463	2765	100
		Aquatic invertebrates	1.59	Acute	0.463	3434	100
		Algae	0.75	Acute	0.463	1620	10

[1] indicate whether Northern of Southern

[2] include critical groups which fail at Step 1.

[3] maximum values have been used (in µg/L!).

[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

[5] only required for herbicides

[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used

[7] Toxicity expressed in mg a.s./L

Bioconcentration			
	Active substance	FA-1-1	imidazole

Bioconcentration			
log $P_{O/W}$	4.8	-	-
Bioconcentration factor (BCF)[1] ‡	1417		
Annex VI Trigger for the bioconcentration factor	100		
Clearance time (days) (CT_{50})	At target concentration of 0.6 µg as/L: 5.8 d (fast phase and 38 d (slow phase) At target concentration of 6.0 µg as/L: 7.5 d		
(CT_{90})	At target concentration of 0.6 µg as/L: 19.3 d (fast phase and 126 d (slow phase) At target concentration of 6.0 µg as/L: 24.9 d		

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

* based on total ^{14}C or on specific compounds

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

Test substance	Acute oral toxicity (LD_{50} µg a.s./bee)	Acute contact toxicity (LD_{50} µg a.s./bee)
a.s. ‡	14*	20
Field or semi-field tests		
not required		

* from a test with the preparation Rocket EC

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

Crop and application rate

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	12	50
a.s.	oral	17	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g as/ha[1])
Typhlodromus pyri ‡		Mortality	63

Species	Test Substance	End point	Effect (LR_{50} g as/ha[1])
Aphidius rhopalosiphi ‡		Mortality	165

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Crop and application rate

Test substance	Species	Effect (LR_{50} g as/ha)	HQ in-field	HQ off-field[1]	Trigger
Rocket EC	*Typhlodromus pyri*	63	not relevant, because only IPM-issue	not relevant, because only IPM-issue	2
Rocket EC	*Aphidius rhopalosiphi*	165	not relevant, because only IPM-issue	not relevant, because only IPM-issue	2

[1] indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)[1,2]	End point	% effect[3]	Trigger value
Encarsia formosa	<24h	Rocket EC 150 g a.s./L,glass plate	30	mortality	4.8 (1 and 4d aging)	30 %
				reproduction	27 (1d aging) +47 (4d aging)	30 %
		directly on pupae	30	reproduction	13	30 %
Encarsia formosa	<24h	Rocket EC 150 g a.s./L, glass plate	180	mortality	98	30 %
Encarsia formosa		Rocket EC 150 g a.s./L, directly on pupae	350	reproduction	2	30%
Encarsia formosa	<24h	Rocket EC 150 g a.s./L, aged residue (3 days) on leaves	1320	mortality	1.3	25%

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)[1,2]	End point	% effect[3]	Trigger value
Phytoseiulus persimilis	1d juveniles	Rocket EC 150 g a.s./L, aged residue (3 days) on bean leaves	180	mortality reproduction	8 6	25% 25%

[1] indicate whether initial or aged residues

[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

[3] indicate if positive percentages relate to adverse effects or not

Field or semi-field tests
not required

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

No studies on earthworms, other soil macro-organisms and soil micro-organisms available. Since the application of Triflumizole involves only indoor treatment on artificial substrate, the risk of Triflumizole for soil organisms is considered not relevant and is therefore not required.

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

No studies on non-target plants available. Since the application of Triflumizole involves only indoor treatment on artificial substrate, the risk of Triflumizole for non-target plants is considered not relevant and is therefore not required.

