CONCLUSION ON PESTICIDES PEER REVIEW

efsa JOURNAL

APPROVED: 5 July 2023

doi: 10.2903/j.efsa.2023.8141

Peer review of the pesticide risk assessment of the active substance metconazole

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Abstract

The conclusions of the EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State, Belgium, and co-rapporteur Member State, the United Kingdom, for the pesticide active substance are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The conclusions were reached on the basis of the evaluation of the representative uses of metconazole as a fungicide on cereals and oilseed rape and as a plant growth regulator on oilseed rape. The reliable end points appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are reported where identified.

Keywords: metconazole, peer review, risk assessment, pesticide, fungicide, plant growth regulator

Requestor: European Commission

Question number: EFSA-Q-2015-00588

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Note/Update: This scientific output, approved on 5 July 2023, supersedes the previous output published on 22 February 2006 (EFSA, 2006).

Declaration of interest: If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

Acknowledgements: EFSA wishes to thank the rapporteur Member State, Belgium, for the preparatory work on this scientific output.

Suggested citation: EFSA (European Food Safety Authority), Álvarez, F., Arena, M., Auteri, D., Binaglia, S. B. L. M., Castoldi, F. A., Chiusolo, A., Colagiorgi, A., Colas, M., Crivellente, F., De Lentdecker, C., De Magistris, I., Egsmose, M., Fait, G., Ferilli, F., Gouliarmou, V., Halling, K., Nogareda, L. H., Ippolito, A., … Villamar-Bouza, L. (2023). Peer review of the pesticide risk assessment of the active substance metconazole. *EFSA Journal, 21*(8), 1–30. https://doi.org/10.2903/j.efsa.2023.8141

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.

Summary

Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659, lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Metconazole is one of the active substances listed in Regulation (EU) No 686/2012.

In accordance with Article 1 of Regulation (EU) No 844/2012, the rapporteur Member State (RMS), Belgium, and co-rapporteur Member State (co-RMS), the United Kingdom, received an application from BASF Agro BV for the renewal of approval of the active substance metconazole.

An initial evaluation of the dossier on metconazole was provided by the RMS in the renewal assessment report (RAR), and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 13 of Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The following conclusions are derived.

The uses of metconazole according to the representative uses as a fungicide on cereals and oilseed rape and as a plant growth regulator on oilseed rape, as proposed at EU level result in a sufficient fungicidal efficacy against the target organisms and a sufficient activity as a plant growth regulator.

The assessment of the data package revealed no issues that could not be finalised or that need to be included as critical areas of concern with respect to **identity, physical/chemical properties and analytical methods**.

In the **mammalian toxicology** section, the exposure estimates for bystander and residential children are above the (A)AOEL for the use on oilseed rape.

In area of **residues**, data gaps were identified for additional confirmation on the presence of metabolites M11 and M21 among the monohydroxylated compounds recovered as a group, additional trials in primary and rotational crops analysing for all compounds covered by the residue definition for risk assessment including triazole derivative metabolites (TDMs). Although the consumer risk assessment has not been finalised, the estimated calculations did not indicate an exceedance of toxicological reference values of metconazole and its monohydroxylated metabolites relevant for risk assessment. The consumer risk assessment related to the TDMs resulting from the use of metconazole should be regarded as provisional only.

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 a data gap was identified for information on the effect of water treatment processes on the nature of residues of both the active substance and its identified metabolites potentially present in surface water, when surface water is abstracted for the production of drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses.

In the area of **ecotoxicology**, a low risk to birds, wild mammals, bees and non-target arthropods other than bees, earthworms, soil macro- and microorganisms, non-target terrestrial plants and sewage treatment organisms is concluded for all the representative uses. Low risk was also concluded for aquatic organisms with the implementation of mitigation measures for the majority of the relevant FOCUS scenarios for all representative uses. Data gaps were identified for birds and mammals, bees and aquatic organisms for the exposure to some of the relevant metabolites in the relevant matrices.

Regarding the endocrine disruption (ED) properties of metconazole, it is concluded that metconazole does not meet the ED criteria for humans and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.

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Background

Commission Implementing Regulation (EU) No 844/2012[1], as amended by Commission Implementing Regulation (EU) No 2018/1659[2] (hereinafter referred to as 'the Regulation') lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009[3]. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3). Furthermore, in accordance with Article 13(3a), where the information available in the dossier is not sufficient to conclude the assessment on whether the approval criteria for endocrine disruption are met, additional information can be requested to be submitted in a period of minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS, Belgium, and co-RMS, the United Kingdom, received an application from BASF Agro BV for the renewal of approval of the active substance metconazole. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (the United Kingdom), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on metconazole in the RAR, which was received by EFSA on 26 February 2018 (Belgium, 2018).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, BASF Agro BV, for consultation and comments on 1 August 2018. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 1 October 2018. At the same time, the collated comments were 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 13(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 20 November 2018. 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 that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues and ecotoxicology.

In addition, following a consultation with Member States in the Pesticides Peer Review Experts' meeting 06 (June 2019), it was considered necessary to apply an additional clock stop of 30 months in accordance with Commission Implementing Regulation (EU) No 2018/1659, to be able to conclude whether the approval criteria for endocrine disruption in line with the scientific criteria for the determination of endocrine-disruption properties, as laid down in Commission Regulation (EU) 2018/605[4], are met.

[1] Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

[2] Commission Implementing Regulation (EU) No 2018/1659 of 7 November 2018 amending Implementing Regulation (EU) No 844/2012 in view of the scientific criteria for the determination of endocrine-disruption properties introduced by Regulation (EU) 2018/605.

[3] Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

[4] Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No 1107/2009 by setting out scientific criteria for the determination of endocrine-disruption properties. OJ L 101, 20.4.2018, p. 33–36.

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, were compiled by EFSA in the format of an evaluation table.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, together with the outcome of the expert consultation and the written consultation on the assessment of additional information, 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 June 2023.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of metconazole as a fungicide on cereals and oilseed rape and as a plant growth regulator on oilseed rape, as proposed by the applicant. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR and considered during the peer review, if any, are presented in the conclusion.

A list of the relevant end points for the active substance and the formulation is provided in Appendix B.

A key supporting document to this conclusion is the peer review report (EFSA, 2023), 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 comprises the following documents, in which all views expressed during the course of the peer review, including minority views, where applicable, can be found:

- the comments received on the RAR;
- the reporting tables (23 November 2018 and 19 September 2022[5]);
- the evaluation table (4 July 2023);
- 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 revisions (Belgium, 2023), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

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

The active substance and the formulation for representative uses

Metconazole is the ISO common name for a mixture of four diastereomers (1*RS*,5*RS*;1*RS*,5*SR*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol (IUPAC). The pair of enantiomers (1*R*,5*R*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol and (1*S*,5*S*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol are referred as *trans*-metconazole and the pair of enantiomers (1*R*,5*S*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol and (1*S*,5*R*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol as *cis*-metconazole.

The representative formulated product for the evaluation was 'BAS 555 01 F', an emulsifiable concentrate (EC) containing 90 g/L metconazole.

The representative uses evaluated were spraying application for control of a broad range of fungal diseases in cereals and oilseed rape and as a plant growth regulator in oilseed rape. Full details of the good agricultural practices (GAPs) can be found in the list of end points in Appendix B.

Data were submitted to conclude that the use of metconazole according to the representative uses proposed at EU level results in a sufficient fungicidal efficacy against the target organisms and a sufficient activity as a plant growth regulator, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014).

[5] Reporting table following consultation on the revised RAR on the assessment of the endocrine-disruption properties made available after the 30-month clock stop.

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: European Commission, 2000a,b, 2010.

The proposed specification for metconazole is based on batch data from industrial scale production. The proposed minimum purity of the technical material is 940 g/kg with a range of 800–950 g/kg for *cis*-metconazole (1*SR*,5*RS*). Toluene and ethylcyclohexane are toxicological relevant impurities with the maximum levels of 2 g/kg. These impurities are also part of the current reference specification (the same levels) however, their consideration as relevant triggers an update of the current reference specification. The RMS proposed that the minimum purity of the active substance and the maximum levels of the significant impurities to be kept as in the current reference specification. However, EFSA noted that based on the data of the renewal procedure, a higher minimum purity of the active substance and lower maximum levels for some of the significant impurities could be set. The batches used in the (eco) toxicological assessment support the current and the newly proposed reference specification (See Sections 2 and 5). There is no FAO specification available for metconazole.

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

Adequate methods are available for the generation of data required for the risk assessment. Methods of analysis are available for the determination of the active substance and impurities in the technical material and for determination of the active substance in the formulation for the representative uses. Data gap for analytical methods for analysis of the relevant impurities in the representative formulation was set (see Section 10).

