

APPROVED: 2 July 2018

doi: 10.2903/j.efsa.2018.5379

### Peer review of the pesticide risk assessment of the active substance BAS 750 F (mefentrifluconazole)

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#### Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, the United Kingdom, for the pesticide active substance BAS 750 F (mefentrifluconazole) are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions were reached on the basis of the evaluation of the representative use(s) of BAS 750 F (mefentrifluconazole) as a fungicide on cereals. The reliable endpoints, appropriate for use in regulatory risk assessment are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

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**Keywords:** BAS 750 F (mefentrifluconazole), peer review, risk assessment, pesticide, fungicide

**Requestor:** European Commission

**Question number:** EFSA-Q-2016-00254

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**Suggested citation:** EFSA (European Food Safety Authority), Arena M, Auteri D, Barmaz S, Brancato A, Brocca D, Bura L, Carrasco Cabrera L, Chiusolo A, Civitella C, Court Marques D, Crivellente F, Ctverackova L, De Lentdecker C, Egsmose M, Erdos Z, Fait G, Ferreira L, Goumenou M, Greco L, Ippolito A, Istace F, Jarrah S, Kardassi D, Leuschner R, Lythgo C, Magrans JO, Medina P, Mineo D, Miron I, Molnar T, Padovani L, Parra Morte JM, Pedersen R, Reich H, Riemenschneider C, Sacchi A, Santos M, Serafimova R, Sharp R, Stanek A, Streissl F, Sturma J, Szentes C, Tarazona J, Terron A, Theobald A, Vagenende B, Van Dijk J and Villamar-Bouza L, 2018. Conclusion on the peer review of the pesticide risk assessment of the active substance BAS 750 F (mefentrifluconazole). *EFSA Journal* 2018;16(7):5379, 25 pp. <https://doi.org/10.2903/j.efsa.2018.5379>

**ISSN:** 1831-4732

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## Summary

BAS 750 F (mefentrifluconazole) is a new active substance for which, in accordance with Article 7 of Regulation (EC) No 1107/2009 of the European Parliament and of the Council (hereinafter referred to as 'the Regulation'), the rapporteur Member State (RMS), the United Kingdom, received an application from BASF Agro B.V. on 29 February 2016 for approval. Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 30 March 2016.

The RMS provided its initial evaluation of the dossier on BAS 750 F (mefentrifluconazole) in the draft assessment report (DAR), which was received by the European Food Safety Authority (EFSA) on 25 April 2017. The peer review was initiated on 24 May 2017 by dispatching the DAR for consultation to the Member States and the applicant, BASF Agro B.V.

Following consideration of the comments received on the DAR, 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 accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether BAS 750 F (mefentrifluconazole) can be expected to meet the approval criteria provided for in Article 4 of the Regulation taking into consideration recital (10) of the Regulation. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of BAS 750 F (mefentrifluconazole) as a fungicide on cereals as proposed by the applicant. Full details of the representative uses can be found in Appendix A of this report.

Data were submitted to conclude that the use of mefentrifluconazole according to the representative uses proposed at the European Union (EU) level results in a sufficient fungicidal efficacy against the target organisms.

In the area of identity, physical/chemical properties and analytical methods data gaps were identified for spectra data for the relevant impurities, for information on the content of the relevant impurities after the storage, for methods of analysis 1,2,4-(1*H*)-triazole in the representative formulation and for monitoring methods for determination of metabolites M750F015, M750F016 and M750F017 in body fluids.

No data gaps or areas of concerns were identified in the mammalian toxicology area.

In the area of residues, data gaps were identified with regard to the formed triazole derivative metabolite (TDM) of mefentrifluconazole, specifically with regard to storage stability data in animal commodities and a feeding study with triazole lactic acid (TLA), and for residue data in pollen and bee products. Despite these data gaps, the residue situation for the representative uses and the resulting consumer risk assessment did not indicate any potential for exceedance of toxicological reference values of mefentrifluconazole and its metabolites relevant for risk assessment.

The data available on environmental fate and behaviour were sufficient to carry out the required environmental exposure assessments at EU level, with the exception that a data gap was identified for information on the consideration of chlorination and ozonation processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water. This gap leads to the consumer risk assessment from the consumption of drinking water being not finalised for all the representative uses.

The risk to birds, mammals, non-target arthropods, earthworms and other soil dwelling meso- and macrofauna, soil nitrification, non-target plants and biological methods of sewage treatment was assessed as low. The risk to aquatic organisms was assessed as low in most scenarios for the active substance. A high risk was indicated only in some scenarios for the long-term risk to fish and daphnids requiring risk mitigation (D2 ditch for fish, D1 and D2 ditch for invertebrates). The acute toxicity of the formulation is about 10 times greater than the technical active substance and a high acute risk to fish and invertebrates was indicated with FOCUS step 1 calculations. The risk to aquatic organisms was assessed as low for all metabolites except for M750F005 for which a high acute risk to fish was indicated for the scenario D2 ditch. A 5-m no-spray buffer zone was not sufficient and no larger no-spray buffer zones were calculated. The refined acute risk assessment for the formulation was based on spray drift entry. The acute risk to aquatic invertebrates from exposure to the formulation from spray drift was assessed as low. Risk mitigation comparable to a 5-m no spray buffer zone are needed for fish to mitigate the acute risk from spray drift. Toxicity data were submitted for honeybees but no

risk assessment was conducted to address the risk from chronic exposure, the risk to larvae and to non-apis bees. Therefore, a data gap was identified to conduct a risk assessment according to EFSA 2013 (EFSA Bee Guidance Document).

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## Background

Regulation (EC) No 1107/2009 of the European Parliament and of the Council<sup>1</sup> (hereinafter referred to as 'the Regulation') lays down, *inter alia*, the detailed rules as regards the procedure and conditions for approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the initial evaluation in the draft assessment report (DAR), provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 12 of the Regulation, EFSA is required to adopt a conclusion on whether an active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation (also taking into consideration recital (10) of the Regulation) within 120 days from the end of the period provided for the submission of written comments, subject to an extension of 30 days where an expert consultation is necessary, and a further extension of up to 150 days where additional information is required to be submitted by the applicant(s) in accordance with Article 12(3).

BAS 750 F (mefentrifluconazole) is a new active substance for which, in accordance with Article 7 of the Regulation, the RMS, the United Kingdom (hereinafter referred to as the 'RMS'), received an application from BASF Agro B.V. on 29 February 2016 for approval of the active substance BAS 750 F (mefentrifluconazole). Complying with Article 9 of the Regulation, the completeness of the dossier was checked by the RMS and the date of admissibility of the application was recognised as being 30 March 2016.

The RMS provided its initial evaluation of the dossier on BAS 750 F (mefentrifluconazole) in the DAR, which was received by EFSA on 25 April 2017 (United Kingdom, 2017). The peer review was initiated on 24 May 2017 by dispatching the DAR for consultation of the Member States and the applicant, BASF Agro B.V., for consultation and comments. EFSA also provided comments. In addition, EFSA conducted a public consultation on the DAR. The comments received were collated by EFSA and forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant 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 12(3) of the Regulation were considered in a telephone conference between EFSA, the RMS, on 6 September 2017. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicant and EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues and ecotoxicology.

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 where this took place, were reported in the final column of the evaluation table.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether BAS 750 F (mefentrifluconazole) can be expected to meet the approval criteria provided for in Article 4 of the Regulation, taking into consideration recital (10) of the Regulation. A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in May/June 2018.

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 of BAS 750 F (mefentrifluconazole) as a fungicide on cereals as proposed by the applicant. Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005, provided the active substance will be approved under Regulation (EC) No 1107/2009 without restrictions affecting the residue assessment. In the event of a non-approval of the active substance or an approval with restrictions that have an impact on the residue assessment, the maximum residue level (MRL) proposals from this conclusion might no longer be relevant and a

<sup>1</sup> 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.

new assessment under Article 12 of Regulation (EC) No 396/2005 will be required. A list of the relevant end points for the active substance and the formulation is provided in Appendix A.

