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CONCLUSION ON PESTICIDES PEER REVIEW

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

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The declarations of interest of all scientific experts active in EFSA's work are available at https://open.efsa.europa.eu/experts

Abstract

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State, the United Kingdom and Poland, after Brexit and co-rapporteur Member State, France, for the pesticide active substance prothioconazole 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 prothioconazole as a fungicide on barley, wheat, oats, spelt, rye and triticale field crops and seeds. 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

fungicide, peer review, pesticide, prothioconazole, risk assessment

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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. Prothioconazole 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), the United Kingdom, and co-rapporteur Member State (co-RMS), France, received an application from Bayer CropScience AG for the renewal of approval of the active substance prothioconazole. Since April 2019, following Brexit, Poland is the new RMS and no new co-RMS has been appointed.

An initial evaluation of the dossier on prothioconazole 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 prothioconazole according to the representative uses as a fungicide on barley, wheat, oats, spelt, rye and triticale field crops and seeds, as proposed at EU level, result in a sufficient fungicidal efficacy against the target diseases.

The assessment of the data package revealed no issues that could not be finalised or that needed to be included as critical areas of concern with respect to **identity, physical–chemical and technical properties of the active substance and the formulation** for representative uses, and analytical methods.

In the area of **mammalian toxicology**, no issues that could not be finalised or that need to be included as critical areas of concern were identified.

In the **residue** section, the overall risk assessment is provisional because clarification of the genotoxic potential of M15, M17, M33 and M35 is missing. The consumer risk assessment is pending the finalisation of the residue definitions for risk assessment for plants and animals; currently, the consumer exposure to M04 (prothioconazole-desthio) is less than 15% of the toxicological reference values (TRVs). As regards triazole derivative metabolites (TDMs), the consumer risk assessment conducted based on the results from the prothioconazole use resulted in a lower exposure compared with the outcome on the TDMs peer review (EFSA, 2018).

In the area of **environmental fate and behaviour**, the information available was considered sufficient to complete the assessments necessary regarding the environmental exposure assessment at the EU level for the representative uses assessed.

In the area of **ecotoxicology**, a high long-term risk to birds and mammals was identified for the seed treatment uses on winter cereals. In addition, a high long-term risk to aquatic organisms was identified for the metabolite M04 for the spray uses on winter cereals.

In the area of **environmental fate and behaviour**, the assessment was not finalised for soil, surface water and sediment as one formulation for the representative uses contains the active substance bixafen, and the available evaluations did not include exposure and risk assessments for this active substance from the representative uses. EFSA used information from a previous EFSA assessment of bixafen to conclude on the groundwater exposure assessment of the product for representative uses.

With regard to the assessment of **the endocrine disruption (ED) properties**, based on the available data and assessment, it can be concluded that prothioconazole 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. Although further confirmation is needed regarding the conclusion for the T-modality in non-mammalian species, based on the available data, it is unlikely that prothioconazole is an endocrine disruptor.

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 a minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS the United Kingdom and co-RMS France received an application from Bayer CropScience AG for the renewal of approval of the active substance prothioconazole. Since April 2019, following Brexit, Poland is the new RMS and no new co-RMS has been appointed. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicant, the co-RMS (France), the European Commission and EFSA about the admissibility.

The initial RMS the United Kingdom provided its initial evaluation of the dossier on prothioconazole in the RAR, which was received by EFSA on 22 February 2018 (United Kingdom, 2018).

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicant, Bayer CropScience AG, for consultation and comments on 12 June 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 12 August 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 initial RMS, the United Kingdom, on 15 October 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, environmental fate and behaviour and ecotoxicology.

In addition, following a consultation with Member States in the Pesticides Peer Review Experts' teleconference (TC) 26 (October 2020), it was considered necessary to apply an additional clock stop of up to 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-disrupting properties, as laid down in Commission Regulation (EU) 2018/605,[4] are met.

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 April/May 2025.

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 prothioconazole as a fungicide on barley, wheat, oats, spelt, rye and triticale field crops and seeds, as proposed by the applicant. In accordance with Article

[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, pp. 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 disrupting 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, pp. 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 disrupting properties. OJ L 101, 20.4.2018, pp. 33–36.

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, 2025), 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 (18 October 2028 and 10 July 2023[5]);
- the evaluation table (27 May 2025);
- 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 RAR, including its revisions (Poland, 2024) and the peer review report, both documents are considered 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 FORMULATIONS FOR REPRESENTATIVE USES

Prothioconazole is the ISO common name for (*RS*)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione (IUPAC); it is noted that this ISO common name corresponds to a racemic mixture of (*R*)- and (*S*)- prothioconazole.

The formulations for the representative uses were 'Aviator EC 225' and 'Redigo FS 100'. 'Aviator EC 225' is an emulsifiable concentrate (EC) formulation containing 150 g/L of pure prothioconazole and 75 g/L of pure bixafen,[6] and 'Redigo FS 100' is a flowable concentrate (FS) formulation containing 100 g/L of pure prothioconazole.

The information on the active substances and the formulations for representative uses, including the co-formulants in these formulations, was considered in the overall assessment during the peer review. It is noted that the applicant did not indicate the actual co-formulants contained in the formulations for the representative uses, instead provided a list of alternative co-formulants.[7] None of the known co-formulants is an unacceptable co-formulant listed in Annex III of Regulation (EC) No 1107/2009;[8] however, one component of some co-formulants contained in the formulation 'Redigo FS 100' is a non-approved active substance under Regulation (EC) 1107/2009.[9]

Details on the composition of the formulations cannot be reported in conclusions because of the provisions in Article 63(2)(d) of Regulation (EC) No 1107/2009; however, this information was available and evaluated during the peer review. A proposal for classification of the formulation(s) according to Regulation (EC) 1272/2008 was provided by the applicant and assessed by the RMS (please see Volumes 3 CP of the RAR).

The representative uses evaluated for 'Aviator EC 225' were foliar spray applications on barley, wheat, oats, spelt, rye and triticale crops in south and central EU zone; and the representative EU uses evaluated for 'Redigo FS 100' were seed treatment applications of barley, wheat, oats, spelt, rye and triticale. 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 uses of prothioconazole according to the representative uses proposed at EU level result in a sufficient fungicidal efficacy against the target diseases, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014a).

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

[6]The peer review process for the approval of bixafen was completed and an EFSA Conclusion was issued on 15 October 2012 (EFSA, 2012). The peer review process for the renewal of the approval is ongoing (EFSA-Q-2023-00823).

[7]See Evaluation Table Section 1, Data requirement 1.17 (EFSA, 2025).

[8]Commission Regulation (EU) 2021/383 of 3 March 2021 amending Annex III to Regulation (EC) No 1107/2009 of the European Parliament and Council listing co-formulants which are not accepted for inclusion in plant protection products. OJ L 74, 4.3.2021, pp. 7–26.

[9]Please see Regulation (EC) No 1107/2009 for acceptability criteria for co-formulants and Section 2.13.6 of the Technical report on the outcome of the pesticides peer review meeting on general recurring issues in physical and chemical properties and analytical methods. EFSA supporting publication 2019:EN-1623. 32 pp. https://doi.org/10.2903/sp.efsa.2019.EN-1623.

CONCLUSIONS OF THE EVALUATION

General aspects

With regard to the toxicological information available for the formulations for representative uses 'Aviator EC 225' and 'Redigo FS 100', studies were performed on acute toxicity endpoints. Regarding the co-formulants contained in the formulations for representative uses, based on the available information, sufficient toxicological data were available for the majority of them. However, for three co-formulants in 'Aviator EC 225' and three co-formulants in 'Redigo FS 100', the experts considered that the available toxicological information did not sufficiently address the genotoxicity and repeated dose toxicity potential of the two formulations over the short- and long-term and that they might be considered for further assessment. The collected information, including information from the existing uses other than plant protection products, under regulated EU frameworks, did not highlight any concern (see Section 10).[10]

The availability of ecotoxicity data with the formulations for representative uses was discussed at the experts' meeting.[11] It was noted that, based on the available acute data (see Section 5), overall, the formulations for representative uses are not more acutely toxic than the active substance. Furthermore, the data retrieval search and the available data for the individual components were also discussed, and the experts concluded that no concerns were identified. However, pending the outcome of the data gap identified in mammalian toxicology for several components of the formulations for representative uses as described in previous paragraphs, further consideration to non-target organisms may be necessary.

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, 2000b, 2010).

An updated common reference specification was proposed for all manufacturing sources and it was based on batch data from industrial plant productions. The proposed minimum purity of the active substance as manufactured is 970 g/kg; prothioconazole-desthio and toluene were still considered as relevant impurities with maximum levels of 0.5 g/kg and 5 g/kg, respectively. In addition, prothioconazole-deschloro (AE 1344264) and prothioconazole-triazolidinethione (AE 1344254) were considered as new relevant impurities specified at maximum levels of 12 and 5 g/kg, respectively (see Section 2). The current and the proposed reference specification are supported by the batches used in the (eco)toxicological assessment (see Sections 2 and 5).

The proposed minimum purity of 970 g/kg met the requirements of the FAO specification 745/TC (FAO, 2021), covering prothioconazole technical materials of Bayer AG, Division Crop Science (BCS). The FAO specification contains only prothioconazole-desthio as a relevant impurity specified at a maximum of 0.5 g/kg.

The main data regarding the identity of prothioconazole and its physical and chemical properties are given in Appendix B. A data gap was set for the relevant impurities prothioconazole-deschloro (AE 1344264) and prothioconazole-triazolidinethione (AE 1344254) for spectral data and content of the impurities before and after storage of the formulations (**data gap**, see Section 10).