Metconazole residues in food and feed of plant origin can be monitored by DFG S19 method using liquid chromatography with tandem mass spectrometry (LC–MS/MS) with a limit of quantification (LOQ) of 0.005 mg/kg (for each *cis*- and *trans*- isomers) in all commodity groups. However, a data gap was identified for verification of the efficiency of the extraction procedure used in the monitoring method (see Section 10). Metconazole residues in food of animal origin can be determined by DFG S19 LC–MS/MS with LOQ of 0.005 mg/kg (for each *cis*- and *trans*- isomers) in all animal matrices. The efficiency of the extraction procedure used was not verified (data gap, see Section 10).

Metconazole residues in environmental compartments could be monitored by LC–MS/MS with LOQ of 0.002 mg/kg (for each of four enantiomers, using chiral column) and 0.002 mg/kg (for each *cis*- and *trans*- isomers, not chiral column) in soil, 25 ng/L (for each of four enantiomers, using chiral column) in water and 0.0429 μg/m^3 (total metconazole) in air.

LC–MS/MS method can be used for monitoring of metconazole in body fluids (blood and urine) with an LOQ of 0.005 mg/L (for each *cis*- and *trans*- isomers). Metconazole in body tissues could be analysed by the monitoring methods for residue in food of animal origin.

2. Mammalian toxicity

The toxicological profile of the active substance metconazole and its metabolites was discussed at the Pesticides Peer Review Experts' Meeting 07 in June 2019, and, assessed based on the following guidance documents: European Commission (2003, 2012), EFSA PPR (2017, 2014), EFSA (2014) and ECHA, 2017.

Regarding the proposed reference specification, the impurities toluene and ethylcyclohexane are identified as relevant, with a maximum acceptable level of 2 g/kg for both (as specified). The test material used in toxicity studies is considered sufficiently representative of the original and newly proposed reference specification for the active substance and associated impurities. The analytical methods used in feed, body fluids and tissues, air and any additional matrices used in support of the toxicity studies are considered fit-for-purpose.

Key toxicological studies were performed with either the 85:15% ratio *cis*/*trans* (called *cis*/*trans* hereafter) or the 95:5% ratio *cis*/*trans* (called *cis* hereafter). Based on the available toxicological data, indicating that the *trans*-isomer is less potent than the *cis* isomer, it can be assumed that any shift from *cis* to *trans* is unlikely to be more toxic.[6]

[6] Refer to experts' consultation 2.17 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

Absorption, distribution, metabolism and excretion were investigated for metconazole (both *cis/trans* and *cis*). The oral absorption of metconazole is estimated to account for > 80% of the administered low dose.[7] Excretion occurs predominantly through the bile, with smaller amount excreted in urine. In the rat, metconazole is widely distributed throughout the body, with highest levels in the gastro-intestinal tract, liver and adrenals, showing no evidence of bioaccumulation. There was no indication that the metabolism of the cis/trans mixture was different than the cis isomer, including predominantly phase-I metabolism (rather than conjugations). No major metabolite, i.e. at a level higher than 10% of the administered dose of the parent, was identified. Therefore, the residue definition for body fluids and tissues should include only metconazole (sum of isomers). Based on comparative *in vitro* metabolism, no major metabolic inter-species (human, rat, rabbit) differences have been observed and no unique human metabolites have been identified.

The **acute** oral toxicity data provided for metconazole (*cis/trans* and *cis*) support the harmonised classification[8] as harmful if swallowed (Acute Tox. 4). Metconazole (*cis/trans* and *cis*) is not acutely toxic after dermal or inhalatory exposure, not skin or eye irritant nor skin sensitiser. Testing for phototoxicity is not required for metconazole (based on UV absorption data).

Short-term toxicity studies with metconazole (*cis/trans* and *cis*) were provided for rats, mice and dogs. The main target organs were liver (with hepatocellular vacuolation/hypertrophy) and adrenal (vacuolation) in rats, liver (hypertrophy/vacuolation) and spleen (lymphoid hyperplasia) in mice; while in dogs, critical effects included reduction in body weight gain; increased level of alkaline phosphatase (AP); and lens degeneration. The relevant short-term no observed adverse effect level (NOAEL) (oral) for the most sensitive species (90-day mouse study) was set at 4.6 mg/kg body weight (bw) per day. In a 21-day dermal rat study, the relevant NOAEL was 250 mg/kg bw per day based on liver and thymus weight changes.

Based on the overall weight of evidence from the available genotoxicity studies (addressing mutagenic, clastogenic and aneugenic potential), metconazole (both cis/trans and cis) is considered unlikely to be genotoxic in humans.

Long term toxicity of metconazole (*cis/trans*) was investigated in rats and mice. The liver was the main target organ, with both neoplastic and non-neoplastic effects. The relevant NOAEL for general toxicity is 4.3 mg/kg bw per day in rats based on effects in liver and spleen at 13.1 mg/kg bw per day. For the carcinogenic findings, despite the presence of some preneoplastic changes in the liver, no tumours were observed in rats.[9] In mice, liver tumours were considered treatment-related and not sufficiently demonstrated as not relevant to humans due to the lack of experimental data on the mode of action. No consensus was reached by the experts on whether these effects may trigger a proposal for classification.[10] The relevant NOAEL for systemic toxicity and carcinogenicity in mice is 4.4 mg/kg bw per day based on neoplastic and non-neoplastic effects in the liver.

For the assessment of **reproductive** toxicity, several one- and two-generation studies with rats were provided for metconazole (*cis/trans* and *cis*). Based on the two-generation study with the *cis/trans*, the overall parental NOAEL is 10 mg/kg bw per day based on mortality, decreased body weight, increased ovary and liver weight, hepatocyte fatty change and centrilobular hypertrophy, increased ovary follicular and lutein cysts. The overall NOAEL for the offspring is 10 mg/kg bw per day based on decreased viability index, body weight and brain weight. The overall NOAEL for reproductive toxicity is also 10 mg/kg bw per day based on decreased oestrus cycle length, increased gestation length, decreased gestation index, decreased number of live litters born. These effects were concluded as not triggering a classification as hazardous for fertility. Based on hepatocellular and adrenocortical vacuolation in rats and mice (short- and long-term studies) and maternal toxicity in a rat multigenerational study, the majority of the experts supported that the criteria for classification as STOT-RE2 may be triggered.[11]

[7] Refer to experts' consultation 2.1 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

[8] Commission Regulation (EC) No 790/2009 of 10 August 2009 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures. OJ L 235, 5.9.2009, p.1–439.

[9] Refer to experts' consultation 2.8 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

[10] Refer to experts' consultation 2.7 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

[11] 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.

Both metconazole *cis/trans* and *cis* were tested in **developmental** toxicity studies. In the rat, severe effects on development (e.g. ventricular septal defects) were only observed at maternal toxic doses in one study only. In the rabbit, developmental effects included hydrocephaly (at 10 mg/kg bw per day), a finding considered treatment related and occurring even at doses similar or below maternal toxicity. The experts agreed that the overall developmental toxicity data support the current harmonised classification Repr. Cat 2. The agreed NOAELs for developmental and maternal toxicity were both 10 mg/kg bw per day in rats and 4 mg/kg bw per day in rabbits.

No potential for **neurotoxicity** or **immunotoxicity** was observed in the available toxicity studies. In the 2-week and 4-week neurotoxicity studies, no neurotoxic effects were observed up to the highest dose tested (47 mg/kg bw per day). No studies on delayed neurotoxicity or developmental neurotoxicity were required.

The potential concern for an increasing prevalence of azole-resistant strains in *A. fumigatus* was discussed by the experts.[12] It was considered necessary to reflect it in the EFSA conclusion even though there is currently no clear evidence for the potential link between the occurrence of azole-resistant *A. fumigatus* in the environment and the spread of azole-resistant *Aspergillus* in infected patients. Indeed, ongoing research has already shown that the mutation seen in the fungus in the clinical setting and in the environment is the same.

All toxicological reference values (i.e. the **acceptable daily intake** (ADI), the **acute reference dose** (ARfD), the **acceptable operator exposure level** (AOEL) and the **acute acceptable operator exposure level** (AAOEL)) are 0.01 mg/kg bw per day based on developmental effects in the rabbit studies, applying an increased uncertainty factor (UF) of 400 in order to obtain a higher margin of safety (1000x) compared to the dose level where the effect was observed.[13] No correction for oral absorption was necessary for the (A)AOEL. These reference values are the same as those derived during the first peer review (European Commission, 2021).