In addition, a key supporting document to this conclusion is the peer review report (EFSA, 2018a), 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 DAR;
- the reporting table (6 September 2017);
- the evaluation table (25 June 2018);
- the report(s) 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 DAR including its revisions (United Kingdom, 2018) and the peer review report, both documents are considered as background documents to this conclusion.

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

## The active substance and the formulated product

Mefentrifluconazole is the provisionally approved ISO common name for (2*RS*)-2-[4-(4-chlorophenoxy)- $\alpha,\alpha,\alpha$ -trifluoro-*o*-tolyl]-1-(1*H*-1,2,4-triazol-1-yl)propan-2-ol (IUPAC).

The representative formulated product for the evaluation was 'BAS 750 01 F', an emulsion concentrate (EC) containing 100 g/L mefentrifluconazole.

The representative use evaluated was by foliar spray for the control of *Septoria tritici* in cereals. Full details of the good agricultural practices (GAPs) can be found in the list of end points in Appendix A.

Data were submitted to conclude that the use of mefentrifluconazole according to the representative uses proposed at EU level result in a sufficient fungicidal efficacy against the target organisms, following the guidance document SANCO/10054/2013 - rev. 3 (European Commission, 2013).

## Conclusions of the evaluation

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

The following guidance documents were followed in the production of this conclusion: SANCO/3029/99-rev. 4 (European Commission, 2000a), SANCO/3030/99-rev. 4 (European Commission, 2000b) and SANCO/825/00-rev. 8.1 (European Commission, 2010).

The proposed specification for mefentrifluconazole is based on batch data from a pilot plant. The proposed minimum purity of the technical material is 970 g/kg. *N,N*-Dimethylformamide (DMF), toluene and 1,2,4-(1*H*)-triazole are considered relevant impurities with maximum amounts 0.5 g/kg for DMF and 1 g/kg for the others. The proposed specification is supported by (eco)toxicological assessment (Sections 2 and 5). It should be noted that data on five representative batches should again be provided once industrial scale production methods and procedures are stabilised. Based on this data the specification might need to be modified. There is no FAO specification available for mefentrifluconazole.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of mefentrifluconazole or the representative formulation. However, it should be noted that data gaps were identified for spectra data for the relevant impurities and for information on the content of the relevant impurities after the storage. The main data regarding the identity of mefentrifluconazole and its physical and chemical properties are given in Appendix A.

Adequate methods are available for the generation of pre-approval data required for the risk assessment. However, validation data for the analytical method used in the key toxicity studies, in particular the 1-year dog, and developmental toxicity studies in rats and rabbits were not provided

(data gap). Methods of analysis are available for the determination of the active substance and the relevant impurity in the technical material and of the active substance and some of the relevant impurities (DMF and toluene) in the representative formulation. Therefore, a data gap for a method of analysis of 1,2,4-(1*H*)-triazole in the representative formulation was identified.

Mefentrifluconazole residues can be monitored in food and feed of plant origin by a quick, easy, cheap, effective and safe (QuEChERS) method using liquid chromatography with tandem mass spectrometry (LC–MS/MS) with a limit of quantification (LOQ) of 0.01 mg/kg in each commodity group. Mefentrifluconazole residues in food of animal origin can be determined by LC–MS/MS with a LOQ of 0.01 mg/kg in all animal matrices.

Mefentrifluconazole residues in soil and in drinking and surface water can be monitored by LC–MS/MS with LOQs 0.002 mg/kg and 0.030 µg/L, respectively.

An appropriate LC–MS/MS method exists for monitoring mefentrifluconazole residues in air with a LOQ of 0.01 ng/L.

A LC–MS/MS method can be used for monitoring of mefentrifluconazole residue in body fluids (urine and blood) with a LOQ of 0.01 mg/L. The method for monitoring of mefentrifluconazole in food of animal origin can be used for the determination of mefentrifluconazole in body tissues. However, it has been concluded that metabolites M750F015, M750F016 and M750F017 should be also included in the residue definition for body fluids, as a consequence a data gap for monitoring methods for their determination in body fluids was identified.

## 2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000-rev. 10-final (European Commission, 2003), SANCO/10597/2003-rev. 10.1 (European Commission, 2012), Guidance on dermal absorption (EFSA PPR Panel, 2012) and Guidance on the Application of the CLP Criteria (ECHA, 2017).

Mefentrifluconazole was discussed during the Pesticides Peer Review Meeting 172 in February 2018.

The technical specification is not supported by the batches used in the toxicological studies according to a Tier I analysis; however a detailed quantitative structure–activity relationship (QSAR) analysis supportive to a Tier II analysis has been provided indicating that the impurities (except the ones of known toxicological relevance listed below) are unlikely to be relevant in comparison with the toxicity profile of the parent substance. It can therefore be concluded that the technical specification is supported by the toxicological assessment. DMF (harmonised classification as reproductive toxicant category 1B according to Regulation 1272/2008<sup>2</sup>), toluene and 1,2,4-(1*H*)-triazole (reproductive toxicants category 2) are considered relevant impurities. Their levels should remain below the levels stated in Section 1 in the technical specification. No toxicological concern is identified at these specified concentration levels. Validated analytical methods have been provided for the analysis of dietary preparations and capsule administration used in key toxicological studies, confirming the quality of the toxicological assessment.

Mefentrifluconazole absorption is extensive, the active substance is widely distributed and metabolised, a preferential metabolism and elimination is observed for the *S*-enantiomer in rats; the active substance is rapidly excreted to a major extent via the biliary pathway. Comparative interspecies *in vitro* metabolism did not detect human-specific metabolites. Mefentrifluconazole is metabolised to a high number of metabolites, being the major ones M750F015, M750F016 and M750F017, a residue definition for body fluids (blood, plasma and urine) should include the parent and these three metabolites for the purpose of human biomonitoring.

Low acute toxicity was observed when mefentrifluconazole was administered by the oral, dermal or inhalation routes, no skin or eye irritation, or phototoxic potential were attributed to the active substance, but potential for skin sensitisation was observed and classification as skin sensitiser (skin sens 1, H317 'may cause an allergic skin reaction') is in agreement with the proposed harmonised classification (ECHA, 2018). The liver is the main target organ of mefentrifluconazole upon short to long term exposure, in all species tested, rat, mouse and dogs, mice being the more sensitive species. The applicant provided mechanistic studies to demonstrate that liver effects in mice (increased serum alanine aminotransferase (ALT) levels, increased liver weight, hypertrophy and liver cell proliferation) are constitutive androstane receptor (CAR) mediated and of limited relevance for human risk

<sup>2</sup> 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.

assessment. The RMS did not assess these studies, justifying that the studies are not relevant to the risk assessment since necrosis was observed in some repeated-dose mouse studies, while it is generally accepted that the CAR mode of action does not result in cytotoxicity; in addition, liver dysfunction (increased liver weight, hypertrophy and changes in clinical chemistry parameters) was observed in the dog studies. Therefore, it is concluded that the liver effects observed in the toxicological studies in several species cannot be attributed to CAR-mediated processes and should be considered to be potentially relevant to humans. The relevant no-observed adverse effect level (NOAEL) upon short- and long-term exposure is 3.5 mg/kg body weight (bw) per day overall from the 90-day and 18-month studies in mice. Genotoxicity studies covering bacterial and mammalian gene mutation assays *in vitro*, and clastogenicity and aneugenicity *in vitro* and *in vivo* were all negative; accordingly the active substance is unlikely to be genotoxic, it is also unlikely to be photogenotoxic. No carcinogenic effects were observed up to 36 mg/kg bw per day in mice and 163 mg/kg bw per day in rats. Mefentrifluconazole did not exert adverse effects on the reproduction or fertility; the majority of the experts concluded that developmental toxicity (visceral and skeletal variations) was observed in the presence of maternal toxicity in rats and rabbits, while the RMS disagreed, considering the developmental NOAEL as the highest dose tested in both rats and rabbits. No potential for neurotoxicity or immunotoxicity were observed in the overall data package, including an acute neurotoxicity study in rats.