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

Test type/organism	end point	
Activated sludge	EC_{10} (30 min)	EC_{50} (30 min)
mixed population of micro-organisms (activated sludge)	61 mg form/L	157 mg form/L

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

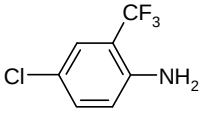
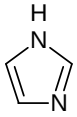
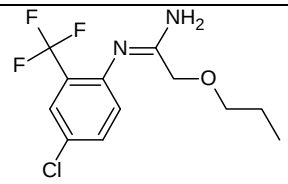
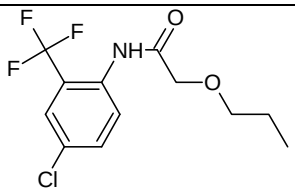
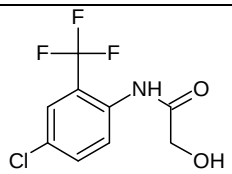
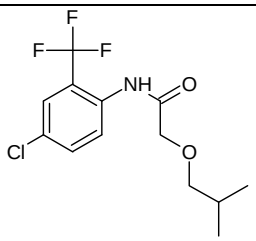
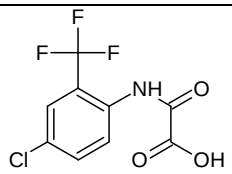
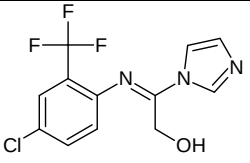
Compartment	
soil	No data, not required for the intended uses
water	triflumizole, metabolite FA-1-1, metabolite imidazole
sediment	metabolite FA-1-1, metabolite imidazole
groundwater	triflumizole due to toxicity to aquatic organisms

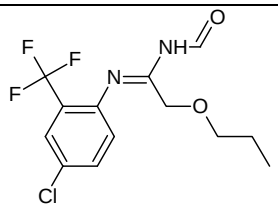
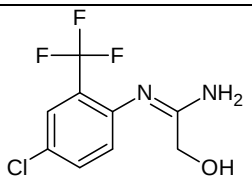
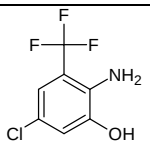
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50/53

	RMS/peer review proposal
Preparation	R50/53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
FA-1-1	4-chloro-α,α,α-trifluoro-*o*-toluidine	
imidazole	imidazole	
FM-6-1	(1*E*)-*N*'-[4-chloro-2-(trifluoromethyl)phenyl]-2-propoxyethanimidamide	
FD-1-1	*N*-[4-chloro-2-(trifluoromethyl)phenyl]-2-propoxyacetamide	
FD-2-1	*N*-[4-chloro-2-(trifluoromethyl)phenyl]-2-hydroxyacetamide	
FD-6-1	*N*-[4-chloro-2-(trifluoromethyl)phenyl]-2-(2-methylpropoxy)acetamide	
FD-7-1	*N*-(4-chloro-2-trifluoromethylphenyl)-oxalamic acid or {[4-chloro-2-(trifluoromethyl)phenyl]amino}(oxo)acetic acid	
FM-2-1	(2*E*)-2-{[4-chloro-2-(trifluoromethyl)phenyl]imino}-2-(1*H*-imidazol-1-yl)ethanol	

FM-5-1	(1*E*)-*N*'-[4-chloro-2-(trifluoromethyl)phenyl]-*N*-formyl-2-propoxyethanimidamide	
FM-8-1	(1*E*)-*N*'-[4-chloro-2-(trifluoromethyl)phenyl]-2-hydroxyethanimidamide	
FA-1-5	2-amino-5-chloro-3-(trifluoromethyl)phenol	

* The metabolite name is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT50	period required for 50 percent disappearance (define method of estimation)
DT90	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC50	effective concentration (biomass)
EC50	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate/effective rate, median
ErC50	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography

GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-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)
Kdoc	organic carbon linear adsorption coefficient
kg	kilogram
KFoc	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC50	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD50	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
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level

OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PECair	predicted environmental concentration in air
PECgw	predicted environmental concentration in ground water
PECsed	predicted environmental concentration in sediment
PECsoil	predicted environmental concentration in soil
PECsw	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pKa	negative logarithm (to the base 10) of the dissociation constant
Pow	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
r2	coefficient of determination
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
t1/2	half-life (define method of estimation)
TER	toxicity exposure ratio
TERA	toxicity exposure ratio for acute exposure
TERLT	toxicity exposure ratio following chronic exposure
TERST	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 Organisation
wk	week
yr	year