For the formulation for the representative use 'BAS 555 01 F', the dermal absorption values are 5.1% for the concentrate, 35% for the dilution applied on cereals and 48% for the dilution applied on oilseed rape (considering pro-rata correction).[14] For the use on cereals, all exposure estimates for operators, workers, residents and bystanders are below the (A)AOEL. For the use on oilseed rape, the exposure estimates for bystander and residential children are above the (A)AOEL.

For the **metabolites** of metconazole (M11, M21, M30 and M31), no genotoxic potential was identified on the basis of Ames tests and quantitative structure–activity relationship (QSAR) analysis. Their general toxicity profile could not be concluded on the basis of the available data (acute oral toxicity study for M11).[15] Consequently, a data gap is set for further assessment of the general toxicity of the metabolites M11 and M21 (see also Section 3). For the triazole derivative metabolites (TDMs), triazole acetic acid (TAA), triazole alanine (TA), 1,2,4-triazole (1,2,4-T) and triazole lactic acid (TLA), their respective toxicological reference values were previously adopted during the Pesticides Peer Review Experts' Meeting 162 (EFSA, 2018; see Appendix B).

3. Residues

The assessment in the residues section is based on the following guidance documents: OECD, 2009, 2011; European Commission, 2011 and JMPR, 2004, 2007.

Metconazole was discussed at the Pesticides Peer Review Experts' Meeting 09 in June 2019.

Metabolism in primary crops was investigated in fruits (banana and mandarin), pulses/oilseeds (oilseed rape and peas) and cereals/grass crops (wheat) labelled to all rings, 14C-cyclopentyl or 14C-chlorophenyl and 14C-triazolyl metconazole (or cis-metconazole) at sufficient dose rate following foliar applications. Metconazole was the major residue in most of the investigated crops (e.g. 87% of total

[12] Refer to experts' consultation 2.18 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

[13] Refer to experts' consultation 2.19 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

[14] It was noted that based on the BfR template (excel file to support calculations for dermal absorption from in vitro studies in EFSA PPR 2017), not available at the time of the peer review of the RAR, the dermal absorption value for the second dilution could be revised to 33% which may lead to non-dietary exposure estimates below the (A)AOEL for the use on oilseed rape. However, discussion on dermal absorption did not take place during the peer review since comments were not raised at that time (calculations based on the BfR template were made available at the publication stage, not peer-reviewed). The update of the dermal absorption value is supported by EFSA and RMS and may be further considered by risk managers.

[15] Refer to experts' consultation 2.15 in the Report of the Pesticides Peer Review Experts' Meeting 07 session 2 in June 2019 (EFSA, 2023).

radioactive residue (TRR) in banana) except wheat grain where triazole alanine (TA) and triazole acetic acid (TAA) were found the major components (69% and 25% of TRR, respectively). TA was found relevant in oil rape seeds and peas seeds too. Different monohydroxylated metconazole compounds (free and conjugates) such as M11 and M21 were recovered in various amounts in all matrices[16] except in wheat grain. M11 and M21 were found individually in fruits crops and wheat feed items (up to 10% of TRRs). Since in peas seeds significant amount of radioactivity (67% of TRR) was recovered as group of monohydroxylated compounds of metconazole (free and conjugates) not individually, a data gap is set to confirm the presence and the ratio of M11 and M21 among these (data gap leading to the consumer risk assessment not finalised, see Section 9.1). Whether these monohydroxylated compounds are covered by the toxicity of the parent compound still needs to be confirmed (see Section 2). The metabolic pattern was comparable for all three crop categories.

In the rotational crop metabolism study in root and tuber crops, leafy crops and cereal (small grain), cultivated after representative soil ageing intervals, metconazole, TA, TAA and M12 a monohydroxylated metabolite were identified as major residues. It was noted that major part of the radioactivity remained unidentified (e.g. 63% of TRR in wheat grains). Nevertheless, considering the information from primary metabolism studies, the experts agreed that an additional study is not required.[17] The overall metabolism in rotational crops is similar to metabolism in primary crops. Additionally, taken into account the outcome of peer review on triazole metabolites (EFSA, 2018) where triazole lactic acid (TLA) was found in residue field trials and that 1,2,4 triazole (1,2,4-T) residues are not stable in rapeseed, the experts agreed that these metabolites should be included in the residue definition (RD) for risk assessment. Considering all the available information on monohydroxylated compounds and pending the confirmation on the presence and the ratio of M11 and M21 among the monohydroxylated compounds recovered as a group and their toxicity, the RD for risk assessment is provisionally proposed as: metconazole (sum of isomers) and its monohydroxylated derivatives (free and conjugated). Tentative conversion factors have been derived, based on relative occurrence of all monohydroxylated metabolites (free and conjugated) compared to the parent compound in the primary crop metabolism studies. The provisional RD for risk assessment may be reconsidered once additional data on the identity, magnitude and toxicity of the main monohydroxylated metabolites would become available (see above-mentioned data gaps on toxicity and identity/relative magnitude). Separately the TDMs TA, TLA, TAA, 1,2,4-T are also included as agreed during the review of TDM covering all primary and rotational crops (EFSA, 2018). The residue definition for enforcement is proposed as metconazole (sum of isomers) only.

The nature of metconazole residues under standard hydrolysis conditions was investigated and metconazole was found stable. Processing trials for metconazole, TA, TAA and TLA in cereals and oilseed rape were submitted and processing factors were derived (see Appendix B).

Field trials covered by validated analytical methods and storage stability were submitted for oilseed rape, wheat and barley in Europe (NEU & SEU). In oilseed rape, analysis of metconazole, TA, TLA, TAA, 1,2,4-T was conducted in seeds in all trials. In cereals, analysis of parent was conducted in grain and straw in all trials and partly the trial's analysis of TA, TLA, TAA, 1,2,4-T was performed using validated analytical methods. Due the insufficient data on TDMs, a data gap was identified for additional GAP compliant residue trials in barley and wheat (see Section 9.1).

Two rotational field trials analysed for metconazole (sum of isomers) investigated in EU at two plant back intervals were submitted. Additional US trials analysed for metconazole and some monohydroxylated compounds but not all were made available. Since the data were not sufficient, a data gap is set for four rotational crops field trials (2NEU/2SEU), analysing for all compounds covered by the RD for risk assessment (including TDMs and monohydroxylated metconazole derivatives and their conjugates). These trials should be conducted in the EU with at least root and tuber vegetables, cereals, oilseeds and leafy vegetables as rotational crops (see Section 9.1).

Metabolism of metconazole has been investigated in ruminants and poultry, using 14C-cyclopentyl or 14C-chlorophenyl and 14C-triazolyl labelled metconazole (or cis-metconazole). High level of excreted radioactivity is noted in all matrices up to 96% of TRRs. Metconazole was found in all matrices, predominantly in egg yolk, fat, goat liver and muscle above 10% of TRRs. 1,2,4-T was found at high proportions in hen matrices (13–77% of TRR), but not in ruminants. Metconazole monohydroxylated

[16] Refer to the experts' consultation 3.2 in the Report of the Pesticides Peer Review Experts' Meeting 09 (24–28 June 2019) (EFSA, 2023).

[17] Refer to the experts' consultation 3.5 in the Report of the Pesticides Peer Review Experts' Meeting 09 (24–28 June 2019) (EFSA, 2023).

individually compounds were found at relevant levels M12 in liver and kidney (max 21% of TRR), while M1, M31, M32 found all in free and conjugated forms up to 24% of TRRs mainly in liver and kidney.

Feeding studies conducted with metconazole in ruminant and laying hens analysed for metconazole, M1 and M12 were provided; no residue above 0.02 mg/kg was found at the 1 N dose rate. Although the studies were considered not fully reliable since the stability of M1 and M12 residues in animal products was not demonstrated, they were sufficient to justify the exclusion of M1 and M12 from the RA-RD. In addition, following the expert consultation, the RMS updated the livestock dietary burden calculation (DB) including all the monohydroxylated compounds showing no significant livestock exposure increase hence significant levels of metabolites M1, M12, M31 or M32 are unlikely to occur in animal products. Therefore, for the risk assessment the residues of metconazole (sum of isomers) and separately the TDMs TA, TLA, TAA, 1,2,4-T are considered, as agreed during the review of TDM. For enforcement, the residue definition is proposed as metconazole (sum of isomers) for all animal matrices.

Studies on the change on isomeric ratio of cis/trans metconazole residues in plants and animals show a small change in plants from ratio of 85/15 to 78/22 in barley grain while in animal, a clear tendency of a preferential metabolism of the cis-isomer(s) was observed with the maximum shift in goat liver of 34/66. From toxicological evaluation, the shift resulted likely no more toxic with no impact on the consumer risk assessment as both isomers are included in the residue definitions.