Mefentrifluconazole is not classified or proposed to be classified as carcinogenic or toxic for reproduction category 2, on this basis, the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine-disrupting (ED) properties are not met. From a scientific perspective, a weak inhibition of aromatase activity seen *in vitro* did not translate to any relevant adverse effect *in vivo* and it was concluded that mefentrifluconazole is unlikely to have ED properties regarding oestrogen, androgen, thyroid and steroidogenesis (EATS) modalities.

Toxicological studies were provided on the metabolite M750F022; it was concluded that the toxicological reference values of the parent are applicable to both metabolites M750F022 and M750F019. Since evidence of enzymatic cleavage of sulfate conjugates metabolites (M750F043 and M750F072) and fatty acid conjugates (M750F023, M750F024 and M750F025) was provided by the applicant, it was concluded that these metabolites share the toxicity profile of the respective (unconjugated) metabolite (M750F022 and M750F039). While the toxicological profile of metabolite M750F039 and its sulfate conjugate M750F072 has not been addressed, it could be concluded that the toxicological reference values of the parent mefentrifluconazole may apply to metabolites M750F015, M750F016 and M750F017 (major rat metabolites); M750F019 (conjugate of major rat metabolites); M750F022; M750F023, M750F024, M750F025 (fatty acid conjugates of M750F022); and M750F043 (sulfate conjugate of M750F022). *In vitro* human recombinant aromatase inhibition was tested on mefentrifluconazole, its *S*- and *R*-enantiomers and metabolite M750F022. The highest activity was observed with the *S*-enantiomer, then mefentrifluconazole, its *R*-enantiomer and M750F022 in a decreasing order of activity. The RMS concluded that the *S*-enantiomer is more toxicologically active than the *R*-enantiomer based on this information. This was not discussed during the experts' meeting, but EFSA is of the opinion that this represents weak evidence for a level of toxicity since only one endpoint has been tested *in vitro* and there is no information of the relative toxicity of each enantiomer *in vivo*. No toxicological information has been provided on the triazole derivative metabolites (TDMs) by the applicant in this dossier; however the toxicity of these metabolites – 1,2,4-triazole (1,2,4-T), triazole alanine (TA), triazole acetic acid (TAA), and triazole lactic acid (TLA) – has been revised under confirmatory data procedure for a number of triazole active substances (EFSA, 2018a); dietary reference values were established for these four metabolites.

The acceptable daily intake (ADI) for mefentrifluconazole is set at 0.035 mg/kg bw per day based on the NOAEL of 3.5 mg/kg bw per day for hepatotoxicity from the 18-month mouse study and applying an uncertainty factor (UF) of 100. This confirms the RMS's proposal in the DAR but rounding of the value is not considered appropriate. In contrast to the acceptable operator exposure level (AOEL) proposed by the RMS, the AOEL is set at 0.035 mg/kg bw per day based on the overall NOAEL of 3.5 mg/kg bw per day from the 90-day and chronic mouse studies, UF of 100 and no correction being needed for oral absorption. The RMS interpreted the liver effects seen in the short-term studies differently and considered that the short-term NOAEL should be set at a higher dose level; the RMS therefore did not agree with the AOEL setting. The acute reference dose (ARfD) is 0.15 mg/kg bw, based on the NOAEL for maternal and developmental toxicity from the rabbit developmental toxicity study at 15 mg/kg bw per day, with an UF of 100; as mentioned above, the RMS did not agree with

the lowering of the respective NOAEL and therefore did not agree with the ARfD set by the majority of experts. Similarly to the ARfD setting, the acute acceptable operator exposure level (AAOEL) is 0.15 mg/kg bw, no correction being needed for the oral absorption, the RMS disagreed.

A non-dietary exposure risk assessment was performed for the representative formulation 'BAS 750 01 F', an EC, containing 100 g/L to be applied in cereals. Estimated operator and worker exposure does not exceed the (A)AOEL according to the EFSA calculator even when no specific personal protective equipment (PPE) is used, but normal work wear (arms, body and legs covered); bystander and resident's exposure represented up to 5% of the AAOEL and 17% of the AOEL respectively, the latter as the sum of routes of exposure (mean) to children (resident).

### 3. Residues

The assessment in the residue section is based on the OECD guidance document on overview of residue chemistry studies (OECD, 2009), the OECD publication on MRL calculations (OECD, 2011), the European Commission guideline document on MRL setting (European Commission, 2011) and the Joint Meeting on Pesticide Residues (JMPR) recommendations on livestock burden calculations (JMPR, 2004, 2007). It is noted that studies with the TDM except a storage stability study with TLA have not been provided by the applicant in this dossier. Reference has been made to the available residue studies regarding these metabolites – 1,2,4-T, TA, TAA and TLA – recently reviewed under the confirmatory data procedure for a number of existing triazole active substances (EFSA, 2018a,b). These studies have been considered where appropriate for assessment of residues of mefentrifluconazole.

Metabolism of BAS 750 F (mefentrifluconazole) was investigated upon foliar application in wheat (cereal crop group), soybean (pulses and oilseed crop group), and grapevine (fruits/fruited vegetable crop group). Comparable results were obtained for all three crop groups.

In most matrices, mefentrifluconazole is the predominant component of the residue (> 60% total radioactive residue (TRR)), notably in forage (wheat, soybean), leaf/stalk (grapevine), straw/hull/chaff (wheat, soybean), green pod (soybean) and grape (grapevine). To the contrary, in wheat grain and soybean seed, mefentrifluconazole is present at very low levels if at all, while the predominant residues are formed by TDM, with triazole alanine as the most abundant compound.

In a rotational crop metabolism study in leafy vegetables, root and tuber vegetables and cereals, cultivated after representative soil ageing intervals, mefentrifluconazole as well as the TDM were identified as major residues. Overall, the metabolism in rotational crops is similar to metabolism in primary crops with no rotational crop specific metabolites.

The ratio of *R*- and *S*-enantiomers of mefentrifluconazole residues in plants remained unchanged compared with the test substance, indicating the absence of preferential metabolism or uptake.

Residues of mefentrifluconazole and the TDM remained stable in hydrolysis studies simulating representative food processing conditions.

For commodities of plant origin, including processed commodities and rotational crops, the residue definition for risk assessment should therefore include mefentrifluconazole (BAS 750 F) and separately the triazole derivative metabolites TA, TLA, TAA, 1,2,4-T considered for assessment as agreed during the recent review of TDM. The residue definition for MRL enforcement/monitoring is proposed as mefentrifluconazole (BAS 750 F) only. Recommendations for monitoring of TDM residues as proposed during the recent review of TDM for a number of existing triazole active substances are applicable also to mefentrifluconazole.

A sufficient number of residue field trials in wheat and barley in northern Europe (NEU and southern Europe (SEU)) are available to support the representative use in cereals. Analysis of BAS 750 F, TA, TLA, TAA, 1,2,4-T was conducted in grain and straw with validated analytical methods. Integrity of residues during freezer storage of the grain and straw samples until analysis was demonstrated for all analytes.

In rotational crop residue trials in wheat, radish, carrot, cauliflower, broccoli, lettuce and spinach in NEU and SEU at a dose level which covers the expected plateau concentration of BAS 750 F in soil, residues of BAS 750 F above LOQ were not found while residues of TDM except 1,2,4-T regularly exceeded the LOQ. The residue levels obtained for the TDM are comparable to the residues in rotational crops considered for other triazole active substances in the TDM review.

With regard to the requirement for residue data in pollen and bee products for human consumption a waiver was submitted that was considered as insufficient evidence to conclusively rule out occurrence of residues of BAS 750 F or its metabolites in pollen and in bee products for human consumption (data gap).

Studies are available to determine the transfer of residues of mefentrifluconazole, TA, TAA and TLA into a variety of wheat and barley processed commodities and to establish respective processing factors.