Adequate methods are available for the generation of data required for the risk assessment. Appropriate methods of analysis are available for the determination of the active substance and impurities in the technical materials, and for the determination of the active substance and prothioconazole-desthio and toluene in the formulations. A data gap was set for the relevant impurities prothioconazole-deschloro (AE 1344264) and prothioconazole-triazolidinethione (AE 1344254) for methods of analysis in the formulations (**data gap**, see Section 10).

Residues of prothioconazole-desthio in food and feed of plant origin can be determined by the QuEChERS LC–MS/MS method with a limit of quantification (LOQ) of 0.01 mg/kg in each matrix group. High-pressure liquid chromatography–mass spectrometry (HPLC-MS/MS) methods were developed for the determination of prothioconazole-desthio in food and feed of animal origin with an LOQ of 0.01 mg/kg in meat, liver, kidney, fat and egg and an LOQ of 0.004 mg/kg in milk.

The compounds of the residue definition in soil can be monitored by HPLC–MS/MS methods, with an LOQ of 0.006 mg/kg for prothioconazole (PTZ) and an LOQ of 0.002 mg/kg for prothioconazole-desthio. Appropriate HPLC–MS/MS methods are available for monitoring residues of prothioconazole and prothioconazole-desthio in groundwater, drinking water and surface water with LOQs of 0.05 µg/L for each substance. Residues of prothioconazole in air can be monitored by HPLC-MS/MS method with an LOQ of 0.015 mg/m^3.

An HPLC–MS/MS method is available to monitor prothioconazole-desthio in blood with an LOQ of 0.05 mg/L, while one of the available methods for monitoring PTZ-desthio in food and feed of animal origin can be used also for monitoring in body tissues. No method was available for monitoring prothioconazole in body fluids and tissues (**data gap**, see Section 10).

[10]Refer to experts' consultation 2.17 in the Report of the Pesticides Peer Review TC 125 (EFSA, 2025).

[11]Refer to experts' consultation 5.9 in the Report of the Pesticides Peer Review TC 124 – TC 129 (EFSA, 2025).

2 | MAMMALIAN TOXICITY

The toxicological profile of the active substance prothioconazole and its metabolites was discussed at the Pesticides Peer Review Experts' TC 22 (September 2020) and TC 124 and 125 (January 2024). The assessment is based on the following guidance documents: European Commission (2003, 2012a), EFSA (2014b, 2017), EFSA PPR Panel (2012), ECHA (2017) (and the available draft Technical Guidance Document on assessment of negligible exposure, European Commission, 2015).

Regarding the new proposed reference specification, the impurities PTZ-desthio, PTZ-deschloro (AE 1344264; skin sensitisation potential), PTZ-triazolidinethione (AE 1344254; skin sensitisation potential) and toluene are identified as relevant, with maximum acceptable levels of 0.5, 12, 5 and 5 g/kg, respectively. The test materials used in toxicity studies are considered representative of the current and newly proposed reference specifications for the active substance and associated impurities. Although the impurity PTZ-deschloro (AE 1344264) showed slightly positive results in a skin sensitisation study, it is noted that negative results were obtained in a skin sensitisation study with a PTZ batch representative of the new reference specification.

All toxicological studies were performed with 50:50 racemic prothioconazole and prothioconazole-desthio. For both substances, no information has been submitted on the relative toxicity of their enantiomers (see data gaps identified in Sections 3 and 4).

The oral **absorption** of prothioconazole is estimated to account for > 90% of the administered low dose (2 mg/kg bw). **Excretion** occurs predominantly through the biliary route (90% of the administered dose), with appreciable amounts excreted in urine (2%).

In the rat, prothioconazole is widely distributed throughout the body, with the highest levels being reached in the liver and kidney. There was no evidence of bioaccumulation in any organs or tissues.

The main **metabolic** pathway identified is the direct glucuronidation at the sulfur atom of the parent compound to produce prothioconazole-S-glucuronide, which accounted for 46% and 7.8% of the administered dose in bile and urine, respectively.

Assessment of the comparative in vitro metabolism was performed on human and rat liver microsomes and hepatocytes. A unique human metabolite (prothioconazole-hydroxymethoxy-glucuronide) was identified to form at a low amount. Despite some uncertainties associated with human unicity for this metabolite, the experts agreed that the hydroxymethoxylation is considered of no concern.[12]

The **residue definition** for body fluids and tissues includes prothioconazole and prothioconazole-desthio (M04) (see data gap set in Section 1).

Prothioconazole has no **acute toxicity** by oral, dermal and inhalation exposure. It is neither a skin or eye irritant, nor a skin sensitiser. Prothioconazole tested negative in an in vitro phototoxicity assay.

Short-term oral toxicity studies were provided for rats, mice and dogs. The liver was the main target organ in mice, showing adverse effects including increased weight, changes in clinical chemistry parameters and histopathological changes. Rats and dogs showed similar hepatic effects and, in addition, adverse effects in the kidney, including increased organ weights and histopathological changes. The dog appeared as the most sensitive species, with a no observed adverse effect level (NOAEL) of 5 mg/kg bw per day from the 1-year dog study. This NOAEL was corrected to 3.6 mg/kg bw per day to adjust for the exposure regime of 5 days/week of the study.

Based on the available **genotoxicity** studies, prothioconazole is unlikely to be genotoxic.

Testing for photogenotoxicity is not required for prothioconazole since the conditions triggering the data requirements at the time of the submission of the application for the renewal of approval are not met.

After **long-term exposure** in the rat and the mouse, target organs for toxicity included the liver and kidney. The relevant NOAEL in a 2-year study in rats is 5 mg/kg bw per day, based on effects observed at 50 mg/kg bw per day, including haematological changes (increased platelet count), increased severity of chronic nephropathy and increased incidence of hepatocyte hypertrophy in males and increased urinary output.

The substance showed no treatment-related tumours in rats and mice and was concluded unlikely to be carcinogenic for humans.

With regard to **reproductive toxicity** studies, fertility and overall reproductive performance were not affected. In the multigeneration rat study, the parental NOAEL is 10 mg/kg bw per day based on decreased body weight (bw) gain and decreased thymus weight observed at 100 mg/kg bw per day. The offspring NOAEL is 100 mg/kg bw per day based on reduced pup weight, decreased spleen weight and a slight delay in preputial separation in F1 males observed at 750 mg/kg bw per day. Finally, the reproductive NOAEL is 100 mg/kg bw per day based on a reduced number of oestrus cycles, implantation sites, litter size, time to insemination, duration of gestation observed at 750 mg/kg bw per day and considered secondary to maternal toxicity.

With regard to fetal development, microphthalmia, delayed ossification and skeletal variations were observed in one developmental study in rats at ≥ 80 mg/kg bw per day. In a follow-up study (in a different rat substrain), skeletal variations were observed only at 750 mg/kg bw per day and no microphthalmia was observed. The maternal NOAEL in the rat teratogenicity studies is identified at 80 mg/kg bw per day based on decreased body weight gain, increased water consumption and urination and changes in clinical chemistry parameters observed at 500 mg/kg bw per day. The rat developmental

[12]Refer to experts' consultation 2.1 in the Report of the Pesticides Peer Review TC 22 (EFSA, 2025).

NOAEL is 20 mg/kg bw per day based on the combined results of the two studies. In the rabbit teratogenicity study, the maternal NOAEL is 80 mg/kg bw per day based on increased mortality, decreased body weight and body weight gain and decreased food consumption at 350 mg/kg bw per day. The developmental NOAEL is 80 mg/kg bw per day based on fetotoxic effects secondary to maternal toxicity (350 mg/kg bw per day).

The substance was concluded to be unlikely to be a reproductive and developmental toxicant in humans.

With respect to **immunotoxicity**, prothioconazole does not show any potential for immunotoxic effects in the standard regulatory toxicity studies.

With respect to **neurotoxicity**, no neurotoxic effects are observed in the acute neurotoxicity study. In the rat 13-week neurotoxicity study, reduced motor/locomotor activity is observed, triggering a NOAEL of 357 mg/kg bw per day (following adjustment for the exposure regime of 5 days/week of the study). General toxicity was observed at and above this dose (NOAEL for general toxicity 71 mg/kg bw per day, adjusted for the applied exposure regime of 5 days/week).

The **acceptable daily intake** (**ADI**) is 0.036 mg/kg bw per day, based on the NOAEL identified in the 1-year study in dogs, applying a standard uncertainty factor (UF) of 100. This value differs from the previous peer review where the ADI of 0.05 mg/kg bw per day was based on the NOAEL from the 2-year study in rats and that from the 1-year study in dogs (not adjusted for the 5/7 days of treatment), applying an UF of 100 (EFSA, 2007).

The **acute reference dose** (**ARfD**) is 0.2 mg/kg bw, based on the developmental NOAEL from the developmental study in rats and applying a standard UF of 100. This value is the same as the previous peer review (EFSA, 2007).

The **acceptable operator exposure level** (**AOEL**) is 0.036 mg/kg bw per day, based on the same NOAEL and study used for the ADI derivation and without correction for oral absorption. This value differs from the previous peer review where the AOEL of 0.2 mg/kg bw per day was based on the NOAEL from the developmental study in rats, applying a standard UF of 100 (EFSA, 2007).

The **acute AOEL** (**AAOEL**) is 0.2 mg/kg bw, based on the same NOAEL and study used for the ARfD derivation and without correction for oral absorption. No AAOEL was established in the previous peer review (EFSA, 2007).

For the **dermal absorption** of prothioconazole in the first representative product ('**Aviator EC 255**'), the default dermal absorption values are applicable (EFSA, 2007), i.e. 25% for the concentrate and 70% for the spray dilution. For prothioconazole-desthio, based on an in vitro study with human skin, the dermal absorption value for the spray dilution is 18% (EFSA PPR Panel, 2012).[13]

For the **dermal absorption** of prothioconazole in the second representative product ('**Redigo FS 100**'), the default dermal absorption value to be used for risk assessment is 10% for the formulated product (EFSA, 2017). For prothioconazole-desthio, based on an in vitro study with human skin, the dermal absorption value to be used for risk assessment is 6% (EFSA, 2017).[14] These two values are used for all aspects of the risk assessment as the product is applied undiluted.