Two provisional consumer risk assessment calculations were performed for metconazole residues with EFSA PRIMo rev.2 and PRIMo rev 3.1 using toxicological reference values of metconazole, inputs values from the residue trials for the representative use and conversion factor derived from the metabolism studies to compensate the contribution of monohydroxylated derivatives of metconazole. For these calculations, it was provisionally assumed the monohydroxylated compounds are covered by the toxicity of metconazole. The dietary intake calculations should be regarded as provisional, and they should be revisited when all missing data are provided (see Section 9.1). The estimated intakes of metconazole and the monohydroxylated metconazole derivatives in primary were below the toxicological reference values for all European groups (see detailed calculations in Appendix B). Tentative estimation intakes for rotational crops affected by a high level of uncertainty were made for metconazole and monohydroxylated compounds of metconazole resulting in an exposure below the toxicological reference values for all European groups.[18]

Regarding residues of TDMs, although is not expected to exceed the toxicological reference values the current consumer risk assessment is also considered provisional pending the additional residue trials in wheat/barley, honey and the rotational crops field studies (see Section 9.1).

Metabolism studies for fish were not submitted since the calculated dietary burden was below 0.1 mg/kg dry feed. Regarding the magnitude of residues in pollen and bee's products for human consumption, four trials analysed for metconazole were submitted which were found acceptable. However, since the studies provided cover only metconazole but not the TDMs, additional trials for pollen and bee products analysing for all compounds covered by the residue definition for risk assessment are needed to cover these metabolites (data gap, see Section 10).

The consumer risk assessment from the consumption of drinking water is not finalised considering the lack of appropriate information to address the effect of water treatment processes on the nature of residues, potentially present in surface water and groundwater, when surface water or groundwater is abstracted for drinking water (see Sections 4 and 9.1).

It is highlighted that under the current renewal of the approval of metconazole, it is provisionally proposed to include the monohydroxylated metconazole derivatives in the risk assessment residue definition in plants. This proposal could have an impact on the maximum residue levels (MRLs) derived during the review of the existing MRLs under Art 12 of the Regulation (EC) No 396/2005 (EFSA, 2011).

4. Environmental fate and behaviour

Metconazole is a mixture of two pairs of diastereomers, no shift in the isomeric and enantiomeric ratio during incubation was observed in soil, water and sediment.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, metconazole exhibited medium to high persistence, forming the major (> 10% applied

[18] See a detailed roughly estimations on the consumer dietary intakes from rotational crops provided by the RMS in Vol. 1 of the Renewal Assessment Report.

radioactivity (AR)) metabolite 1,2,4-triazole (max. 9% AR), which exhibited moderate to high persistence. Mineralisation of the 3,5-triazole ring ^{14}C radiolabel to carbon dioxide accounted for 1–10% AR after 120 days, and of the phenyl ring ^{14}C radiolabel accounted for 14% AR after 119 days. The formation of unextractable residues (not extracted by acetonitrile/water) for these radiolabels accounted for 39–42% AR after 120 days and for 23.1% after 119 days, respectively. The formation of unextractable residues (not extracted by acetonitrile/water) for the cyclopentanol ring ^{14}C radiolabel accounted for 12–28% AR after 112 days. Under dark anaerobic conditions and in laboratory soil photolysis studies, no novel breakdown products were identified.

Metconazole exhibited low mobility in soil. It was concluded that the adsorption of metconazole was not pH dependent. A data gap was identified for a batch adsorption study for 1,2,4-triazole in at least three soils (see Section 10).

In satisfactory field dissipation studies carried out at four sites in Germany, four in the UK and two in France (spray application to the soil surface on bare soil plots in late spring), and two in Germany, one in Denmark, one in France, one in Italy and one in Spain (sand covered), metconazole exhibited low to very high persistence. In satisfactory field dissipation studies carried out at one site in Germany, one in the UK, one in Italy and one in Spain (spray application to the soil surface on bare soil plots in late spring), metabolite 1,2,4-triazole exhibited low to moderate persistence.[19] Field study DegT50 values were derived following normalisation to FOCUS reference conditions (20°C and pF2 soil moisture) according to the EFSA (2014) DegT50 guidance. The field data endpoints were not combined with lab values to derive modelling endpoints.

In laboratory incubations in dark aerobic natural sediment water systems, metconazole exhibited high to very high persistence, forming the major metabolite M555F013 cis (max. 9% AR in water). The unextractable sediment fraction (not extracted by acetonitrile/water) was the major sink for the triazole ring ^{14}C and phenyl ring radiolabels, accounting for 15–20% AR at study end (182 days) and for 13–20% AR at study end (99 days), respectively. Mineralisation of phenyl ring radiolabel accounted for only 0.9–1.2% AR at the end of the study. In laboratory sterile aqueous photolysis experiment, no chromatographically resolved component (excluding metconazole) accounted for > 10% AR.

The necessary surface water and sediment exposure assessments (Predicted environmental concentrations (PEC) calculations) were carried out for the metabolites M555F013 cis and 1,2,4-triazole using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator). For the active substance metconazole, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available.[20] The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of up to 10 m being implemented for the drainage scenarios (representing a 58–86% spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of up to 10 m (reducing solute flux in run-off by 80% and erosion run-off of mass adsorbed to soil by 95%) being implemented for the run-off scenarios. The SWAN tool (version 4.0.1) was appropriately used to implement these mitigation measures in the simulations. However, risk managers and others may wish to note that while 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. metconazole), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.[20] The potential for groundwater exposure from the representative uses by metconazole above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios for metconazole and metabolite 1,2,4-triazole.

The applicant did not provide appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water. This has led to the identification of a data gap and results in the consumer risk assessment not being finalised regarding treatment of surface water (see Section 9.1).

[19] Endpoints for 1,2,4-triazole accepted at EU level [CRD (2014): Triazole derived metabolite: 1,2,4-Triazole. Proposed revision to DT50 Summary, Scientific evaluation and Assessment July 2011, revised September 2011 (after comments from MS and EFSA) and further revised January 2013 (minor clarifications added post-commenting), 24 Oct. 2014].

[20] Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix B of this conclusion. A key to the wording used to describe the persistence and mobility of the compounds assessed can be found in Appendix C of this conclusion.

5. Ecotoxicology

The risk assessment was based on the following documents: European Commission (2002), SETAC (2001), EFSA (2009), EFSA PPR Panel (2013), EFSA (2013) and ECHA/EFSA (2018).

Metconazole has been discussed at the Pesticides Peer Review Experts' Meeting 08 (June 2019).

The batches used in the ecotoxicity studies are considered sufficiently representative of the proposed and current technical specification.

All the available ecotoxicity studies were conducted either with metconazole 85:15 *cis:trans* or metconazole 87:13 *cis:trans* or metconazole 95% *cis*. Although in the majority of the cases, metconazole 85:15 *cis:trans* was used for risk assessment, no major difference in terms of toxicity was noted.

For **birds**, acute toxicity studies with bobwhite quail were available for the active substance metconazole and the formulation for the representative uses 'BAS 555 01 F'. Short-term dietary and long-term toxicity data were also available for metconazole with bobwhite quail and mallard duck. The findings of these studies were discussed by the experts during the meeting. Owing to the higher toxicity observed in the avian short-term dietary studies relative to the acute studies, the experts agreed to use a geometric mean of the available LC50 values for the acute risk assessment. A long-term no observed effect concentration (NOEC) was also agreed for use in risk assessment.[21] Based on the available data and the risk assessment, a low acute and long-term risk via dietary exposure to birds was concluded for all representative uses of 'BAS 555 01 F'.

Regarding **wild mammals**, acute, reproductive and developmental toxicity, as well as oral exposure data were available for metconazole. An acute toxicity study with 'BAS 555 01 F' to rats was also available. Considering the effects seen in the developmental, reproductive and oral exposure studies, an ecotoxicologically relevant chronic toxicity endpoint for wild mammals was agreed by the experts.[22] On the basis of the available data and risk assessment, a low acute and long-term risk via dietary exposure to mammals was concluded for all representative uses of 'BAS 555 01 F'.

A low risk to birds and mammals from secondary poisoning and from consumption of contaminated water was concluded for metconazole.

Based on the lower or similar toxicity of the pertinent plant metabolites TA, TLA, TAA, 1,2,4-T to birds and mammals compared to metconazole and the expected lower level of exposure, low risk from exposure to metabolites to birds and wild mammals is concluded. No toxicity data and risk assessment were available on monohydroxylated derivatives (free and conjugated) (data gap, see Section 10).