Metabolism studies with BAS 750 F in goat and hen indicated common basic metabolite routes while species-typical conjugation reactions and a different transformation rate among the two species were observed. In poultry matrices, the metabolite M750F022 (and its fatty acid conjugates) is the predominant component of the residue, with unmodified parent mefentrifluconazole and 1,2,4-T also present as significant components. In goat matrices, unmodified parent mefentrifluconazole and 1,2,4-T were the predominant components of the residue, with M750F022 present at much lower levels. A metabolism study in fish upon dietary exposure to BAS 750 F showed that mefentrifluconazole and 1,2,4-T were the major residues in fish matrices.

Chiral analysis of mefentrifluconazole revealed a significant change of the ratio in most goat matrices, with proportion of the *R*-enantiomer of 70–80% in cream, muscle, liver, kidney and fat. In contrast, the racemate was maintained in goat faeces, indicating a preferential metabolism of the *S*-enantiomer. Such a change was not observed in poultry and was not analysed for in fish.

Exposure of poultry and ruminant to TDM via the diet was significant with regard to the representative uses. The metabolic pathway of TDM in poultry and ruminant has been assessed under the recent review of TDM and the conclusions should apply accordingly, while information is currently not available for metabolism of TDM in fish.

For commodities of animal origin, the residue definition for risk assessment should include mefentrifluconazole (BAS 750F) and separately the triazole derivative metabolites (TA and TLA, TAA, 1,2,4-T) as agreed during the recent review of TDM. For fish, this residue definition is provisional but considered sufficiently precautionary. The residue definition for animal commodities for MRL enforcement/monitoring is proposed as mefentrifluconazole (BAS 750 F). Recommendations for monitoring of TDM residues as proposed during the recent review of TDM for a number of existing triazole active substances are applicable also to mefentrifluconazole.

The transfer of residues in animal commodities was assessed based on feeding studies with mefentrifluconazole in ruminant and poultry, conducting analysis of parent or formed TDM in animal matrices. The integrity of TDM residues except 1,2,4-T during sample storage until analysis of defined animal commodities has still to be demonstrated (data gap). Considering exposure from plant commodities, the maximum dietary burden of TA and TAA resulting from the representative uses are within the maximum levels determined in the TDM review, and the assessment of residue transfer in animal commodities for these compounds should apply accordingly. Feeding studies dosed with TLA are not available, while in the context of this assessment the dietary burden based on use of mefentrifluconazole exceeds the trigger value in cattle, sheep and poultry. Therefore, in accordance with the conclusions in the TDM review a data gap is identified to further address transfer of residues of TLA in animal commodities.

The consumer dietary risk assessment was performed with the EFSA PRIMo rev.2. Estimated intakes of mefentrifluconazole were well below the toxicological reference values for all European sub-population groups. In the chronic assessment, the highest TMDI was 4.3% ADI (IE adult). In the acute assessment, for children, the highest international estimated short-term intake (IESTI) was corresponding to 1.8% ARfD for consumption of bovine liver, and for adults 2.0% ARfD for consumption of barley.

With regard to residues of TDM, the RMS did not consider necessary to undertake a new dietary risk assessment for TDMs arising from the application of mefentrifluconazole, as this is deemed covered by the risk assessment performed in the TDM review because data obtained on the levels of TDM residues from use of mefentrifluconazole are comparable to the TDM data previously considered in the TDM review. Nonetheless, it should be noted that mefentrifluconazole is an additional compound contributing to the pool of TDM residues in plant and animal commodities and that the available single substance residue trials are not taking into account multiple applications of different triazole pesticides per crop or per season.

#### 4. Environmental fate and behaviour

Mefentrifluconazole is a racemic mixture of an (*R*)-enantiomer and an (*S*)-enantiomer. The methods of analyses used in the radiolabelled soil and water studies were able to distinguish between the enantiomers and there was no significant change in the isomeric ratio over the duration of the studies.

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, mefentrifluconazole exhibited high to very high persistence in soil. No major (> 10% applied radioactivity (AR)) metabolites were formed. However, applicant proposed to consider metabolite 1,2,4-T (M750F001) (which occurred at a maximum concentration of 5.1% AR at a single time point) within the present assessment due to its widespread occurrence in the environment. Metabolite 1,2,4-triazole exhibited moderate to high persistence in soil exhibiting a biphasic pattern of decline. Mineralisation of the <sup>14</sup>C-radiolabelled triazole, chlorophenyl and trifluoromethylphenyl rings to carbon dioxide accounted for 0.2–9.7% AR after 121 days. The formation of unextractable residues (not extracted by acetonitrile/water) for these radiolabels accounted for 12.6–26.7% AR after 121 days. For the metabolite, 1,2,4-T EU agreed endpoints were used in the present assessment (EFSA, 2013a).

In anaerobic soil incubations, degradation of mefentrifluconazole was slow, with the degradation pathway similar to that under aerobic conditions and no major metabolites were detected. In a soil photolysis study, no new metabolites requiring further investigation were detected. The contribution of photolytic transformation processes on soil surfaces to the dissipation of mefentrifluconazole from the soil environment is regarded as negligible.

Mefentrifluconazole exhibited slight mobility in soil. Metabolite 1,2,4-T exhibited very high to high soil mobility. It was concluded that the adsorption of mefentrifluconazole and metabolite 1,2,4-T was not pH dependent.

In satisfactory field dissipation studies carried out at six sites in the EU, mefentrifluconazole exhibited high to very high persistence. Following the EFSA guidance (EFSA, 2014a), the field data endpoints were not combined with laboratory values to derive modelling endpoints as the geometric mean of normalised laboratory DT<sub>50</sub> was > 240 days. In European field dissipation studies at four sites where 1,2,4-T was dosed, this metabolite exhibited a biphasic pattern of decline having moderate to high persistence (EFSA, 2013a).

In laboratory incubations in dark aerobic natural sediment water systems, mefentrifluconazole exhibited high persistence, forming the major metabolites 1,2,4-T (max. 10.2% AR in water and 4.9% AR in sediment) and M750F003 (max. 3.8% AR in water and 5.4% AR in sediment). The unextractable sediment fraction was the major sink for both <sup>14</sup>C-radiolabelled triazole and chlorophenyl rings, accounting for 17–26.6% AR at study end (100 days). Mineralisation of these radiolabels accounted for 0.5–9.6% AR at the end of the study.

The rate of decline of mefentrifluconazole in a laboratory sterile aqueous photolysis experiment was significantly fast relative to that occurred in the aerobic sediment water incubations. Irradiation of triazole and chlorophenyl-labelled mefentrifluconazole in sterile water resulted in formation of the major photodegradation products M750F005 (max. 32.2% AR), M750F006 (max. 30.7% AR), M750F007 (max. 43.9% AR), and M750F008 (max. 7.3% AR).

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for the metabolites 1,2,4-T and M750F003, using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1-2 in FOCUS calculator). For metabolites M750F005, M750F006, M750F007, and M750F008, appropriate step 3 (FOCUS, 2001) calculations were available. PEC<sub>SW</sub> for these photolytic metabolites were calculated converting the maximum parent PEC<sub>SW</sub> values based on the molecular weight correction and peak occurrence in the aqueous photolysis study (i.e. metabolite PEC<sub>SW</sub> = parent PEC<sub>SW</sub> × molar correction factor × peak occurrence in water as a fraction). The K<sub>OC</sub> values of the photolytic metabolites were derived using EPI Suite and were high for all metabolites. For the active substance, mefentrifluconazole step 4 calculations were performed following the FOCUS (2007) guidance, with no-spray drift buffer zones of up to 5 m being implemented (representing a 57–91% spray drift reduction). The SWAN tool (version 4.0) was appropriately used to implement these mitigation measures in the simulations.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (2009) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4 for the active substance mefentrifluconazole and metabolite 1,2,4-T. Four tiers of groundwater modelling were proposed based on refining the formation fraction of metabolite 1,2,4-T and taking into account its biphasic degradation:

- At tier 1, the formation fraction was set to 1 and the geometric mean of slow phase DT<sub>50</sub> values was used;

- At tier 2, the formation fraction was set to 1 and degradation rates of the fast and slow phases were calculated based on the formation fraction and the 'g' value;
- At tier 3, the formation fraction was set to 0.65 (based on the worst case formation fraction) and degradation rates of the fast and slow phases were calculated based on the formation fraction and the 'g' value;
- At tier 4, the formation fraction was set to 0.4 (based on the arithmetic mean formation fraction) and degradation rates of the fast and slow phases were calculated based on the formation fraction and the 'g' value.