For '**Aviator EC 225**', used on cereals, the **non-dietary exposure** estimates are including a 45% conversion of prothioconazole to prothioconazole-desthio. With EFSA calculator (EFSA, 2014b) estimates for the operators are below the (A) AOELs, for both prothioconazole and prothioconazole-desthio, with the use of gloves during mixing/loading and application (in addition to standard workwear). For the workers, the use of workwear is sufficiently protective during the inspection activities (no refinement for the 45% conversion was necessary); for residents and bystanders, drift reducing nozzles are required (after inclusion of the 45% conversion). On this basis, the Hazard Indexes of combined prothioconazole and prothioconazole-desthio acute and repeated exposures were less than one. In relation to the presence of bixafen in 'Aviator EC 225', it is noted that liver is the main toxicological target organ for prothioconazole, prothioconazole-desthio and bixafen, and therefore, combined exposure assuming additive effects is recommended. For the non-dietary exposure, the Hazard Index for the combined repeated exposures including bixafen were also less than one.

For '**Redigo FS 100**', used for seed treatment, the **non-dietary exposure** estimates for the operators are below the (A) AOELs for both prothioconazole and prothioconazole-desthio, with the use of gloves and protective clothing (coveralls) during mixing/loading, calibration, cleaning or handling contaminated surfaces (in addition to standard workwear), based on the results of a valid operator exposure study. For the workers, the use of standard workwear is sufficiently protective during seed sowing activities, according to a seed sowing study. For residents and bystanders, also based on a valid exposure study during sowing, exposures were well below the (A)AOELs. For bystanders in seed treatment plants, based on the Seed TROPEX model, the estimated exposure is below both the prothioconazole and prothioconazole-desthio AOELs, considering a 100% conversion of prothioconazole to prothioconazole-desthio as first tier. Again, on the same basis, the Hazard Indexes of combined prothioconazole and prothioconazole-desthio exposures were less than one.

Toxicological studies and information have been provided for metabolites prothioconazole-desthio (M04), M02, M03, M09, M14, M15, M16, M17, M18, M19, M30 and thiocyanate, as reported in Appendix B. With respect to metabolites identified as relevant residues in Section 3, a genotoxic potential could be excluded, and toxicological reference values were derived for M04, M18, M14 and M16 (see Table 1). Data gaps have been set for the genotoxic potential of the metabolites M15, M17, M33 and M35 (see Sections 3 and 9.1). Data are missing (no data gap identified; not critical for the representative uses) for M02 (clastogenicity), M03, M09 and M19 (clastogenicity and repeated toxicity) and thiocyanate (genotoxicity).

[13]Refer to experts' consultation 2.14 in the Report of the Pesticides Peer Review TC 22 (EFSA, 2025).

[14]Refer to experts' consultation 2.15 in the Report of the Pesticides Peer Review TC 22 (EFSA, 2025).

TABLE 1 Overview table of the toxicological profile of metabolites found as residues in livestock and/or crops.

Metabolite	Genotoxicity	General toxicity Reference values (RV)
Prothioconazole-desthio, JAU 6476-desthio (M04)	Negative in in vitro assays (Ames test, mammalian cell mutation assay, UDS assay, chromosome aberration) and in in vivo micronucleus test	**General toxicity** No acute toxicity; no skin irritation; slight eye irritation; no sensitisation potential Liver target organ following short- and long-term exposure Relevant NOAELs: • Short-term: 2.2 mg/kg bw per day • Long-term: 1.1 mg/kg bw per day Reproductive toxicity: ↑ dystocia and cleft palate; decreased pup viability and delayed growth. Relevant NOAEL (parental, based on hepatic effects and decreased food intake): 2.7 mg/kg bw per day Developmental toxicity: Rats: ↑ rudimentary supranumerary ribs and delayed ossification Rabbits: ↑ arthrogryposis, and multiple abnormalities Relevant NOAEL (foetal, rats): 1 mg/kg bw per day **TRVs:** ADI: 0.01 mg/kg bw per day ARfD: 0.01 mg/kg bw AOEL: 0.01 mg/kg bw per day AAOEL: 0.01 mg/kg bw per day
JAU 6476-α-hydroxy-desthio (M18)	Negative Ames test In silico analysis indicates no difference with prothioconazole-desthio Genotoxicity considered addressed due to structural similarity with prothioconazole and prothioconazole-desthio	Oral LD50 (rat) > 2000 mg/kg Same TRVs as prothioconazole-desthio apply
JAU 6476-desthio-3-hydroxy (M14)	Genotoxicity considered addressed due to close structural similarity with prothioconazole-desthio (M04)	Structurally closely related to prothioconazole-desthio (M04) Same TRVs as prothioconazole-desthio apply
JAU 6476-desthio-4-hydroxy (M15)	The genotoxic potential cannot be excluded due to the in silico structural alert for clastogenicity related to the 3-chlorophenol structure **Data gap** for genotoxicity	No conclusion, pending data gap in genotoxicity
JAU 6476-desthio-5-hydroxy (M16)	Genotoxicity considered addressed due to close structural similarity with prothioconazole-desthio	Structurally closely related to prothioconazole-desthio Same TRVs as prothioconazole-desthio apply
JAU 6476-desthio-6-hydroxy (M17)	The genotoxic potential cannot be excluded due to the in silico structural alert for clastogenicity related to the 3-chlorophenol structure **Data gap** for genotoxicity	No conclusion, pending data gap in genotoxicity
JAU 6476-desthio-3,4-dihydroxy (M33)	No data available **Data gap** for genotoxicity	No conclusion, pending data gap in genotoxicity
JAU 6476-desthio-4,5-dihydroxy (M35)	No data available **Data gap** for genotoxicity	No conclusion, pending data gap in genotoxicity

3 | RESIDUES

The assessment in the residue section is based on the following guidance documents: OECD (2009, 2011), European Commission (2011), JMPR (2004, 2007).

Prothioconazole was discussed at the Peer Review Experts' TC 25 in (28–29 September 2020).

Metabolism in primary crops was investigated in wheat, sugar beet and peanuts after foliar applications of prothioconazole labelled ^{14}C-phenyl and ^{14}C-3,5-triazole at sufficient dose rates compared with the representative GAP. Two additional metabolism studies on wheat were provided: one with seed treatment with only phenyl labelled prothioconazole, and the other with foliar application of triazole labelled M04.

Prothioconazole was found in almost all investigated crops at levels < 10% of total radioactive residues (TRRs). Metabolite M04 was the major residue in most of the investigated crops (e.g. 58% TRR in sugarbeet root, 16% TRR in wheat grain). Prothioconazole-desthio hydroxylated derivatives (M14, M15, M16, M17 and M18) were recovered in significant concentrations mainly in feed items, wheat forage, straw and peanut hay, while the glucoside conjugates of hydroxylated derivatives

(M21, M22, M23) were recovered in crops relevant for human consumption such as peanut meat, wheat grain and beet tops. M14, M15, M16, M17 and M18 were analysed in the field trials in wheat and barley and their presence is confirmed only for feed items.

In the seed treatments study, residue levels in grain were very low (0.01 mg/kg) and therefore not further investigated.

In grain from foliar treated wheat, triazole alanine (TA) and triazole acetic acid (TAA) represented major residues, with 71% and 19% of TRR, respectively. These triazoles represented the major radioactivity in wheat grain also in the M04 triazole labelled metabolism studies. Triazole lactic acid (TLA) was also recovered but represented less than 10% TRR in wheat and up to 24% TRR in peanut meat. 1,2,4-triazole (1,2,4-T) was not found in any of the crops in the metabolism studies but it was found in the field residue trials. Based on overall findings from metabolism studies and field trials, the residue definition for **enforcement is proposed** as prothioconazole-desthio (**M04**). For risk assessment, **the relevant residues** are **prothioconazole-desthio (M04), M14, M15, M16, M17**, **including their glucoside conjugates** (**M21, M22, M23**) and **M18**. Provisionally, these residues are expressed as **prothioconazole-desthio** (M04) **equivalents**, pending data to address the genotoxic potential of M15 and M17 (see Section 2). Separately, the triazole derivative metabolites (TDMs) **TA, TLA, TAA and 1,2,4-T are also included in the risk assessment residue definition** in line with the conclusion on TDMs (EFSA, 2018). These proposals cover all the crop categories following foliar and seed treatments as the metabolic patterns are similar.

Confined rotational crop studies were conducted on wheat, Swiss chard and turnips with triazolyl and phenyl-labelled prothioconazole at all three plant back intervals (PBIs) at 1.5N and 2.2N of the seasonal application rates. The overall metabolism was similar to the primary crops. Prothioconazole was almost not found (less than 1% TRR), while M04 was found at a maximum level of 37% TRR in Swiss chard. The hydroxylated derivatives of M04 were found in lower proportions compared to M04 (maximum 10% TRR for M14 in turnip roots). M64 occurred at a proportion above 10% TRR in wheat straw, but its absolute amount did not exceed 0.05 mg/kg. For the triazole moiety, TDMs represented the majority of the recovered residues, reaching 93% TRR in turnip roots for TA.

Field rotational crop trials were conducted at overdosed rates (3.4N) when compared to the seasonal rate in lettuce, carrots, turnips and barley, and covering all PBIs. They were analysed for M04 and all TDMs. M04 was never detected, while TA, TLA and TAA were present > 0.01 mg/kg in most of the samples. Although hydroxylated metabolites were not measured in the rotational trials, their presence is not expected considering that M04 was not detected and the fact that hydroxylated metabolites were found in similar amounts to M04 in primary crops. Based on the information from the metabolism studies and the results from the field trials, **the same residue definitions as proposed for the primary crops are applicable to rotational crops**.