Acute and chronic toxicity studies were conducted with **aquatic organisms** (fish, aquatic invertebrates, including sediment dwellers and algae) for the active substance metconazole and the formulation for the representative uses 'BAS 555 01 F'. Toxicity data with *Lemna gibba* were also available for metconazole.

A low acute risk to fish was indicated at FOCUS Step 2 for the representative uses of 'BAS 555 01 F'.

For **fish**, three early life stage studies and a full life cycle study were available. The chronic endpoint was discussed and agreed in the Pesticides Peer Review Experts' Meeting 08 (June 2019).[23] Based on that, a high chronic risk to fish was concluded for all the FOCUS scenarios at Step 3 for all the representative uses of 'BAS 555 01 F', except for the scenarios D5 for the representative use on winter oilseed rape (spring application). The implementation of mitigation measures up to 10 m no spray buffer zone and 10 m vegetative filter strip was needed to conclude low chronic risk to fish for the majority of the relevant FOCUS scenarios for all representative uses (7 of 9 FOCUS scenarios for the representative use on winter cereals; 4 of 5 for the representative use on spring cereals; 5 of 6

[21] Refer to the experts' consultations 5.1 and 5.3 in the Report of the Pesticides Peer Review Experts' Meeting 08 in June 2019 (EFSA, 2023).

[22] Refer to the experts' consultation 5.5 in the Report of the Pesticides Peer Review Experts' Meeting 08 in June 2019 (EFSA, 2023).

[23] Refer to the experts' consultation 5.6 in the Report of the Pesticides Peer Review Experts' Meeting 08 in June 2019 (EFSA, 2023).

for the representative use on winter oilseed rape (autumn application); 4 of 5 for the representative use on winter oilseed rape (spring application)).[24]

Low risk was also concluded for **aquatic invertebrates** including **sediment dwellers**. Low risk was indicated for **algae**, and **aquatic macrophytes** (*Lemna*) at FOCUS Step 1 for the representative uses of 'BAS 555 01 F'.

The risk to fish, aquatic invertebrate and algae from the pertinent surface water metabolite M555F020 (1,2,4 triazole) was assessed to be low at FOCUS Step 2. No toxicity data with the metabolite M555F013 cis and aquatic organisms were available. The risk from the metabolite M555F013 cis was therefore assessed by considering 10 times higher toxicity than the parent. Based on this, low acute risk to fish and low risk to algae were indicated. The risk to aquatic invertebrates and a chronic risk to fish, however, could not be excluded from metabolite M555F013 cis (data gap, see Section 10).

Sufficient acute, oral and contact, toxicity data for metconazole and the formulation for the representative uses 'BAS 555 01 F' were available with honey**bees**. Data on chronic toxicity to adult honeybees from metconazole were also available. For honeybee larvae, there were 72-h and 22-day (repeated exposure) toxicity data with metconazole.

The risk assessment to honeybees was performed in accordance with European Commission (2002) and a low acute risk to adult honeybees via oral and contact exposure to metconazole was indicated.

The risk assessment was also conducted in accordance with EFSA (2013). A low risk to adult (acute oral, acute contact and chronic) honeybees and honeybee larvae (chronic oral) was concluded at the screening step for all representative uses of metconazole.

One semi-field (tunnel test) study on flowering *Phacelia tanacetifolia* during active honeybee foraging conditions in line with OECD test guideline 75 (OECD, 2007) was available with the different formulation 'BAS 555 00 F', which was noted to be of equivalent acute toxicity to 'BAS 555 01 F'. The results of this study did not contradict the low risk indicated in the Tier 1 risk assessment.

Acute oral and contact toxicity data with adult bumblebees and risk assessment in accordance with EFSA (2013) were also conducted by RMS for metconazole. Based on these, a low acute risk to adult bumblebees was concluded.

Data on the assessment of sublethal effects on honeybees were not available (see Section 10).

No assessment of the accumulative effects was available. No risk assessment following exposure to possible metabolites was available (data gap, see Section 10). No data were available for solitary bees.

For **non-target terrestrial arthropods**, Tier 1 toxicity data for the representative formulation 'BAS 555 01 F' were available with the two standard test species *Typhlodromus pyri* and *Aphidius rhopalosiphi* and two additional test species *Chrysoperla carnea* and *Aleochara bilineata*. For 'BAS 555 01 F', extended laboratory tests with *Typhlodromus pyri* and *Aphidius rhopalosiphi*, and an aged residue test with *Typhlodromus pyri* were also available.

The in-field risk to non-target terrestrial arthropods was assessed as high at Tier 1. Refinement was available considering the data with the two additional test species and the available Tier 2 data with the standard test species. It was concluded that a low in-field risk to non-target terrestrial arthropods can be anticipated for the representative uses of 'BAS 555 01 F'. Low off-field risk to non-target terrestrial arthropods was identified at Tier 1 from exposure to metconazole for all the representative uses of 'BAS 555 01 F'.

Standard toxicity data for the formulation for the representative uses 'BAS 555 01 F', for 'BAS 555 00 F', the active substance metconazole and the pertinent soil metabolite 1,2,4 triazole were available with **earthworms**. Low risk to earthworms was concluded based on the available data for all the representative uses. However, an earthworm field study was also available with the formulation 'BAS 555 00 F' and was applied at single rate of 180 g metconazole/ha. A decrease in the abundance of earthworm juveniles after 1 year following application was observed, but the application regime differed from the representative uses. Thus, although the results were not considered directly relative to the risk assessment, uncertainties were identified in the outcome of the Tier 1 risk assessment for earthworms.[25]

[24] High risk was concluded for the FOCUS scenarios D1 and D2 for the representative use on winter cereals; D1 for the representative use on spring cereals; D2 for the representative use on winter oilseed rape (autumn application and spring application).

[25] Refer to the experts' consultation 5.7 in the Report of the Pesticides Peer Review Experts' Meeting 08 in June 2019 (EFSA, 2023).

For **soil macro-organisms** other than earthworms, experimental data were available with *Folsomia candida* and *Hypoaspis aculeifer* for 'BAS 555 01 F', metconazole and 1,2,4 triazole. On the basis of these data, the risk to soil macro-organisms other than earthworms from metconazole and 1,2,4 triazole for all the representative uses of 'BAS 555 01 F' was assessed as low.

Experimental data were available for 'BAS 555 01 F', and 1,2,4 triazole with **soil microorganisms** and a low risk from metconazole and 1,2,4 triazole was concluded.

A vegetative vigour and a seedling emergence study were available with 'BAS 555 01 F' and the risk to **non-target terrestrial plants** was assessed as low for all the representative uses of 'BAS 555 01 F'.

On the basis of the available data with metconazole and risk assessment, a low risk is concluded regarding biological methods in **sewage treatment plants.**

6. Endocrine disruption properties

An assessment of the endocrine disruption potential of metconazole **for humans and non-target organisms** according to the ECHA/EFSA guidance (2018) was available.

The assessment of the endocrine disruption (ED) potential of metconazole was discussed at the Pesticides Peer Review Experts' meeting 07 for Mammalian Toxicology and in the Pesticides Peer Review Experts' meeting TC 93 in January 2023 for the Ecotoxicology.

Regarding the assessment of the ED potential of metconazole for **humans** according to the ECHA/ EFSA (2018) guidance, in determining whether metconazole interacts with the oestrogen, androgen, steroidogenesis (EAS) and thyroid (T) mediated pathways, the number and type of effects induced, and the magnitude and pattern of responses observed across the available information were considered. Additionally, the conditions under which effects occur were considered; in particular, whether or not endocrine-related responses occurred at dose(s) that also resulted in overt toxicity. The assessment is therefore providing a weight-of-evidence analysis of the potential interaction of metconazole with the EAS and T signalling pathways, using the available evidence in the data set.

With regard to the T-modality, the data set was considered complete. No evidence of T-mediated endocrine activity was observed and changes in T-mediated parameters were confined to increase in thyroid weight not accompanied by histopathological correlates. Therefore, overall, it was concluded that there is no pattern of T-mediated adversity.

With regard to EAS-modalities, the data set was also considered complete; some changes in EAS-mediated parameters were observed, however mainly above the maximum tolerated dose (MTD) or at doses where maternal toxicity was also observed. Therefore, it was concluded that there was no pattern of EAS-mediated adversity.

The outcome of the assessment reported above for humans also applies to **wild mammals as non-target organisms**.