In order to minimise the influence of non-linear sorption of metabolite 1,2,4-T, in tiers 2–4 the amount of active substance applied was doubled and the predicted concentrations of parent and metabolite in leachate were divided by 2. Results coming from tier 4 were used in the present assessment. The potential for groundwater exposure from the representative uses by mefentrifluconazole 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 mefentrifluconazole and metabolite 1,2,4-T.

The applicant provided some information to address the effect of water treatments processes on the nature of the residues that might be present in surface water and groundwater. However, appropriate information were not provided on the consideration of chlorination and ozonation 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 (see Section 7) and results in the consumer risk assessment not being finalised (see Section 9).

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

## 5. Ecotoxicology

The risk assessment was based on the following documents: Guidance Document on Terrestrial Ecotoxicology (European Commission, 2002a), Guidance Document on Aquatic Ecotoxicology (European Commission, 2002b), Guidance Document on non-target arthropods (SETAC, 2001), Guidance Document on Birds and Mammals (EFSA, 2009), Guidance on tiered risk assessment for aquatic organisms (EFSA PPR Panel, 2013).

According to Regulation (EU) No. 283/2013, data should be provided regarding the acute and chronic toxicity to honeybees and data to address the development of honeybee brood and larvae. As the European Commission (2002a) does not provide a risk assessment scheme which is able to use the chronic toxicity data for adult honeybees and the honeybee brood, when performing the risk assessment according to European Commission (2002a), the risk to adult honeybees from chronic toxicity and the risk to bee brood, could not be finalised due to the lack of a risk assessment scheme. Therefore, the EFSA (2013b) should be used for risk assessment in order to reach a conclusion for the representative uses.

BASF 750 F (mefentrifluconazole) was discussed at the Pesticides Peer Review Experts' teleconference 170 in March 2018.

Acute oral toxicity studies with mallard duck, bobwhite quail and canary birds were available. Only one study is required and the possibility of combining the studies to derive an endpoint based on the geometric mean value of available endpoints was discussed. Diarrhoea was observed in the canary and bobwhite quail studies. Furthermore, there were concerns about the health of the birds used in the canary study and hence this study was considered unreliable. Some experts considered that the endpoints of bobwhite quail and mallard duck could be combined. However, the majority of experts were of the opinion that this is not appropriate because of differences in the quality of the two studies and that the lowest endpoint of 816 mg/kg bw from the study with bobwhite quail should be used. The acute and long-term (reproductive) risk to birds from oral exposure via residues in food and water was assessed as low.

The relevant endpoint from the rabbit developmental study was decreased from 25 mg a.s./kg bw per day to 15 mg a.s./kg bw per day based on maternal bodyweight effects and skeletal variations at 25 mg a.s./kg bw per day. The effects on maternal bodyweight were assessed as treatment related by toxicology. The effects on maternal body weight gain at the dose of 25 mg a.s./kg bw per day were > 10% (13% reduction with respect to control for days 0–29 and 11% reduction with respect to control for treatment days 6–28). In the absence of set triggers/threshold for ecological relevance of body weight effects, the majority of the experts agreed to use the endpoint of 15 mg a.s./kg bw per day in the mammalian risk assessment.

The log Pow of BAS 750F is 3.4. Therefore, a risk assessment for earthworm- and fish-eating birds was conducted and assessed as low.

The risk to **birds and mammals** from oral exposure to BASF 750F via food, contaminated drinking water and secondary poisoning was assessed as low.

The risk to birds and mammals from oral exposure to plant metabolites M750F001, M750F029, M750F030 and M750F031 was assessed as low.

The formulation BAS70501F is acutely up to 10 times more toxic to **aquatic organisms** than the active substance. The risk to aquatic plants and algae was assessed as low for the active substance and the formulation with FOCUS step 1 PEC<sub>sw</sub>. A refinement of the risk assessment was needed for fish and aquatic invertebrates. The acute and chronic risk to fish from the active substance was assessed as low with FOCUS step 3 PEC<sub>sw</sub> except for D2 ditch where risk mitigation is needed. Risk mitigation equivalent to a 5-m buffer zone is not sufficient for the D2 ditch scenario. No larger buffer distances were calculated. The acute risk to daphnids was assessed as low for the active substance. Risk mitigation comparable to a 5-m no-spray buffer zone is needed to mitigate the long-term risk to aquatic invertebrates in scenario D1 ditch. A 5-m no spray buffer zone is not sufficient for scenario D2 ditch. No risk assessment was conducted for buffer zones larger than 5 m.

The refined acute risk assessment for the formulation was based on spray drift entry for a pond, ditch and stream scenario. A low risk was indicated for fish in the pond scenario and in all three scenarios for invertebrates. Risk mitigation comparable to a 5-m no spray buffer zone would be needed to achieve PEC<sub>sw</sub> values below the RAC for fish in the stream and ditch scenario.

The risk to sediment dwelling invertebrates was assessed as low.

The risk to aquatic organisms from the metabolites M750F001, M750F003, M750F006, M750F007 and M750F008 was assessed as low. The acute risk to fish from metabolite M750F005 was assessed as high for the scenario D2 ditch. A 5-m no-spray buffer zone was not sufficient as a risk mitigation for scenario D2 ditch. No risk assessment was provided for larger no-spray buffer zones. For all other scenarios and other groups of aquatic organisms, the risk from M750F005 was assessed as low.

The risk of bioaccumulation of mefentrifluconazole was assessed as low.

A fish full life cycle test (FFLC) and a test according to OECD TG 234 were submitted in order to address potential endocrine effects on fish. In the FFLC, effects on reproduction and growth were observed at the highest tested concentration of 45.5 µg a.s./L. However, the available FFLC lacks important ED-related parameters such as vitellogenin levels, and oestrogen level in females. The available test according to OECD TG 234 does not cover the reproductive life stages of fish. Considering the results of *in vitro* data (positive for aromatase inhibition) further information, e.g. a test according to OECD 229, should be provided in order to draw a firm conclusion the endocrine potential of mefentrifluconazole in fish.

Toxicity data on **honeybees** (acute, chronic, larvae) and acute toxicity data on bumblebees were available and evaluated in the DAR. A risk assessment was conducted according to the guidance document on terrestrial ecotoxicology (European Commission, 2002a). No risk assessment was provided for chronic risk to adult bees, larvae or non-apis bees. A data gap for a risk assessment according to the Guidance Document on Bees (EFSA, 2013a,b) is identified. Although it is acknowledged that the EFSA Bee Guidance Document is yet to be implemented, it was agreed at the Pesticides Peer Review Expert Meeting 133 (September 2015) that it should be used (at least the first tier schemes and the general principles for the higher tier). The previous risk assessment schemes are not able to consider various aspects which are now considered to be important in the risk assessment for bees (e.g. chronic, larvae, additional exposure scenarios). Furthermore, it is now necessary to provide chronic adult and larvae data according to Regulation 283/2013. Therefore, in the absence of an alternative risk assessment scheme which would be able to address these points, it was agreed that the EFSA Bee Guidance should be used.

The risk to other **non-target arthropods** was assessed as low for the off-field in a first tier assessment. A low in-field risk was demonstrated in a refined risk assessment with extended laboratory studies.

The risk to **earthworms and other soil dwelling meso- and macrofauna** was assessed as low for exposure to the active substance and the metabolite BAS750F 01 (1,2,4-T).

The risk to **soil nitrogen transformation, non-target plants and biological methods of sewage treatment** was assessed as low.