Storage stability data under freezer conditions were submitted for the prothioconazole, M04, its hydroxylated metabolites and TDMs across several crops and time intervals (see Appendix B). For hydroxylated metabolites, only one study in potatoes is not sufficient to cover cereals; therefore, an additional commodity from the category of high starch content or one from the high protein content category would be needed to extrapolate to all crops (**data gap**, see Section 10). Sufficient field trials covered by validated analytical methods and storage stability were submitted for wheat and barley in Europe (NEU & SEU) to support the foliar and seed treatment uses. In cereals, analysis of M04 and its hydroxylated metabolites was conducted in grains and straw in all trials, and partly, the trial's analysis of TA, TLA, TAA and 1,2,4-T was performed using validated analytical methods.

Livestock studies with prothioconazole triazolyl- and phenyl-labelled were conducted on goats and poultry, while with M04 only in goats. M04 was the major compound in the feed items, thus metabolism studies with M04 are most relevant for depicting the metabolic pattern. In goats, M04 was found in the liver and fat, up to 31% TRR. Additionally, M33, M35 and M32, along with their glucuronide conjugates, were found in all matrices either greater than 10% TRR or above 0.01 mg/kg. Triazole derivatives, mainly 1,2,4-T and TA, were also found in relevant amounts (i.e. 32.6% TRR in milk for 1,2,4-T). The fate and transfer of M04 residues in poultry was not investigated, although it is triggered (**data gap** leading to an issue not finalised, see Section 9.1).

Considering the overall results, the residue definition for **enforcement was proposed as M04** for both poultry and ruminants. For risk assessment in ruminants, the most relevant residues are: **M04 free and conjugated, M14, M15, M33 and M35, free and their conjugates. Provisionally, these residues are expressed as M04 equivalents**, pending the data to address the genotoxic potential of M15, M33 and M35 (see Section 2). Metabolism studies conducted with TDMs were not available. However, their presence in livestock metabolism studies conducted with M04 is noted. Considering that TDMs were present in the feed items and included in the risk assessment residue definition for plants, all experts agreed that TDMs need to be included in the residue definition for risk assessment for livestock, in line with the EFSA outputs on TDMs (EFSA, 2018).

Since residue definitions for enforcement and risk assessment for plant and animal commodities are different, conversion factors were proposed (see Appendix B).

Feeding studies to investigate the transfer of residues in animal commodities were available at three dosing levels for poultry with prothioconazole and for ruminants with M04. In ruminant commodities, M04, M14 and M15 were analysed in milk, muscle, liver, kidney and fat, but residues above 0.01 mg/kg were found in liver and kidney only (see detailed Appendix B). These findings do not impact the existing MRL in animal commodities, which also cover the authorised uses. In poultry commodities, prothioconazole, M04 and M15 were analysed in eggs, liver, muscle and fat, but no residues above 0.01 mg/kg were found.

M04 residues investigated under standard hydrolysis conditions were found to be stable. Processing trials were submitted for M04, TA, TAA and TLA in cereals and oilseed rape, and processing factors were derived (see Appendix B).

Fish metabolism studies were not available although they are required in line with the risk assessment residue definition (**data gap**, see Section 10). As regards the residue level in pollen and bee products in four residue trials on honey resulting from bees visiting the oilseed rape treated before the flowering and analysed for prothioconazole and M04, they were provided. The residues were below 0.005 mg/kg. However, the study provided was not good laboratory practice (GLP) compliant and thus is considered only supportive. Therefore, residue trials on bee products for human consumption, covering the representative use and analysed according to plant risk assessment residue definitions, are needed (**data gap**, see Section 10). RMS disagrees with the data gap on the magnitude of residues in bees products for human consumption.

An indicative consumer risk assessment was conducted with PRIMo rev. 3.1 too using the ADI of 0.01 mg/kg bw per day and ARfD of 0.01 mg/kg bw of M04, residues of M04 in wheat, barley, rye and oat, and residues in animal commodities except poultries (see Appendix B). The chronic exposure (TMDI) resulted in a maximum of 7% of the ADI (NL, toddler), while the acute intake IESTI was calculated at 12% of the ARfD. The overall consumer risk assessment is not finalised due to the identified data gaps (see Section 9.1) and pending the finalisation of the risk assessment residue definitions in plant and animal. To finalise the consumer risk assessment, it is essential to clarify the genotoxic potential of M15, M17, M33 and M35 (see Sections 2 and 9.1).

A consumer risk assessment was conducted also for residues of TDMs, see Appendix B. The consumer risk assessment conducted based on the results from the prothioconazole use led to a lower exposure when compared with the outcome on the TDMs peer review (EFSA, 2018).

As regards the preferential isomeric degradation of (R)- and (S)- enantiomer of prothioconazole and M04 in plant and animal matrices, no information was provided; therefore, a **data gap** was identified (see Section 10).

The representative formulation contains a second active substance, bixafen. Although bixafen was applied together with prothioconazole and analysed in some of the field trials, the data were not included in the RAR. However, the rate of application of bixafen under this evaluation was less critical than the application for MRL use. Under the Article 12 MRL review of bixafen (EFSA, 2020) an application rate in cereals of 2×125 g/ha was assessed and found to be within $\pm 25\%$ deviation compared to the representative GAPs. Therefore, residues of bixafen expected from the representative uses are unlikely to significantly change the risk assessment presented in the Article 12 MRL review of bixafen that did not indicate specific concerns.

Prothioconazole and bixafen share the same toxicological profile targeting the liver (see Section 2), and a combined risk assessment for consumers would be appropriate; however, such an approach for use in the regulatory context has not yet been agreed and implemented.

4 | ENVIRONMENTAL FATE AND BEHAVIOUR

Prothioconazole was discussed at the Pesticides Peer Review TC 23 in September 2020.

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, prothioconazole exhibited very low to moderate persistence, forming the major (> 10% applied radioactivity (AR)) metabolites **M01** (max. 15% AR, low to high persistence) and **M04** (max. 50% AR, moderate to high persistence). Prothioconazole is a racemic mixture of (*R*)- and (*S*)-enantiomer (50/50), and metabolite M04 is rapidly formed also as a racemic mixture. Due to the very fast degradation of prothioconazole in soil, any eventual selective degradation was not deemed to influence the risk assessment for this active substance, while appropriate information to address the stereospecific degradation of metabolite M04 in soil was not provided; therefore, a **data gap** was identified (see Section 10). Mineralisation of the phenyl- and triazole-^{14}C radiolabels to carbon dioxide accounted for 3%–11% AR, and for 0.3%–2% AR after 120 days, respectively. The formation of unextractable residues (not extracted by acetonitrile/water) for the phenyl ring ^{14}C radiolabel accounted for 36%–46% AR after 120 days, and for the triazole ring ^{14}C radiolabel for 42%–48% AR after 120 days. In anaerobic soil incubations, prothioconazole degraded more slowly than under aerobic conditions, with the route of degradation being the same as in the aerobic investigations. The soil photolysis of prothioconazole was not a significant route of degradation. Reliable adsorption endpoints were not available for prothioconazole; therefore, a **data gap** was identified (see Section 10). However, default worst-case values were used in the environmental exposure modelling. Metabolite M01 exhibited slight to low soil mobility, and metabolite M04 exhibited low soil mobility. Adsorption of these two metabolites to soil was not considered to be pH dependent.

Satisfactory field dissipation studies were carried out at three sites in France, 2 sites in Germany, and in the United Kingdom, and one site in Italy (spray application to the soil surface). Sample analyses were carried out for the parent prothioconazole and metabolites M01 and M04. However, during the TC 23 experts agreed that the degradation endpoints for prothioconazole from the field studies would be unreliable, and then, degradation endpoints from the laboratory studies were used in the environmental exposure modelling for prothioconazole.[15] Metabolite M04 exhibited moderate persistence. Field study DegT50 values for metabolite M04 were derived following normalisation to FOCUS reference conditions

[15]Refer to experts' consultation 4.2 in the Report of the Pesticides Peer Review TC 23 (EFSA, 2025).

(20°C and pF2 soil moisture) following the EFSA (2014a) DegT50 guidance and were used to derive modelling endpoints for M04.

In laboratory incubations in dark aerobic natural sediment water systems, prothioconazole exhibited very low to low persistence, forming the major metabolites **M01** (max. 9.6% in sediment, exhibiting moderate to high persistence), **M04** (max. 32% in water and max. 27% in sediment, exhibiting medium to medium persistence), **M13** (max. 37% in water and max. 6% in sediment) and **M42** (max. 8% in water and max. 6% in sediment). Appropriate information to address the stereospecific degradation of prothioconazole and metabolite M04 in surface water/sediment was not provided; therefore, a **data gap** was identified (see Section 10). The unextractable sediment fraction (not extracted by acetonitrile/water) was the major sink for the phenyl and 3,5-triazole ^{14}C radiolabels, accounting for 31%–53% AR at study end (121 days). Mineralisation of these radiolabels accounted for 15%–29% AR at the end of the study. The rate of decline of prothioconazole in a laboratory sterile aqueous photolysis experiment was slow relative to that which occurred in the aerobic sediment water incubations. Chromatographically resolved components accounting for > 10% AR were metabolites **M04** (max. 56% AR), **M12** (max. 14% AR) and **M13** (max. 12% AR). The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC) calculations) were carried out for prothioconazole and for the metabolites M01, M12, M42 and M13 using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator). For metabolite M04, appropriate step 3 (FOCUS, 2001) and step 4 calculations were available.[16] The step 4 calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of up to 20 m being implemented for the drainage scenarios (representing a 91%–93% spray drift reduction), and combined no-spray buffer zones with vegetative buffer strips of up to 20 m (reducing solute flux in run-off by 80% and erosion run-off of mass adsorbed to soil by 95%) being implemented for the run-off scenarios. The SWAN tool (version 5.0.1) 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 KFoc < 2000 mL/g (i.e. prothioconazole-desthio), 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, 2014a) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.[17] The potential for groundwater exposure from the representative uses by prothioconazole and its soil metabolites M01 and M04 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.