For non-target organisms other than wild mammals, the data set was complemented with the submission of a Xenopus Eleutheroembryonic Thyroid Assay (XETA, OECD TG 248) and a Fish Short-Term Reproduction Assay (FSTRA, OECD TG 229) for the T- and EAS-modalities, respectively. For the EAS-modalities, a fish life cycle toxicity test (EPA TG OPPTS 850.1500) was already available but showed several deficiencies related to the VTG measurements.[26] The newly submitted information was discussed in the Pesticides Peer-Review meeting TC 93 in January 2023.

No evidence of T-mediated endocrine activity was observed in the valid XETA,[27] and consequently, it could be concluded that metconazole does not interfere in the hypothalamus–pituitary–thyroid (HPT) axis for non-mammalian non-target organisms. For EAS-modalities, although some uncertainties were noted in the available studies[28] and there is evidence of aromatase inhibition from US EPA ToxCast Program, a clear pattern of EAS-mediated adversity could not be identified based on a complete data set; therefore, it could be concluded that metconazole does not meet the ED criteria for non-mammalian non-target organisms for the EAS-modalities.

Overall, it is concluded that metconazole does not meet the ED criteria for humans and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605.

[26] Refer to the Experts' consultation 5.4 in the report of the Pesticides Peer Review Experts' Meeting TC 06–08 (EFSA, 2023).
[27] Refer to the Experts' consultation 5.8 in the report of the Pesticides Peer Review Experts' Meeting TC 93 (EFSA, 2023).
[28] Refer to the Experts' consultation 5.9 in the report of the Pesticides Peer Review Experts' Meeting TC 93 (EFSA, 2023).

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 1–4)

Table 1: Soil

Compound (name and/or code)	Ecotoxicology
Metconazole	Low risk to soil organisms
1,2,4 triazole	Low risk to soil organisms

Table 2: Groundwater[(a)]

Compound (name and/or code)	> 0.1 µg/L at 1 m depth for the representative uses[(b)] Step 2	Biological (pesticidal) activity/ relevance Step 3a.	Hazard identified Steps 3b. and 3c.	Consumer RA triggered Steps 4 and 5	Human health relevance
Metconazole	No	Yes	–	–	Yes
1,2,4-triazole	No	Yes	ADI = 0.023 mg/kg bw per day ARfD = 0.1 mg/kg bw		No

(a): Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).
(b): FOCUS scenarios or relevant lysimeter.

Table 3: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Metconazole	Low risk to aquatic organisms (with mitigation measures) for the majority of the FOCUS scenarios for all representative uses
1,2,4-triazole	Low risk to aquatic organisms
M555F013 cis	Data gap

Table 4: Air

Compound (name and/or code)	Toxicology
Metconazole	> 5.2 mg/L air /4 h

8. Particular conditions proposed to be taken into account by risk managers

Risk mitigation measures (RMMs) identified following consideration of Member State (MS) and/or applicant's proposal(s) during the peer review, if any, are presented in this section. These measures applicable for human health and/or the environment leading to a reduction of exposure levels of operators, workers, bystanders/residents, environmental compartments and/or non-target organisms for the representative uses are listed below. The list may also cover any RMMs as appropriate, leading to an acceptable level of risks for the respective non-target organisms.

It is noted that final decisions on the need of RMMs to ensure the safe use of the plant protection product containing the concerned active substance will be taken by risk managers during the decision-making phase. Consideration of the validity and appropriateness of the RMMs remains the responsibility of MSs at product authorisation, taking into account their specific agricultural, plant health and environmental conditions at national level.

Table 5: Risk mitigation measures proposed for the representative uses assessed

Representative use	Wheat	Oilseed rape
	Spraying	**Spraying**
Operator risk	Drift reduction and gloves during mixing/ loading and application	Drift reduction and gloves during mixing/ loading and application
Worker exposure		
Bystander/ resident exposure	Drift reduction and buffer zone 5 m	(insufficient)[29]
Risk to aquatic organisms	RMM equivalent to 5 m no-spray buffer zone for 7 of 9 FOCUS scenarios for the representative use on winter cereals; 4 of 5 for the representative use on spring cereals	RMM equivalent to 10 m no-spray buffer zone and 10 m vegetative filter strip for the representative use on winter oilseed rape (5 of 6 for the representative use on winter oilseed rape (autumn application); 4 of 5 for the representative use on winter oilseed rape (spring application)

9. Concerns and related data gaps

9.1. Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for one or more of 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[30] and if 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 'could not be finalised' if 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.

The following issues or assessments that could not be finalised have been identified, together with the reasons including the associated data gaps where relevant, which are reported directly under the specific issue to which they are related:

1) The overall consumer risk assessment for metconazole and for triazole metabolites resulting from the metconazole use could not be finalised due to:

   a) Insufficient GAP compliant residue trials in barley and wheat,
   b) Four rotational crops field trials (2NEU/2SEU), analysing for all compounds covered by the RD for risk assessment (including TDMs and monohydroxylated metconazole derivatives and their conjugates). These trials should be conducted in the EU, with at least root and tuber vegetables, cereals, oilseeds and leafy vegetables as rotational crops,
   c) Further confirmation on the presence of M11, M21 and their ratio among the monohydroxylated metconazole compounds recovered as a group in peas seeds,
   d) Satisfactory information to address the effect of water treatment processes on the nature of residues present in surface water and groundwater, when surface water or groundwater are abstracted for drinking water was not available. Probably in the first instance, a consideration of the processes of ozonation and chlorination would appear appropriate. If an argumentation is made that concentrations at the point of abstraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in groundwater and surface water, as well as the active substance. Should this consideration indicate that novel compounds might be expected to be formed from water treatment, the risk to human or animal health through the consumption of drinking water containing them should be addressed (relevant to

[29] See further details in Section 2 regarding possible revision of dermal absorption value.
[30] 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.

comply with the conditions of approval, not dependent of any specific uses, see Section 4),

e) Further assessment of the general toxicity profile of the metabolites M11 and M21 is required (see Section 2).

9.2. Critical areas of concern

An issue is listed as a critical area of concern if 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, and if this assessment does not permit the conclusion 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 if the assessment at a higher tier level could not be finalised due to lack of information, and if the assessment performed at the lower tier level does not permit the conclusion 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 if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

The following critical areas of concern are identified, together with any associated data gaps, where relevant, which are reported directly under the specific critical area of concern to which they are related:

No critical area of concern was identified.

9.3. Overview of the concerns identified for each representative use considered (Table 6)

(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 Table 6.)

Table 6: Overview of concerns reflecting the issues not finalised, critical areas of concerns and the risks identified that may be applicable for some but not for all uses or risk assessment scenarios

Representative use		Wheat, barley, rye, triticale, oats	Oilseed rape
Operator risk	Risk identified		
	Assessment not finalised		
Worker risk	Risk identified		
	Assessment not finalised		
Resident/ bystander risk	Risk identified		X[(c)]
	Assessment not finalised		
Consumer risk	Risk identified		
	Assessment not finalised	X[1]	X[1]
Risk to wild non-target terrestrial vertebrates	Risk identified		
	Assessment not finalised		
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified		
	Assessment not finalised		

Representative use		Wheat, barley, rye, triticale, oats	Oilseed rape
Risk to aquatic organisms	Risk identified	X (2/9 FOCUS scenarios for the representative use on winter cereals; 1/5 FOCUS scenario for the representative use on spring cereals)	X (1/6 FOCUS scenarios for the representative use on winter oilseed rape (autumn application) 1/5 FOCUS scenarios for spring application)
	Assessment not finalised		
Groundwater exposure to active substance	Legal parametric value breached		
	Assessment not finalised		
Groundwater exposure to metabolites	Legal parametric value breached[(a)]		
	Parametric value of 10 µg/L[(b)] breached		
	Assessment not finalised		

The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2.
(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.
(b): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission, 2003.
(c): See further details in Section 2 regarding possible revision of dermal absorption value.

10. List of other outstanding issues

Remaining data gaps not leading to critical areas of concern or issues not finalised but considered necessary to comply with the data requirements, and which are relevant for some or all of the representative uses assessed at EU level. Although not critical, these data gaps may lead to uncertainties in the assessment and are considered relevant.