## 6. 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)	Persistence	Ecotoxicology
<b>Mefentrifluconazole</b>	High to very high persistence Biphasic kinetics DT <sub>50</sub> 104–477 days (DT <sub>90</sub> > 1,000 days, 20°C and pF2) European field dissipation studies single first order and biphasic kinetics DT <sub>50</sub> 185–846 days (DT <sub>90</sub> 616 to > 1,000 days)	Low risk to soil dwelling organisms
<b>1,2,4-triazole</b>	Moderate to high persistence Biphasic kinetics DT <sub>50</sub> 59.2–247.6 days (20°C and 40% maximum water holding capacity soil moisture) European field dissipation studies biphasic kinetics DT <sub>50</sub> 25.1–126 days (normalised to 20°C and pF2)	Low risk to soil dwelling organisms

DT<sub>50</sub>: period required for 50% dissipation; DT<sub>90</sub>: period required for 90% dissipation.

**Table 2:** Groundwater

Compound (name and/or code)	Mobility in soil	> 0.1 µg/L at 1 m depth for the representative uses <sup>(a)</sup>	Pesticidal activity	Toxicological relevance
<b>Mefentrifluconazole</b>	Slight mobility K <sub>Foc</sub> 2,010–4,930 mL/g	No	Yes	Yes
<b>1,2,4-triazole</b>	Very high to high mobility K <sub>Foc</sub> 43–120 mL/g	No	Yes	Yes (harmonised classification: reproductive toxicant cat 2)

K<sub>Foc</sub>: Freundlich organic carbon adsorption coefficient.

(a): At least one FOCUS scenario or a relevant lysimeter.

**Table 3:** Surface water and sediment

Compound (name and/or code)	Ecotoxicology
<b>Mefentrifluconazole</b>	The risk to aquatic organisms was low in most scenarios. A high risk was indicated only in scenarios D2 ditch for fish, D1 and D2 ditch for invertebrates requiring risk mitigation. Risk mitigation equivalent to a 5-m no-spray buffer zone is sufficient as a risk mitigation for D1 scenarios but not for D2 ditch
<b>1,2,4-triazole</b> (soil, surface water/sediment)	The risk to aquatic organisms was assessed as low
<b>M750F003</b> (surface water/sediment)	The risk to aquatic organisms was assessed as low
<b>M750F005</b> (aqueous photolysis)	The risk to aquatic organisms was assessed as low except for the scenario D2 ditch for which a high acute risk to fish was indicated
<b>M750F006</b> (aqueous photolysis)	The risk to aquatic organisms was assessed as low
<b>M750F007</b> (aqueous photolysis)	The risk to aquatic organisms was assessed as low
<b>M750F008</b> (aqueous photolysis)	The risk to aquatic organisms was assessed as low

**Table 4:** Air

Compound (name and/or code)	Toxicology
<b>Mefentrifluconazole</b>	Rat LC <sub>50</sub> inhalation > 5.3 mg/L air (nose only), no classification required

 LC<sub>50</sub>: lethal concentration, median.

## 7. Data gaps

This is a list of data gaps identified during the peer review process, including those areas in which a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 56 of the Regulation concerning information on potentially harmful effects).

- Spectra data for the relevant impurities (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- Information on the content of the relevant impurities after the storage (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- Method of analysis of 1,2,4-(1*H*)-triazole in the representative formulation (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 1).
- Monitoring methods for determination of metabolites M750F015, M750F016 and M750F017 in body fluids (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Sections 1 and 2).
- Poultry and ruminants feeding studies conducted with TLA or, alternatively metabolism studies performed in accordance with the current recommendations as a surrogate to these feeding studies to determine the magnitude of TLA residues in products of animal origin (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Sufficient storage stability data to demonstrate integrity of residues of TA, TAA, TLA in the relevant poultry and ruminant matrices during the sample storage in the feeding studies with mefentrifluconazole.
- Data or information addressing residue levels of mefentrifluconazole and its metabolites in pollen and in bee products for human consumption, obtained from primary and rotational crops (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 3).
- Appropriate information on the consideration of chlorination and ozonation processes on the nature of the residues that might be present in surface water, when surface water is abstracted for drinking water (Article 4 (approval criteria for active substances) 3(b) of Regulation (EC) No 1107/2009) were not provided (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see Section 4).
- Further information on endocrine disruption in fish, e.g. a test according to OECD 229, should be provided.
- A risk assessment according to EFSA, 2013a,b (EFSA Bee Guidance Document) should be performed (relevant for all representative uses proposed; no submission date proposed by the applicant, see Section 5).

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

No particular conditions are proposed for the representative uses.

## 9. Concerns

### 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 the representative uses in line with the uniform principles in accordance with Article 29(6) of the Regulation and as set out in Commission Regulation (EU) No 546/2011<sup>3</sup> 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).

<sup>3</sup> 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.

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 the Regulation.

- 1) The consumer risk assessment is not finalised with regard to the unknown nature of residues that might be present in drinking water, consequent to water treatment following abstraction of surface water that might contain mefentrifluconazole and its metabolites (see Section 4).
- 2) No final conclusion could be drawn with regard to endocrine disruption in fish.

## 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 the Regulation 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 the Regulation.

- None proposed for the representative uses.

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

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in Section 8, has been evaluated as being effective, then 'risk identified' is not indicated in Table 5.)

**Table 5:** Overview of concerns

Representative use		Cereals
<b>Operator risk</b>	Risk identified	
	Assessment not finalised	
<b>Worker risk</b>	Risk identified	
	Assessment not finalised	
<b>Resident/bystander risk</b>	Risk identified	
	Assessment not finalised	
<b>Consumer risk</b>	Risk identified	
	Assessment not finalised	X <sup>1</sup>
<b>Risk to wild non-target terrestrial vertebrates</b>	Risk identified	
	Assessment not finalised	
<b>Risk to wild non-target terrestrial organisms other than vertebrates</b>	Risk identified	
	Assessment not finalised	
<b>Risk to aquatic organisms</b>	Risk identified	
	Assessment not finalised	
<b>Groundwater exposure to active substance</b>	Legal parametric value breached	
	Assessment not finalised	

Representative use	Cereals
Groundwater exposure to metabolites	Legal parametric value breached <sup>(a)</sup>
	Parametric value of 10 µg/L <sup>(b)</sup> breached
	Assessment not finalised

Columns are grey if no safe use can be identified. The superscript numbers relate to the numbered points indicated in Sections 9.1. Where there is no superscript number, see Sections 2–6 for further information.

(a): Based on classification made in the context of this evaluation procedure under Regulation (EC) No 1107/2009. It should be noted that harmonised classification and labelling is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Or it should be noted that the classification proposed in the context of this evaluation procedure under Regulation (EC) No 1107/2009 concurs with the harmonised classification and labelling in accordance with Regulation (EC) No 1272/2008.

(b): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev. 10 final, European Commission, 2003.

## References

- ECHA (European Chemicals Agency), 2017. Guidance on the Application of the CLP Criteria; Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 5.0, July 2017. Reference: ECHA-17-G-21-EN; ISBN: 978-92-9020-050-5; available online: <https://echa.europa.eu/guidance-documents/guidance-on-clp>
- ECHA (European Chemicals Agency), 2018. Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of mefentrifluconazole. [CLH-O-NNNNNNNNNN-NN-NN/X]. Adopted 9 March 2018. Not yet published.
- EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. <https://doi.org/10.2903/j.efsa.2009.1438>
- EFSA (European Food Safety Authority), 2013a. Conclusion on the peer review of the pesticide risk assessment of the active substance ipconazole. EFSA Journal 2013;11(4):3181, 76 pp., <https://doi.org/10.2903/j.efsa.2013.3181>
- EFSA (European Food Safety Authority), 2013b. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA Journal 2013;11(7):3295, 268 pp., <https://doi.org/10.2903/j.efsa.2013.3295>
- EFSA (European Food Safety Authority), 2014a. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp., <https://doi.org/10.2903/j.efsa.2014.3662>
- EFSA (European Food Safety Authority), 2018a. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance BAS 750 F (mefentrifluconazole). Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)
- EFSA (European Food Safety Authority), 2018b. Conclusion on the peer review of the pesticide risk assessment triazole derivative metabolites in light of confirmatory data submitted, under development not yet published.
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2012. Guidance on dermal absorption. EFSA Journal 2012;10(4):2665, 30 pp. <https://doi.org/10.2903/j.efsa.2012.2665>
- EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 186 pp. <https://doi.org/10.2903/j.efsa.2013.3290>
- European Commission, 2000a. Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3029/99-rev. 4, 11 July 2000.
- European Commission, 2000b. Technical material and preparations: guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3030/99-rev. 4, 11 July 2000.
- European Commission, 2002a. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.
- European Commission, 2002b. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001-rev. 4 final, 17 October 2002.
- European Commission, 2003. Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003.
- European Commission, 2010. Guidance Document on residue analytical methods. SANCO/825/00-rev. 8.1, 16 November 2010.
- European Commission, 2011. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. SANCO 7525/VI/95-rev. 9. March 2011. p. 1–46.
- European Commission, 2012. Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1, 13 July 2012.