The applicant provided appropriate information to address the effect of water treatment processes on the nature of the residues that might be present in surface water when surface water is abstracted for drinking water.

The PEC in soil, surface water, sediment and groundwater covering the representative uses assessed can be found in Appendix B of this conclusion. PECs for bixafen, included as a second active substance in the formulation for the representative uses 'Aviator EC 225', and its transformation products are available in the EFSA conclusion (EFSA, 2012). For PEC in groundwater, it is possible to read across the risk assessment carried out for bixafen including data gap identified in the EFSA conclusion. For PEC in soil, surface water and sediment, an additive risk assessment is not available leading to an assessment not finalised (see Section 9.1). 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

For the risk assessments, the following documents were considered: European Commission (2002a, 2002b, 2002c), SETAC (2001), EFSA (2009, 2013), EFSA PPR Panel (2013).

Aspects of the ecotoxicological risk assessments were discussed during the Pesticides Peer Review TC 26 (September–October 2020) with some follow-up during the Pesticides Peer Review TC 69 (January 2022), and at Pesticides Peer Review TC 124 and 129 (January–February 2024).

The batches used in the ecotoxicity studies were sufficiently comparable to the technical specification.

No specific information on the ecotoxicity of enantiomers of prothioconazole and its metabolites was available. Furthermore, no appropriate information to address the stereospecific fate and behaviour in the environment was available (see Section 4); therefore, a **data gap** was identified (see Section 10).

In addition, additive exposure and risk assessments for the bixafen active substance in the formulation for representative uses 'Aviator EC 225' are not available leading to an assessment not finalised (see Sections 4 and 9.1). It is noted that, for some risk cases for certain non-target organisms, effect data for the representative formulation 'Aviator EC 225' are available.

Suitable acute and long-term toxicity data for **birds** and **mammals** were available for the active substance and for the metabolite M04. Furthermore, an acute toxicity study was available for mammals with the representative formulation

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

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

'Aviator EC 225' (spray uses). Some of the endpoints were discussed and agreed during the experts' meeting.[18] For the representative spray uses, the tier 1 risk assessment for the active substance and for the metabolite M04 indicated a low acute and long-term risk to birds and a low acute risk to mammals. Also, a low long-term risk to mammals for the active substance prothioconazole was indicated, while a high risk was concluded for the metabolite M04. A number of pertinent residue studies was available[19] demonstrating a shorter DT_{50} of M04 in plant matrices than the default value used for the tier 1 exposure estimation. Considering these higher tier data, a low long-term risk to mammals was concluded for the metabolite M04. Combined risk assessments considering simultaneous exposure to prothioconazole and M04 were also considered. Simplified methods (TERmix approach) assuming additive toxicity with worst-case parametrisation was applied.[20] These calculations did not indicate additional concern for birds and mammals.

As regards the representative use for seed treatments, the tier 1 risk assessment for **birds** indicated a low acute risk for prothioconazole and for the metabolite M04. Also, low long-term risk was indicated for the seedling consumption scenario; however, for the birds consuming treated seeds scenario, a high long-term risk was indicated for both prothioconazole and the metabolite M04. Higher tier data for refinements were available and discussed during the experts' meetings (i.e. focal species, PT values, PD values, residue data for spring uses).[21] Considering these refinements, a low risk was concluded for birds exposed to prothioconazole and the metabolite M04 via treated spring cereal seeds; however, a low risk could not be concluded for winter cereal seeds. Therefore, this scenario for the representative seed treatment uses represents a **high risk** to birds.

Similar to birds, a low acute risk to **mammals** was indicated by the tier 1 risk assessments for prothioconazole and for the metabolite M04. Also, a low long-term risk was indicated for the seedling consumption scenario for prothioconazole. However, the long-term risk was indicated as high for the mammals consuming treated seeds scenario for both prothioconazole and the metabolite M04, and, in addition, to the seedling consumption scenario for the metabolite M04. Higher tier data for refinements were available and discussed during the experts' meetings (i.e. focal species, PT values, residue data for spring uses).[22] Considering these refinements, a low risk could be concluded for mammals consuming treated spring cereal seeds for prothioconazole and for the metabolite M04. Also, a low risk was demonstrated for winter cereal seeds for prothioconazole, but a low risk was not demonstrated for the metabolite M04. Therefore, this scenario for the representative seed treatment uses represents a **high risk** to mammals. As regards the seedling consumption scenario, a low long-term risk was concluded when the available higher tier residue data were taken into consideration.

A combined risk assessment considering simultaneous exposure to prothioconazole and M04 using the same methodology as for the spray uses was conducted. These assessments indicated a low risk for birds and mammals exposed to prothioconazole and M04 via treated spring cereal seeds. However, a low risk could not be demonstrated to treated winter cereal seeds (i.e. this scenario represents a high risk to birds and mammals as already indicated above).

A low risk to birds and mammals from exposure via secondary poisoning and from consumption of contaminated water was concluded for the representative uses.

Suitable acute and chronic toxicity data for **aquatic organisms** (fish, aquatic invertebrates, algae, aquatic plants and sediment-dwelling organisms) were available with the active substance, prothioconazole and the metabolite M04. In addition, a number of toxicity studies covering fish, aquatic invertebrates and algae were available for the metabolites M12, M42, M13 and for M01, for which toxicity data for sediment-dwellers were also available. Acute studies for fish, aquatic invertebrates and studies on algae were also available for both representative formulations.

Considering these data, a low risk to aquatic organisms was demonstrated for prothioconazole and for all relevant metabolites for the representative uses for seed treatments. As regards the representative spray uses, a low risk was demonstrated for prothioconazole and the relevant metabolites, with the exception for the metabolite M04. At FOCUS Step 3, a high chronic risk was indicated for six of the nine scenarios for fish for this metabolite for the uses on winter cereals. FOCUS Step 4 calculations were available taking into consideration risk mitigation options; however, the risk to fish was still indicated as high for all the six scenarios. As regards the uses on spring cereals, two of the five FOCUS Step 3 scenarios indicated a high chronic risk to fish for the M04 metabolite. With FOCUS Step 4 calculations taking into consideration a 10-m non-spray buffer zone, a low risk was demonstrated for one of those two scenarios (remaining only one scenario indicating high risk). It is noted that for some of the scenarios that indicated a high risk for fish, a high acute risk was indicated also for aquatic invertebrates. No higher tier studies or other refinement options were available; therefore, a **high risk** was concluded for several FOCUS surface scenarios for the representative spray uses (see Appendix B).

Suitable acute (contact and oral) toxicity data with honey **bees** and bumble bees were available for prothioconazole, and suitable acute (contact and oral) toxicity data with honey bees were available for both representative formulations and for the metabolite M04. Furthermore, chronic oral toxicity data were available for honey bees with a suspension concentrate (SC) formulation containing ca. 48% prothioconazole, and a 22-day chronic study on honey bee larvae was available with prothioconazole. Specific assessments for accumulative effects or sublethal effects were not available; however,

[18]Refer to experts' consultations 5.1 and 5.2 in the Report of the Pesticide Peer Review TC 26 (EFSA, 2025) and to follow up experts' consultations 5.1 in the Report of the Pesticide Peer Review TC 69 (EFSA, 2025).

[19]Refer to experts' consultations 5.2 in the Report of the Pesticide Peer Review TC 26 (EFSA, 2025).

[20]Refer to experts' consultations 5.1 and 5.2 in the Report of the Pesticide Peer Review TC 26 and to experts' consultations 5.3 in the Report of Pesticides Peer Review TC 69 (EFSA, 2025).

[21]Refer to experts' consultation 5.1 in the Report of the Pesticide Peer Review TC 26 and to follow up experts' consultations 5.2 in the Report of the Pesticide Peer Review TC 69 (EFSA, 2025).

[22]Refer to experts' consultation 5.2 in the Report of the Pesticide Peer Review TC 26 (EFSA, 2025).

higher tier studies were submitted. A semi-field study and a colony feeder study with honey bees were available with EC and SC formulations different from the representative formulations. No data were available for solitary bees. The risk assessments considering the available laboratory endpoints for honey bees indicated a low acute risk according to the European Commission (2002c). In addition, the RMS performed risk assessments according to the EFSA guidance document of 2013 (EFSA, 2013) for prothioconazole that also indicated a low risk for honey bees. Also, a low acute risk for bumble bees was indicated. No risk assessments were available for other major plant metabolites than M04 (see Section 3); therefore, a **data gap** was identified (see Section 10). As regards the higher tier studies, due to the limitations of the design as described in the EFSA guidance document (i.e. short study duration, low statistical robustness, lack of proper demonstration of the actual exposure), no firm conclusion could be drawn. Nevertheless, the studies did not indicate a particular concern.

As regards **non-target arthropods other than bees**, for the representative spray uses, tier 1 toxicity studies with the two indicator species (*Aphidius rhopalosiphi* and *Typhlodromus pyri*) were available with the representative formulation. In addition, extended laboratory tier 2 studies were available for four species, and aged residue studies were available with the two indicator species. Based on the available tier 1 risk assessments, a low risk to non-target arthropods in the off-field area was indicated, while the in-field risk was indicated as high. Considering the extended laboratory studies, still high risk was indicated for one species (*Typhlodromus pyri*); however, considering the outcomes of the aged residue studies, a low in-field risk could be concluded (a potential for recolonisation within 2 weeks was indicated).