These data gaps refer only to the representative uses assessed and are listed in the order of the sections:

- Analytical method for analysis of the relevant impurities in the formulation for the representative uses (relevant for all representative uses evaluated; see Section 1).
- Extraction efficiency of the procedure used in the monitoring methods for residues in food/feed of plant origin (relevant for all representative uses evaluated; see Section 1).
- Extraction efficiency of the procedure used in the monitoring methods for residues in animal products (relevant for all representative uses evaluated; see Section 1).
- Residue trials for pollen and bee products analysing for all compounds covered by the residue definition for risk assessment, i.e. including TDMSs (relevant for the representative use on oilseed rape; see Section 3).
- A new batch adsorption study for 1,2,4-triazole in at least three soils (relevant for all representative uses evaluated; see Section 4).
- Data to address the risk to aquatic invertebrates and a chronic risk to fish from the metabolite M555F013 cis (relevant for all representative uses, see Section 5).
- Data to address the risk to birds and mammals from exposure to monohydroxylated derivatives (free and conjugated) (relevant for all representative uses, see Section 5).
- Further data to address the risk to honeybees from sublethal effects (relevant for all representative uses, see Section 5).
- Further data to address the risk to bees when exposed to relevant metabolites are needed (relevant for all representative uses, see Section 5).

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Abbreviations

AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
AR	androgen receptor
bw	body weight
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EAS	oestrogen, androgen and steroidogenesis modalities
ECHA	European Chemicals Agency
EEC	European Economic Community
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FSTRA	Fish Short-Term Reproduction Assay
GAP	Good Agricultural Practice
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
JMPR	Joint Meeting of 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
K_{Foc}	Freundlich organic carbon adsorption coefficient
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC–MS	liquid chromatography–mass spectrometry
LC–MS–MS	liquid chromatography with tandem mass spectrometry
LOQ	limit of quantification
mm	millimetre (also used for mean measured concentrations)
mN	milli-newton
MRL	maximum residue level
MTD	maximum tolerated dose
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
Pa	pascal
PEC	predicted environmental concentration
pF2	pF value of 2 (suction pressure that defines field capacity soil moisture)
ppm	parts per million (10^{-6})
QSAR	quantitative structure–activity relationship
r^2	coefficient of determination
RAC	regulatory acceptable concentration
RAR	Renewal Assessment Report
SC	suspension concentrate
SFO	single first-order
SMILES	simplified molecular-input line-entry system
SPG	specific protection goal
TDM	Triazole derivative metabolites
TRR	total radioactive residue
UF	uncertainty factor
UV	ultraviolet
WHO	World Health Organization

Appendix A – Consideration of cut-off criteria for metconazole according to Annex II of Regulation (EC) No 1107/2009 of the European Parliament and of the Council

Properties		Conclusion[(a)]
CMR	Carcinogenicity (C)	Metconazole is not considered to be a carcinogen according to point 3.6.2 of Annex II of Regulation (EC) No 1107/2009.
	Mutagenicity (M)	Metconazole is not considered to be a mutagen according to point 3.6.2 of Annex II of Regulation (EC) No 1107/2009.
	Toxic for reproduction (R)	Metconazole is not considered to be toxic for reproduction according to point 3.6.4 of Annex II of Regulation (EC) No 1107/2009. Harmonised classification according to Regulation (EC) No 1272/2008 and its adaptations to technical process [Table 3.1 of Annex VI of Regulation (EC) No 1272/2008 as amended]: Reproductive category 2; H361d.
Endocrine-disruption properties		Metconazole is not considered to meet the criteria for endocrine disruption for human health and non-target organisms according to points 3.6.5 and 3.8.2 of Annex II of Regulation No 1107/2009, as amended by Commission Regulation (EU) 2018/605.
POP	**Persistence**	Metconazole is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	
	Long-range transport	
PBT	**Persistence**	Metconazole not considered to be a persistent, bioaccumulative and toxic (PBT) substance according to point 3.7.2 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	
	Toxicity	
vPvB	**Persistence**	Metconazole not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	

(a): Origin of data to be included where applicable (e.g. EFSA, ECHA RAC, Regulation).

Appendix B – List of end points for the active substance and the representative formulation

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2023.8141.

Appendix C – Wording EFSA used in Section 4 of this conclusion, in relation to DT and Koc 'classes' exhibited by each compound assessed

Wording	DT_{50} normalised to 20°C for laboratory incubations[31] or not normalised DT_{50} for field studies (SFO equivalent, when biphasic, the DT_{90} was divided by 3.32 to estimate the DT50 when deciding on the wording to use)
Very low persistence	< 1 day
Low persistence	1 to < 10 days
Moderate persistence	10 to < 60 days
Medium persistence	60 to < 100 days
High persistence	100 days to < 1 year
Very high persistence	A year or more

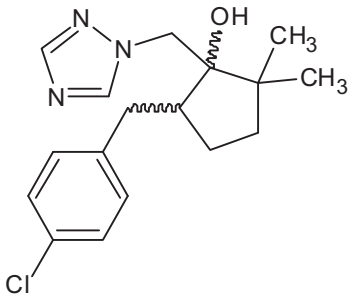
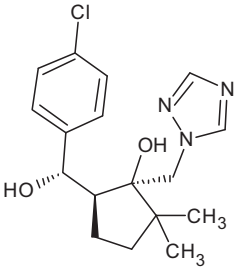
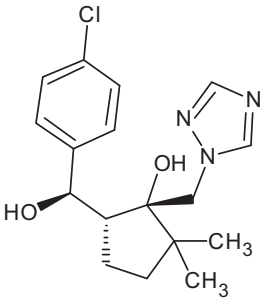
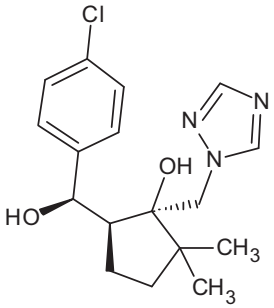
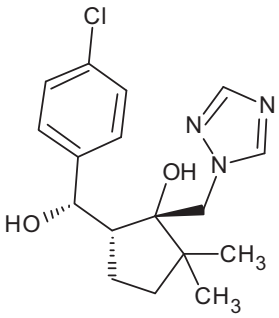
Note these classes and descriptions are unrelated to any persistence class associated with the active substance cut-off criteria in Annex II of Regulation (EC) No 1107/2009. For consideration made in relation to Annex II, see Appendix A.

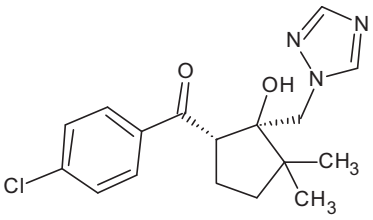
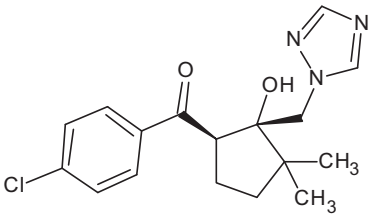
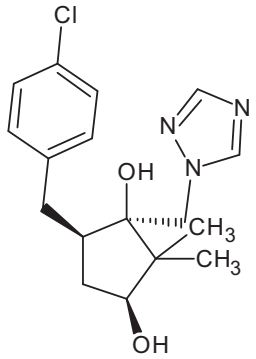
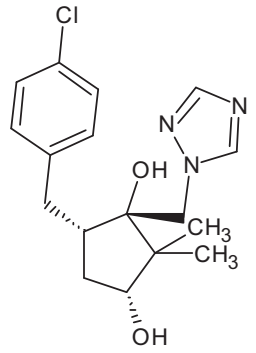
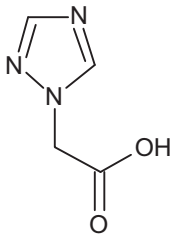
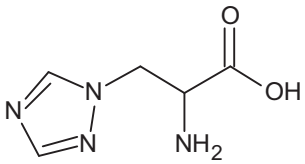
Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0–50
High mobility	51–150
Medium mobility	151–500
Low mobility	501–2000
Slight mobility	2001–5000
Immobile	> 5000

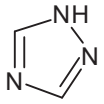
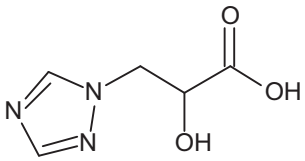
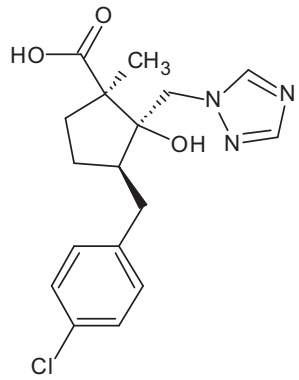
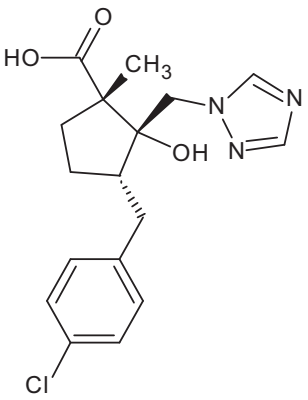
Based on McCall et al. (1980).