- European Commission, 2013. Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products. SANCO/10054/2013-rev. 3, 11 July 2013.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.4, May 2015.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2006. Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005-v. 2.0, 434 pp.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2007. Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. EC Document Reference SANCO/10422/2005 v. 2.0, 169 pp.
- FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2009. Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 1, 604 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.0, January 2011.
- JMPR (Joint Meeting on Pesticide Residues), 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20–29 September 2004, 383 pp.
- JMPR (Joint Meeting on Pesticide Residues), 2007. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 18–27 September 2007, 164 pp.
- OECD (Organisation for Economic Co-operation and Development), 2009. Guidance document on overview of residue chemistry studies. ENV/JM/MONO(2009)31, 28 July 2009.
- OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: [www.oecd.org](http://www.oecd.org)
- SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. ESCORT 2.
- United Kingdom, 2017. Draft Assessment Report (DAR) on the active substance BAS 750 F (mefentrifluconazole) prepared by the rapporteur Member State the United Kingdom in the framework of Regulation (EC) No 1107/2009, April 2017. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)
- United Kingdom, 2018. Revised Draft Assessment Report (DAR) on BAS 750 F (mefentrifluconazole) prepared by the rapporteur Member State the United Kingdom in the framework of Regulation (EC) No 1107/2009, April YYYY. Available online: [www.efsa.europa.eu](http://www.efsa.europa.eu)

## Abbreviations

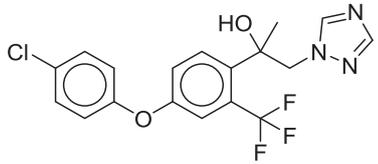
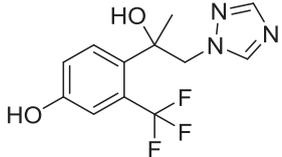
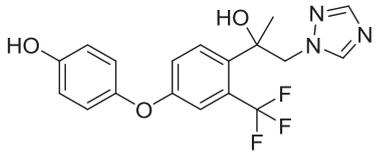
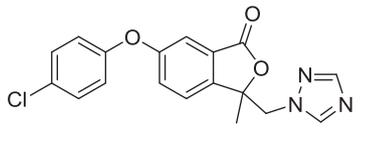
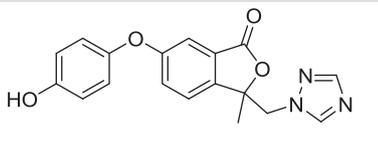
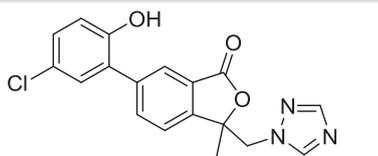
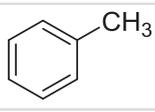
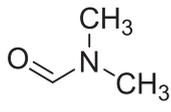
a.s.	active substance
AAOEL	acute acceptable operator exposure level
ADI	acceptable daily intake
ALT	alanine aminotransferase (SGPT)
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
CAR	constitutive androstane receptor
DAR	draft assessment report
DAT	days after treatment
DMF	<i>N,N</i> -Dimethylformamide
DT <sub>50</sub>	period required for 50% dissipation (define method of estimation)
DT <sub>90</sub>	period required for 90% dissipation (define method of estimation)
EATS	oestrogen, androgen, thyroid and steroidogenesis (modalities)
ECHA	European Chemicals Agency
ED	endocrine-disrupting
EEC	European Economic Community
FAO	Food and Agriculture Organization of the United Nations
FFLC	fish full life cycle test

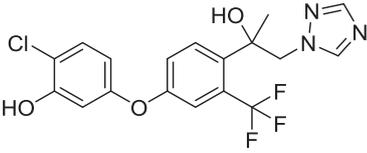
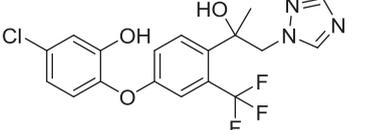
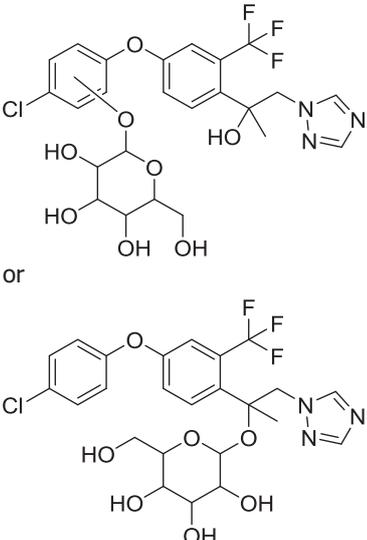
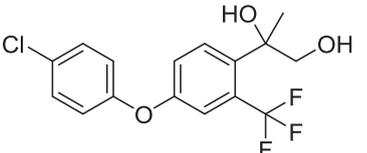
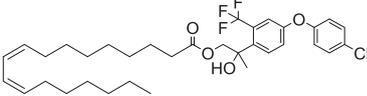
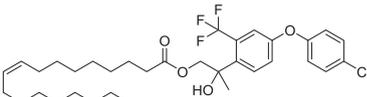
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
IESTI	international estimated short-term intake
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
$K_{Foc}$	Freundlich organic carbon adsorption coefficient
$LC_{50}$	lethal concentration, median
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOQ	limit of quantification
MRL	maximum residue level
NEU	northern Europe
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
$PEC_{air}$	predicted environmental concentration in air
$PEC_{gw}$	predicted environmental concentration in groundwater
$PEC_{sed}$	predicted environmental concentration in sediment
$PEC_{soil}$	predicted environmental concentration in soil
$PEC_{sw}$	predicted environmental concentration in surface water
PPE	personal protective equipment
PRIMo	Pesticide Residue Intake Model
QSAR	quantitative structure–activity relationship
QuEChERS	quick, easy, cheap, effective and safe method
RMS	rappporteur Member State
SEU	southern Europe
SMILES	simplified molecular-input line-entry system
1,2,4-T	1,2,4-triazole
TA	triazole alanine
TAA	triazole acetic acid
TDM	triazole derivative metabolite
TLA	triazole lactic acid
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
UF	uncertainty factor
WHO	World Health Organization

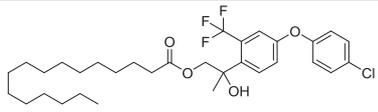
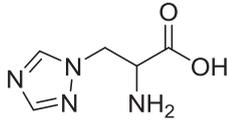
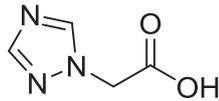
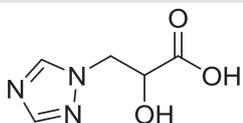
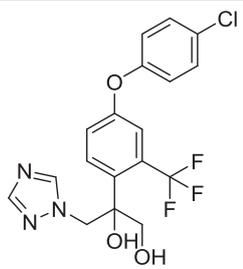
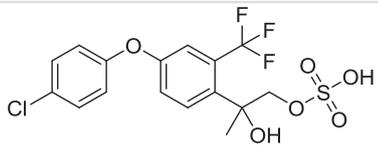
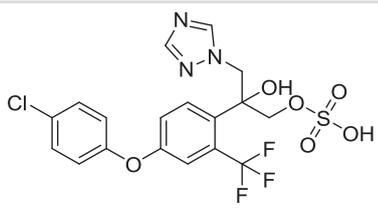
## **Appendix A – List of end points for the active substance and the representative formulation**