As regards the representative seed treatment uses, extended laboratory tier 2 studies were available for three soil-dwelling species. However, since there is no specific guidance for non-target arthropods for seed treatment uses, it was proposed that the risk assessments for the Collembola *Folsomia candida* and the soil predatory mite *Hypoaspis aculeifer* should be considered, which are summarised in the next paragraph.

A number of laboratory chronic toxicity studies with different formulations, the active substance and with the two major soil metabolites, M04 and M01, were available for **soil macroorganisms** (earthworms *Eisenia fetida*, collembola *Folsomia candida* and soil mite *Hypoaspis aculeifer*) and for **soil microorganisms**. Using these data, the tier 1 risk assessments indicated a low risk to soil macro- and microorganisms for the representative uses, with the exception of earthworms for the metabolite M04 for the representative spray uses. However, a field study with earthworms was available to address this issue. The field study was discussed in an experts' meeting[23] and a low risk to earthworms for this metabolite was concluded.

Seedling emergence and vegetative vigour studies with the representative formulation for the spray uses were available, and by using these data, a low risk was demonstrated to **non-target terrestrial plants**. As regards the representative seed treatment uses, no quantitative risk assessment was performed since the exposure to non-target plants was considered minimal. A low risk to **organisms involved in biological methods for sewage treatment** was also concluded.

6 | ENDOCRINE DISRUPTION PROPERTIES

The ED assessment of prothioconazole was discussed in Peer Review Experts' TC 22 and 124.

With regard to the assessment of the endocrine disruption potential of prothioconazole **for humans** and **non-target organisms** according to the ECHA/EFSA guidance (2018), in determining whether prothioconazole interacts with the oestrogen, androgen and steroidogenesis (EAS) and thyroid (T) mediated pathways, the number and type of effects induced and the magnitude and pattern of responses observed across studies 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 (WoE) analysis of the potential interaction of prothioconazole with the EAS and T-signalling pathways using the available evidence in the data set.

With regard to **T modality**, the data set was considered complete, and a pattern of T-mediated adversity was not identified. The minor effects observed in thyroid hormones (THs) below the maximum tolerated dose (MTD), in the absence of any histopathological change in the thyroid follicular cell, were not considered sufficient evidence of adversity and the overall weight-of-evidence (WoE) indicates that prothioconazole is not affecting the T modality.

With regard to **EAS modality**, the data set was considered complete, and a pattern of EAS-mediated adversity was not observed.

Therefore, based on the available and sufficient data set, it was concluded that the ED criteria are not met for the EAST modalities (Scenario 1a of the EFSA/ECHA, 2018, ED Guidance).

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

For **non-target organisms other than mammals**, a *Xenopus* Eleutheroembryonic Thyroid Assay (XETA, OECD TG 248) and a Fish Short-Term Reproduction Assay (FSTRA, OECD TG 229) were available to sufficiently investigate the endocrine activity through the T and EAS modalities, respectively. Additionally, a literature paper was available with lizards (Xie et al., 2019).

A part of the available XETA was not conducted under GLP conditions, as indicated in the provisions of the principles laid down in Directive 2004/10/EC[24] of the European Parliament and of the Council and as implemented by the Commission

[23]Refer to experts' consultation 5.6 in the Report of the Pesticide Peer Review TC 26 (EFSA, 2025).

[24]Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (codified version).

Regulation (EU) No 283/2013.[25] The study was considered fully reliable and no evidence of T-mediated endocrine activity was observed. Nevertheless, a data gap is identified to further confirm the findings in the available study by performing a study in line with the legal requirements, i.e. under GLP (**data gap**, see Section 10).

In the available FSTRA,[26] a slight increase in the severity of oocyte atresia at the highest tested concentration and a dose-dependent decrease in fecundity were observed. Owing to the lack of full reporting of the methods, results of vitellogenin (VTG) were considered questionable; nevertheless, no treatment-related changes could be observed.

The literature study with lizard was not considered reliable due to a number of drawbacks, e.g. unclear origin of animals, single treatment level, only 1 week of acclimation to laboratory conditions (generally 14 days should be considered), a solvent was used but no solvent control was reported, no replication (i.e. total 42 animals – 21 lizards for the treatment and the control), steroid hormones were measured in the control only in the beginning. Therefore, it was not considered to contribute significantly to the overall weight of evidence.

Overall, when considering all evidence[27] in the WoE and its related uncertainties,[28] a clear pattern of endocrine-mediated adversity and endocrine activity was not observed for EAS modalities.

At the Peer Review Experts' TC 22, the experts raised a concern about the potential ED properties of the pertinent metabolite (degradation products in environmental matrices including plants, surface water and soil) prothioconazole-desthio since it was known to be more toxic than the parent compound in vertebrate species.

Based on the available assessment, it could be concluded that prothioconazole does not meet the ED criteria as laid down in 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. Although further confirmation is needed regarding the conclusion for the T-modality in non-mammalian species, based on the available data, it is unlikely that prothioconazole is an endocrine disruptor.

7 | OVERVIEW OF THE RISK ASSESSMENT OF COMPOUNDS LISTED IN RESIDUE DEFINITIONS TRIGGERING ASSESSMENT OF EFFECTS DATA FOR THE ENVIRONMENTAL COMPARTMENTS (TABLES 2–5)

TABLE 2 Soil.

Compound (name and/or code)	Ecotoxicology
Prothioconazole	Low risk
Prothioconazole-desthio (M04)	Low risk
Prothioconazole-S-methyl (M01)	Low risk

TABLE 3 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
Prothioconazole	No	Yes	–	–	Yes
Prothioconazole-desthio (M04)	No	No	Yes Unlikely to be genotoxic Low acute oral toxicity Developmental and reproductive toxicity observed ADI and ARfD 0.01 mg/kg bw (per day)	No	Yes
Prothioconazole-S-methyl (M01)	No	No	No data available	No	No for the representative use(s) assessed

[a]Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).

[b]FOCUS scenarios or relevant lysimeter.

[25]Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.

[26]Refer to experts' consultation 5.8 in the Report of the of the Pesticides Peer Review TC 129 (EFSA, 2025).

[27]Refer to experts' consultation 5.8 in the Report of the Pesticides Peer Review TC 129 (EFSA, 2025) and section B.9.1.5 Vol. 3 B.9 CA of the RAR (Poland, 2024).

[28]See Table B.9.1.5–25 of the Vol. 3 B.9 CA of the RAR (Poland, 2024).

TABLE 4 Surface water and sediment.

Compound (name and/or code)	Ecotoxicology
Prothioconazole	Low risk
Prothioconazole-desthio (M04) (soil, water/sediment, aqueous photolysis)	High risk for 1/5 FOCUS scenarios for spray use on spring cereals High risk for 6/9 FOCUS scenarios for spray use on winter cereals
Prothioconazole-S-methyl (M01) (soil, water/sediment)	Low risk
Prothioconazole-thiazocine (M12) (aqueous photolysis)	Low risk
Prothioconazole-triazolylketone (M42) (water/sediment)	Low risk
1,2,4-triazole (M13) (water/sediment, aqueous photolysis)	Low risk

TABLE 5 Air.

Compound (name and/or code)	Toxicology
Prothioconazole	Rat inhalation LC50 > 4990 mg/m^3 (4h exposure, nose only)
Prothioconazole-desthio (M04)	Rat inhalation LC50 > 5077 mg/m^3 (4h exposure, nose/head-only)

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 6).

TABLE 6 Risk mitigation measures proposed for the representative uses assessed.

Representative use	Spring cereals foliar spray (Aviator EC 225)	Winter cereals foliar spray (Aviator EC 225)	Spring cereals seed treatment (Redigo FS 100)	Winter cereals seed treatment (Redigo FS 100)
Operator risk	Use of PPE is required[a]	Use of PPE is required[a]	Use of PPE is required[b]	Use of PPE is required[b]
Worker exposure	–	–	–	–
Bystander exposure	Use of drift reducing nozzles (50%)	Use of drift reducing nozzles (50%)	–	–
Resident exposure	–	–	–	–

[a]For tractor-mounted applications: gloves during mixing/loading and application (EFSA, 2014b).
[b]For mixing/loading, calibration and cleaning: gloves and coveralls (exposure study).

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[29] 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.

[29]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, pp. 127–175.

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 consumer dietary risk assessment could not be finalised pending the finalisation of the residue definitions for risk assessment for plants and animals (see Section 3) and because of the following data gap:

   a. Appropriate information to address the genotoxicity for the metabolites M15, M17, M33, M35 (relevant for all representative uses, see Section 2).
   b. The fate and the transfer of prothioconazole-desthio (M04) residues in poultry was not investigated although they are triggered (relevant to all representative uses except seed treatment, see Section 3).

2. An additive exposure and risk assessments in soil, surface water and sediment for the active substance bixafen in the formulation for the representative uses 'Aviator EC 225'

   a. Exposure and risk assessments in soil, surface water and sediment for bixafen from the representative uses in the formulation 'Aviator EC 225' is not available (see Sections 4 and 5).

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 areas of concern were identified.

9.3 | Overview of the concerns identified for each representative use considered (Table 7)

(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 7.)

TABLE 7 Overview of concerns reflecting the issues not finalised, critical areas of concern and the risks identified that may be applicable for some but not for all uses or risk assessment scenarios.