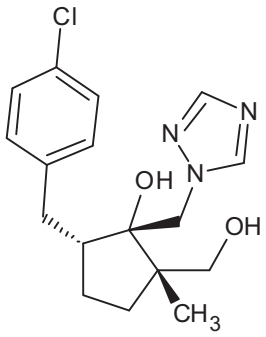
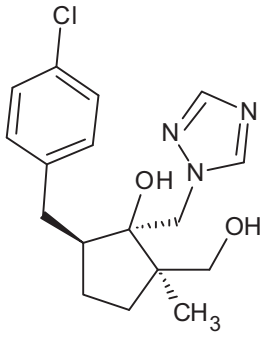
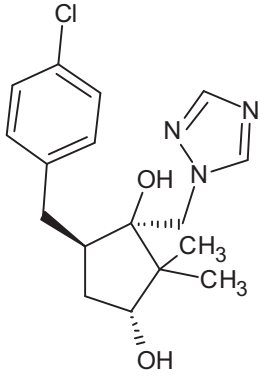
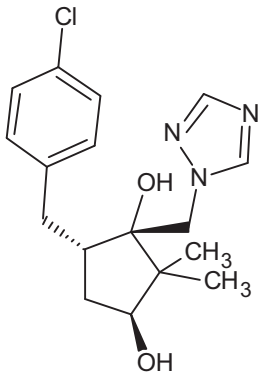
[31] For laboratory soil incubations, normalisation was also to field capacity soil moisture (pF2/10 kPa). For laboratory sediment water system incubations, the whole system DT values were used.

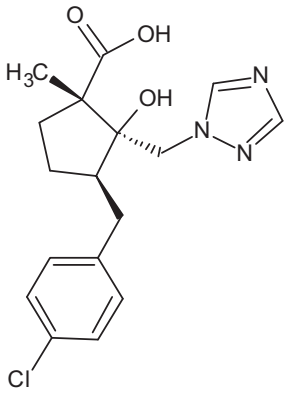
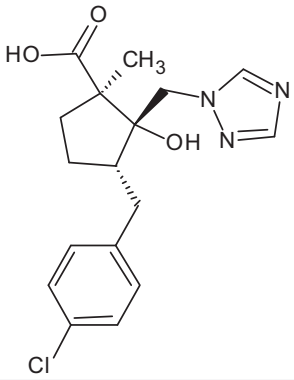
Appendix D – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Metconazole	(1*RS*,5*RS*;1*RS*,5*SR*)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol CC1(C)CCC(CC2=CC=C(C=C2)Cl)C1(CN3C=NC=N3)O XWPZUHJBOLQNMN-UHFFFAOYSA-N	
M11	(1*R*,5*S*)-5-[(*S*)-(4-chlorophenyl)(hydroxy)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentan-1-ol Clc1ccc(cc1)[C@@H](O)[C@@H]1CCC(C)(C)[C@@]1(O)Cn1cncn1 TTYGDFBOWYYCGH-ZMSDIMECSA-N	
	or	
	(1*S*,5*R*)-5-[(*R*)-(4-chlorophenyl)(hydroxy)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentan-1-ol Clc1ccc(cc1)[C@H](O)[C@H]1CCC(C)(C)[C@]1(O)Cn1cncn1 TTYGDFBOWYYCGH-VYDXJSESSA-N	
M21	(1*R*,5*S*)-5-[(*R*)-(4-chlorophenyl)(hydroxy)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentan-1-ol Clc1ccc(cc1)[C@H](O)[C@@H]1CCC(C)(C)[C@@]1(O)Cn1cncn1 TTYGDFBOWYYCGH-YQQAZPJKSA-N	
	or	
	(1*S*,5*R*)-5-[(*S*)-(4-chlorophenyl)(hydroxy)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentan-1-ol Clc1ccc(cc1)[C@@H](O)[C@H]1CCC(C)(C)[C@]1(O)Cn1cncn1 TTYGDFBOWYYCGH-INMHGKMJSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M30	(4-chlorophenyl){(1*S*,2*R*)-2-hydroxy-3,3-dimethyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentyl} methanone Clc1ccc(cc1)C(=O)[C@H]1CCC(C)(C)[C@@]1(O)Cn1cncn1 ZSWLSOCWSGWJQL-RHSMWYFYSA-N	 or
	(4-chlorophenyl){(1*R*,2*S*)-2-hydroxy-3,3-dimethyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentyl} methanone Clc1ccc(cc1)C(=O)[C@@H]1CCC(C)(C)[C@]1(O)Cn1cncn1 ZSWLSOCWSGWJQL-YOEHRIQHSA-N	
M31	(1*R*,3*S*,5*R*)-5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1,3-diol Clc1ccc(cc1)C[C@@H]1C[C@H](O)C(C)(C)[C@@]1(O)Cn1cncn1 NUFCALACVDJTPE-UKPHBRMFSA-N	 or
	(1*S*,3*R*,5*S*)-5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1,3-diol Clc1ccc(cc1)C[C@H]1C[C@@H](O)C(C)(C)[C@]1(O)Cn1cncn1 NUFCALACVDJTPE-LXZKKBNFSA-N	
triazole acetic acid (TAA)	(1*H*-1,2,4-triazol-1-yl)acetic acid O=C(O)Cn1cncn1 RXDBSQXFIWBJSR-UHFFFAOYSA-N	
triazole alanine (TA)	3-(1*H*-1,2,4-triazol-1-yl)alanine NC(Cn1cncn1)C(=O)O XVWFTOJHOHJIMQ-UHFFFAOYSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
1,2,4-triazole (1,2,4-T) M555F020	1*H*-1,2,4-triazole C1ncn[NH]1	
triazole lactic acid (TLA)	2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid OC(Cn1cncn1)C(=O)O KJRGHGWETVMENC-UHFFFAOYSA-N	
M12	(1*R*,2*S*,3*R*)-3-[(4-chlorophenyl)methyl]-2-hydroxy-1-methyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1-carboxylic acid Clc1ccc(cc1)C[C@H]1CC[C@@](C)(C(=O)O)[C@]1(O)Cn1cncn1 CZKUDLLGLJYQBN-COXVUDFISA-N	
	(1*S*,2*R*,3*S*)-3-[(4-chlorophenyl)methyl]-2-hydroxy-1-methyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1-carboxylic acid Clc1ccc(cc1)C[C@@H]1CC[C@](C)(C(=O)O)[C@@]1(O)Cn1cncn1 CZKUDLLGLJYQBN-IAOVAPTHSA-N	or 

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M1	(1*S*,2*S*,5*R*)-5-[(4-chlorophenyl)methyl]-2-(hydroxymethyl)-2-methyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentan-1-ol Clc1ccc(cc1)C[C@H]1CC[C@@](C)(CO)[C@]1(O)Cn1cncn1 FFAVDRUASZEUOU-PVAVHDDUSA-N	 or
	(1*R*,2*R*,5*S*)-5-[(4-chlorophenyl)methyl]-2-(hydroxymethyl)-2-methyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentan-1-ol Clc1ccc(cc1)C[C@@H]1CC[C@](C)(CO)[C@@]1(O)Cn1cncn1 FFAVDRUASZEUOU-USXIJHARSA-N	
M32	(1*R*,3*R*,5*R*)-5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentane-1,3-diol Clc1ccc(cc1)C[C@@H]1C[C@@H](O)C(C)(C)[C@@]1(O)Cn1cncn1 NUFCALACVDJTPE-FRFSOERESA-N	 or
	(1*S*,3*S*,5*S*)-5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-[(1*H*-1,2,4-triazol-1-yl)methyl]cyclopentane-1,3-diol Clc1ccc(cc1)C[C@H]1C[C@H](O)C(C)(C)[C@]1(O)Cn1cncn1 NUFCALACVDJTPE-QRTARXTBSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
M555F013 cis	(1*S*,2*S*,3*R*)-3-[(4-chlorophenyl)methyl]-2-hydroxy-1-methyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1-carboxylic acid Clc1ccc(cc1)C[C@H]1CC[C@](C)(C(=O)O)[C@]1(O)Cn1cncn1 CZKUDLLGLJYQBN-XYPHTWIQSA-N	
		or
M555F013 cis	(1*R*,2*R*,3*S*)-3-[(4-chlorophenyl)methyl]-2-hydroxy-1-methyl-2-[(1*H*-1,2,4-triazol-1-yl)methyl] cyclopentane-1-carboxylic acid Clc1ccc(cc1)C[C@@H]1CC[C@@](C)(C(=O)O)[C@@]1(O)Cn1cncn1 CZKUDLLGLJYQBN-RRQGHBQHSA-N	

(a): The name in bold is the name used in the conclusion.
(b): ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 07 July 2021).
(c): ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021).