Appendix A can be found in the online version of this output ('Supporting information' section):  
<https://doi.org/10.2903/j.efsa.2018.5379>

## Appendix B – Used compound codes

Code/trivial name <sup>(a)</sup>	Chemical name/SMILES notation <sup>(b)</sup>	Structural formula <sup>(b)</sup>
<b>Mefentrifluconazole</b> BAS 750 F	(2 <i>RS</i> )-2-[4-(4-chlorophenoxy)- $\alpha,\alpha,\alpha$ -trifluoro- <i>o</i> -tolyl]-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-ol <chem>CC(CN1C=NC=N1)(c2c(C(F)(F)F)cc(Oc3ccc(Cl)cc3)cc2)O</chem> JERZEQUMJNCPRJ-UHFFFAOYSA-N	
<b>1,2,4-triazole</b> MF750F001	1 <i>H</i> -1,2,4-triazole <chem>N1N=CN=C1</chem> NSPMIYGKQJPBQR-UHFFFAOYSA-N	
<b>M750F003</b> 4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenol	4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenol <chem>OC1=CC=C(C(C)(O)CN2N=CN=C2)C(C(F)(F)F)=C1</chem> WZNDGSSDNFWRU-UHFFFAOYSA-N	
<b>M750F005</b> 4-{4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol	4-{4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol <chem>OC1=CC=C(OC2=CC=C(C(C)(O)CN3N=CN=C3)C(C(F)(F)F)=C2)C=C1</chem> XXTGZVUVWIHRHS-UHFFFAOYSA-N	
<b>M750F006</b> 6-(4-chlorophenoxy)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one	6-(4-chlorophenoxy)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one <chem>O=C1OC(CN2N=CN=C2)(C)C3=CC=C(OC4=CC=C(Cl)C=C4)C=C13</chem> PUYHXMAKCYUBF-UHFFFAOYSA-N	
<b>M750F007</b> 6-(4-hydroxyphenoxy)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one	6-(4-hydroxyphenoxy)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one <chem>O=C1OC(CN2N=CN=C2)(C)C3=CC=C(OC4=CC=C(O)C=C4)C=C13</chem> CVTZVGKIZRMGMX-UHFFFAOYSA-N	
<b>M750F008</b> 6-(5-chloro-2-hydroxyphenyl)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one	6-(5-chloro-2-hydroxyphenyl)-3-methyl-3-[(1 <i>H</i> -1,2,4-triazol-1-yl)methyl]-2-benzofuran-1(3 <i>H</i> )-one <chem>O=C1OC(CN2N=CN=C2)(C)C3=CC=C(C4=CC(Cl)=CC=C4O)C=C13</chem> VNJWOMIREKKDGP-UHFFFAOYSA-N	
<b>Toluene</b>	Toluene <chem>CC1=CC=CC=C1</chem> YXFVVABEGXRONW-UHFFFAOYSA-N	
<b>N,N-dimethylformamide (DMF)</b>	<i>N,N</i> -dimethylformamide <chem>O=CN(C)C</chem> ZMXDDKWLCZADIW-UHFFFAOYSA-N	
<b>M750F015</b> 2-chloro-4-{4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol	2-chloro-4-{4-[2-hydroxy-1-(1 <i>H</i> -1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol <chem>OC1=CC=C(OC2=CC=C(C(C)(O)CN3N=CN=C3)C(C(F)(F)F)=C2)C=C1Cl</chem> BPZYSCSGCSWRX-UHFFFAOYSA-N	

Code/trivial name <sup>(a)</sup>	Chemical name/SMILES notation <sup>(b)</sup>	Structural formula <sup>(b)</sup>
<b>M750F016</b> 2-chloro-5-{4-[2-hydroxy-1-(1H-1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol	2-chloro-5-{4-[2-hydroxy-1-(1H-1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol <chem>OC1=CC(OC2=CC=C(C(C)(O)CN3N=CN=C3)C(C(F)(F)F)=C2)=CC=C1Cl</chem> WEJBGHCFVNQQDI-UHFFFAOYSA-N	
<b>M750F017</b> 5-chloro-2-{4-[2-hydroxy-1-(1H-1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol	5-chloro-2-{4-[2-hydroxy-1-(1H-1,2,4-triazol-1-yl)propan-2-yl]-3-(trifluoromethyl)phenoxy}phenol <chem>OC1=CC(Cl)=CC=C1OC2=CC=C(C(C)(O)CN3N=CN=C3)C(C(F)(F)F)=C2</chem> FQLCIFALHFMSMGH-UHFFFAOYSA-N	
<b>M750F019</b> <b>Glycoside conjugate</b>	Undefined structure and stereochemistry	
<b>M750F022</b> 2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]propane-1,2-diol	2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]propane-1,2-diol <chem>CC(O)(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)CO</chem> MGHXOFWMGUWOW-UHFFFAOYSA-N	
<b>M750F023</b> 2-(4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl)-2-hydroxypropyl (9Z,11Z)-octadeca-9,11-dienoate	2-(4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl)-2-hydroxypropyl (9Z,11Z)-octadeca-9,11-dienoate <chem>OC(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)C(=O)OCCCCC/C=C\C/C=C/C/C=C/C</chem> QFDCNMYVLKAOFE-XESWYYRISA-N	
<b>M750F024</b> oleic acid conjugate of metabolite M750F022	2-(4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl)-2-hydroxypropyl oleate <chem>CCCCCCCC/C=C\C/C=C/C/C=C/C(OC(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)C(=O)O</chem> BYAZFDOZEUFKNN-KHPPLWFESA-N	

Code/trivial name <sup>(a)</sup>	Chemical name/SMILES notation <sup>(b)</sup>	Structural formula <sup>(b)</sup>
<b>M750F025</b> palmitic acid conjugate of metabolite M750F022	2-(4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl)-2-hydroxypropyl palmitate <chem>CCCCCCCCCCCCCCCC(OCC(O)(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)C)=O</chem> VRYGRZWWYDIDOK-UHFFFAOYSA-N	
<b>M750F029</b> 2-amino-3-(1H-1,2,4-triazol-1-yl)propionic acid	3-(1H-1,2,4-triazol-1-yl)alanine <chem>O=C(O)C(N)CN1N=CN=C1</chem> XVWFTOJHOHJIMQ-UHFFFAOYSA-N	
<b>M750F030</b> (1H-1,2,4-triazol-1-yl)acetic acid	(1H-1,2,4-triazol-1-yl)acetic acid <chem>O=C(O)CN1N=CN=C1</chem> RXDBSQXFIWBJSR-UHFFFAOYSA-N	
<b>M750F031</b> 2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propanoic acid	2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propanoic acid <chem>O=C(O)C(O)CN1N=CN=C1</chem> KJRGHWETVMENC-UHFFFAOYSA-N	
<b>M750F039</b> 2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-3-(1H-1,2,4-triazol-1-yl)propane-1,2-diol	2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-3-(1H-1,2,4-triazol-1-yl)propane-1,2-diol <chem>OCC(O)(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)CN3N=CN=C3</chem> JOFSMGNRINQIAS-UHFFFAOYSA-N	
<b>M750F043</b> 2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-2-hydroxypropyl hydrogen sulfate	2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-2-hydroxypropyl hydrogen sulfate <chem>O=S(O)(OCC(O)(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)C)=O</chem> PCUCHYPMMMHHFQ-UHFFFAOYSA-N	
<b>M750F072</b> 2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl hydrogen sulfate	2-[4-(4-chlorophenoxy)-2-(trifluoromethyl)phenyl]-2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propyl hydrogen sulfate <chem>O=S(O)(OCC(O)(C1=CC=C(OC2=CC=C(Cl)C=C2)C=C1C(F)(F)F)CN3N=CN=C3)=O</chem> WXBXGZKUOPBQDO-UHFFFAOYSA-N	

SMILES: simplified molecular-input line-entry system.

(a): The metabolite name in bold is the name used in the conclusion.

(b): Names, SMILES, InChIKey and structures are generated by ChemBioDraw Ultra v. 13.0.2.3021.