Representative use		Spring cereals (Aviator EC 225) foliar spray	Winter cereals (Aviator EC 225) foliar spray	Spring cereals (Redigo FS 100) seed treatment	Winter cereals (Redigo FS 100) seed treatment
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified				
	Assessment not finalised				
Resident/bystander risk	Risk identified				
	Assessment not finalised				
Consumer risk	Risk identified				
	Assessment not finalised	X[1]	X[1]	X[1]	X[1]

(Continues)

TABLE 7 (Continued)

Representative use		Spring cereals (Aviator EC 225) foliar spray	Winter cereals (Aviator EC 225) foliar spray	Spring cereals (Redigo FS 100) seed treatment	Winter cereals (Redigo FS 100) seed treatment
Risk to wild non-target terrestrial vertebrates	Risk identified				X[c]
	Assessment not finalised				
Risk to wild non-target terrestrial organisms other than vertebrates	Risk identified				
	Assessment not finalised				
Risk to aquatic organisms	Risk identified	1/5 FOCUS surface water scenarios	6/9 FOCUS surface water scenarios		
	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				

Note: 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]High risk to mammals was identified as described in Section 5.

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:

- In relation to the formulations for representative uses, for three components of 'Aviator EC 225' and three components of 'Redigo FS 100', the genotoxicity and repeated dose toxicity information over the short and long term was not available. Therefore, in order to allow a final conclusion on the safety assessment of these formulations, genotoxicity and repeated dose toxicity data for these components (short and long term) might be considered for further assessment (to be confirmed by Member States when assessing applications for PPP authorisation; relevant for all representative uses evaluated; see Section 'General aspects').
- For the relevant impurities prothioconazole-deschloro (AE 1344264) and prothioconazole-triazolidinethione (AE 1344254) spectral data and content of the impurities before and after storage of the formulations (relevant for all representative uses, see Section 1).
- Methods of analysis in the formulations for the relevant impurities prothioconazole-deschloro (AE 1344264) and prothioconazole-triazolidinethione (AE 1344254) (relevant for all representative uses, see Section 1).
- No method was available for monitoring prothioconazole in body fluids and tissues (relevant for all representative uses, see Section 1).
- Storage stability data for the hydroxylated metabolites on an additional commodity from the category of high starch content or one from the high protein content category would be needed to extrapolate to all crops (relevant for all representative uses, see Section 3).
- Fish metabolism studies were not available although they are required in line with the risk assessment residue definition (relevant to all representative uses, see Section 3).
- Residues trials on bee products for human consumption, covering the representative use and analysed according to plant risk assessment residue definitions, are needed (relevant to all representative uses except seed treatment, see Section 3).
- Appropriate information to address the stereospecific degradation of prothioconazole and prothioconazole desthio (M04) in plants and in livestock is needed (relevant for all representative uses evaluated, see Section 3).

- Appropriate information to address the stereospecific degradation of prothioconazole in surface water and metabolite prothioconazole-desthio (M04) in soil and surface water/sediment is needed. Depending on the stereospecific fate and behaviour in the environment, further considerations for the risk to non-target organisms may be needed (relevant for all representative uses evaluated; see Sections 4 and 5).
- Reliable adsorption endpoints for prothioconazole on at least four soils with a range of soil pH were not available (relevant for all representative uses; see Section 4).
- An adsorption study for metabolite M12 (JAU 6476-thiazocine) (formed only in aqueous photolysis) using a batch equilibrium method is missing (relevant for all representative uses; see Evaluation Table, Data Requirement 4.8, EFSA, 2025).
- With the exception of prothioconazole-desthio (M04), no risk assessments for bees were available for other major plant metabolites (relevant for all representative uses, see Section 5).
- A new study compliant with the GLP requirement as indicated in the provisions of the principles laid down in Directive 2004/10/EC of the European Parliament and of the Council and as implemented by the Commission Regulation (EU) No 283/2013 is needed to further confirm the findings in the available non-GLP XETA study (relevant for all representative uses, see Section 6).

ABBREVIATIONS

1/*n*	slope of Freundlich isotherm
AAOEL	acute acceptable operator exposure level
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AhR	aryl hydrocarbon receptor
AMA	Amphibian Metamorphosis Assay
AOEL	acceptable operator exposure level
AOP	adverse outcome pathway
AP	alkaline phosphatase
AR	androgen receptor
AR	applied radioactivity
ARfD	acute reference dose
ARSTTA	Stably Transfected Human Androgen Receptor Activation Assay
a.s.	active substance
AST	aspartate aminotransferase (SGOT)
AUC	area under the blood concentration/time curve
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
C&L	classification and labelling
CAS	Chemical Abstracts Service
CFU	colony-forming units
ChE	cholinesterase
CHO	Chinese hamster ovary cells
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
C_{max}	concentration achieved at peak blood level
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DDD	daily dietary dose
DM	dry matter
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EAS	oestrogen, androgen and steroidogenesis modalities
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemicals Agency
EEC	European Economic Community
FAO	Food and Agriculture Organization of the United Nations
FOB	functional observation battery

FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FSTRA	Fish Short-Term Reproduction Assay
GAP	Good Agricultural Practice
GC	gas chromatography
HPLC–MS	high-pressure liquid chromatography–mass spectrometry
HQ	hazard quotient
HR	hazard rate
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
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_{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
LD_{50}	lethal dose, median; dosis letalis media
LOQ	limit of quantification
M/L	mixing and loading
MCV	mean corpuscular volume
MOA	mode of action
MRL	maximum residue level
MS	mass spectrometry
MTD	maximum tolerated dose
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NPD	nitrogen–phosphorus detector
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PHI	preharvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
RAR	Renewal Assessment Report
RBC	red blood cells
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
SC	suspension concentrate
SD	standard deviation
SMILES	simplified molecular-input line-entry system
THs	thyroid hormones
TK	technical concentrate
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time-weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor
UV	ultraviolet
W/S	water/sediment
WBC	white blood cell
WHO	World Health Organization
ε	decadic molar extinction coefficient
λ	wavelength

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NOTE/UPDATE

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

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

Properties		Conclusion[a]
CMR	Carcinogenicity (C)	Prothioconazole is not considered to be a carcinogen according to point 3.6.3 of Annex II of Regulation (EC) No 1107/2009
	Mutagenicity (M)	Prothioconazole 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)	Prothioconazole is not considered to be toxic to reproduction according to point 3.6.4 of Annex II of Regulation (EC) No 1107/2009
Endocrine disrupting properties		Prothioconazole 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. Although further confirmation is needed regarding the conclusion for the T-modality in non-mammalian species, based on the available data, it is unlikely prothioconazole is an endocrine disruptor
POP	**Persistence** **Bioaccumulation** **Long-range transport**	Prothioconazole is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) 1107/2009
PBT	**Persistence** **Bioaccumulation** **Toxicity**	Prothioconazole is 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
vPvB	**Persistence** **Bioaccumulation**	Prothioconazole is not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009

[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.2025.9593

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[30] 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.

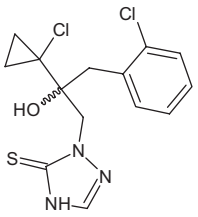
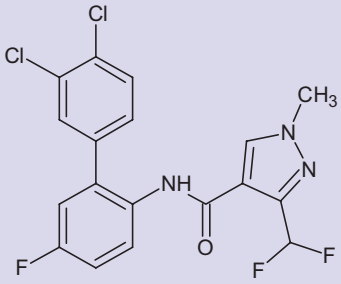
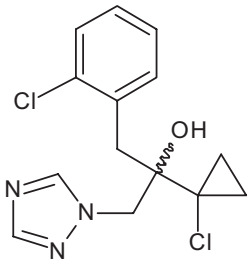
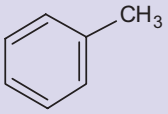
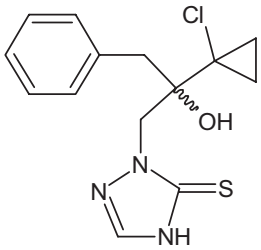
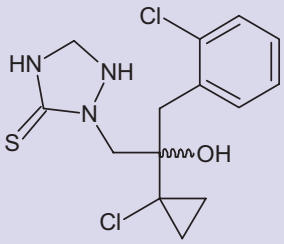
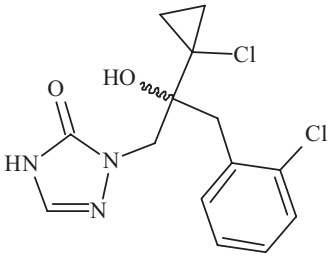
Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0 to 50
High mobility	51 to 150
Medium mobility	151 to 500
Low mobility	501 to 2000
Slight mobility	2001 to 5000
Immobile	> 5000

Note: Based on McCall et al. (1980).

[30] 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,d]	Structural formula[c,e]
Prothioconazole[d,e]	(*RS*)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione S=C1NC=NN1CC(O)(Cc1ccccc1Cl)C1(Cl)CC1 MNHVNIJQQRJYDH-UHFFFAOYSA-N	
Bixafen[b,c]	N-(3′,4′-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxamide O=C(Nc1ccc(F)cc1c1cc(Cl)c(Cl)cc1)c1cn(C)nc1C(F)F LDLMOOXUCMHBMZ-UHFFFAOYSA-N	
Prothioconazole-desthio, JAU 6476-desthio, M04[b,c]	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propan-2-ol OC(Cn1ncnc1)(Cc1ccccc1Cl)C1(Cl)CC1 HHUQPWODPBDTLI-UHFFFAOYSA-N	
Toluene[b,c]	Methylbenzene Cc1ccccc1 YXFVVABEGXRONW-UHFFFAOYSA-N	
Prothioconazole -deschloro, AE 1344264[b,c]	2-[2-(1-chlorocyclopropyl)-2-hydroxy-3-phenylpropyl]-2,4-dihydro-3*H*-1,2,4-triazole-3-thione S=C1NC=NN1CC(O)(Cc1ccccc1)C1(Cl)CC1 LURNYPMEERGXIK-UHFFFAOYSA-N	
Prothioconazole -triazolidinethione, AE 1344254[b,c]	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2,4-triazolidine-3-thione S=C1NCNN1CC(O)(Cc1ccccc1Cl)C1(Cl)CC1 PCARSQBZDYOIPU-UHFFFAOYSA-N	
Prothioconazole-triazolinone, JAU 6476-triazolinone, M03[b,c]	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one OC(CN1N=CNC1=O)(Cc1ccccc1Cl)C1(Cl)CC1 DJTGRQXBACJYBN-UHFFFAOYSA-N	

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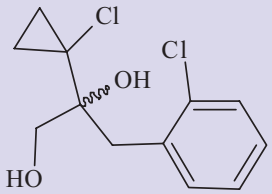
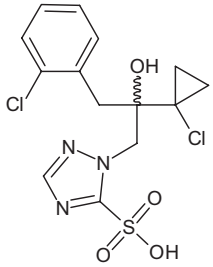
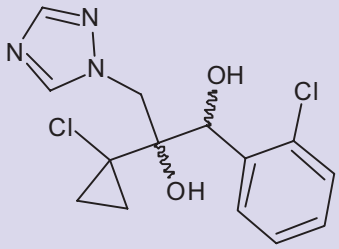
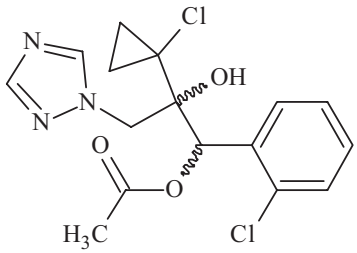
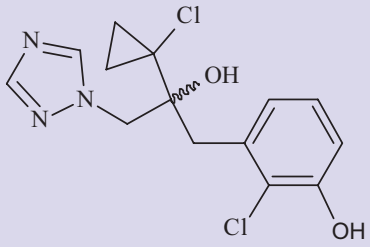
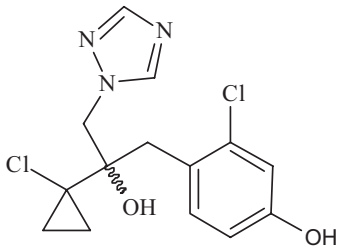
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b,d]	Structural formula[c,e]
Prothioconazole-benzylpropyldiol, JAU 6476-benzylpropyldiol, M09[b,c]	2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)propane-1,2-diol OC(CO)(Cc1ccccc1Cl)C1(Cl)CC1 MAZROLLCBZWRLJ-UHFFFAOYSA-N	
Prothioconazole- sulfonic acid, JAU 6476-sulfonic acid, M02[d,e]	1-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1*H*-1,2,4-triazole-5-sulfonic acid OS(=O)(=O)c1ncnn1CC(O)(Cc1ccccc1Cl)C1(Cl)CC1 IGMSBPDKDGDWJV-UHFFFAOYSA-N	
Prothioconazole- desthio-α-hydroxy, JAU 6476-α-hydroxy-desthio, M18[b,c]	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propane-1,2-diol OC(Cn1cncn1)(C(O)c1ccccc1Cl)C1(Cl)CC1 JOFJRMIXOWNPNA-UHFFFAOYSA-N	
Prothioconazole- desthio-α-acetoxy, JAU 6476-α-acetoxy-desthio, M19[b,c]	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl acetate OC(Cn1ncnc1)(C(OC(=O)C)c1ccccc1Cl)C1(Cl)CC1 GWOABOVCIWBCTM-UHFFFAOYSA-N	
Prothioconazole- desthio-3-hydroxy, JAU 6476-desthio-3-hydroxy, M14[b,c]	2-chloro-3-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenol OC(Cn1cncn1)(Cc1cccc(O)c1Cl)C1(Cl)CC1 OSFCZDFLHQXWKG-UHFFFAOYSA-N	
Prothioconazole- desthio-4-hydroxy, JAU 6476-desthio-4-hydroxy, M15[b,c]	3-chloro-4-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenol OC(Cn1cncn1)(Cc1ccc(O)cc1Cl)C1(Cl)CC1 YZPNFTVYLXGBPC-UHFFFAOYSA-N	

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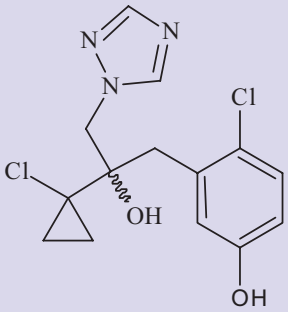
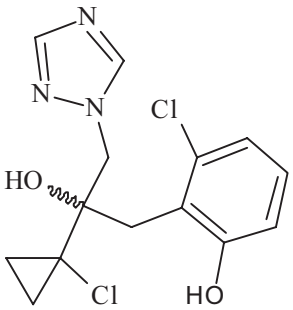
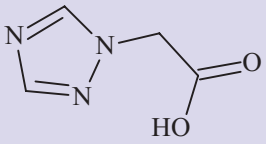
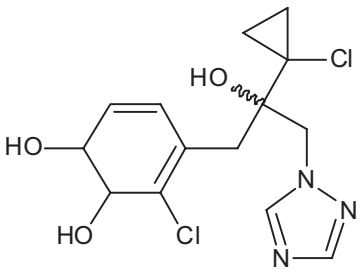
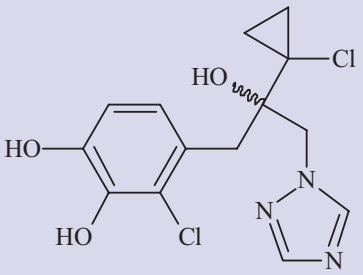
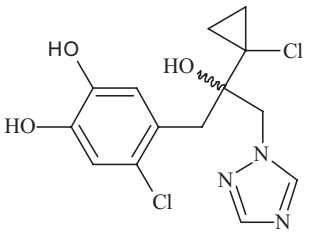
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b,d]	Structural formula[c,e]
Prothioconazole- desthio-5-hydroxy, JAU 6476-desthio-5-hydroxy, M16[b,c]	4-chloro-3-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenol SNUVNTFOEHWABV-UHFFFAOYSA-N OC(Cn1cncn1)(Cc1cc(O)ccc1Cl)C1(Cl)CC1	
Prothioconazole- desthio-6-hydroxy, JAU 6476-desthio-6-hydroxy, M17[b,c]	3-chloro-2-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenol JQRBOBUTGZOYBJ-UHFFFAOYSA-N OC(Cn1cncn1)(Cc1c(O)cccc1Cl)C1(Cl)CC1	
TAA, triazole acetic acid, M29[b,c]	1*H*-1,2,4-triazol-1-ylacetic acid OC(=O)Cn1ncnc1 RXDBSQXFIWBJSR-UHFFFAOYSA-N	
Prothioconazole-desthio-3,4-dihydroxy-diene, JAU 6476-desthio-3,4-dihydroxy-diene, M32[b,c]	3-chloro-4-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]cyclohexa-3,5-diene-1,2-diol OC(Cn1cncn1)(CC=1C=CC(O)C(O)C=1Cl)C1(Cl)CC1 ZLXMQJBUQUSBNC-UHFFFAOYSA-N	
Prothioconazole-desthio-3,4-dihydroxy, JAU 6476-desthio-3,4-dihydroxy, M33[b,c]	3-chloro-4-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]benzene-1,2-diol OC(Cn1cncn1)(Cc1ccc(O)c(O)c1Cl)C1(Cl)CC1 OJZADOBYNJPKNR-UHFFFAOYSA-N	
Prothioconazole-desthio-4,5-dihydroxy, JAU 6476-desthio-4,5-dihydroxy, M35[b,c]	4-chloro-5-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]benzene-1,2-diol OC(Cn1cncn1)(Cc1cc(O)c(O)cc1Cl)C1(Cl)CC1 XRNUGBLYGYCBCO-UHFFFAOYSA-N	

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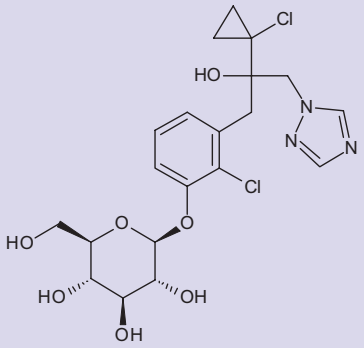
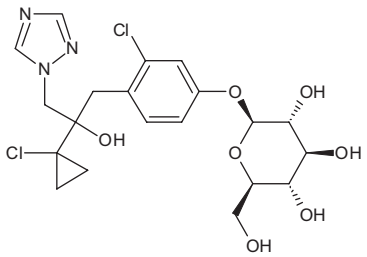
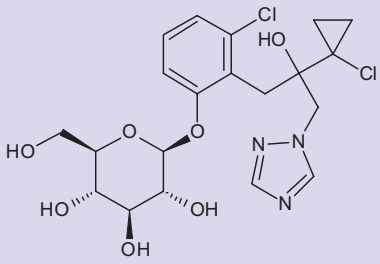
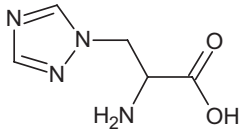
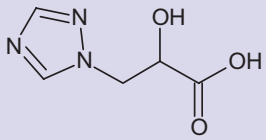
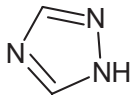
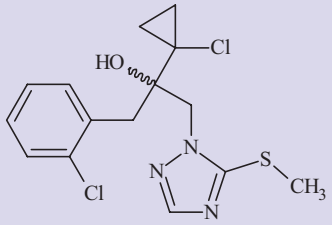
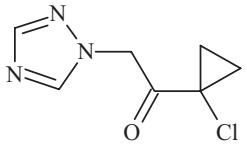
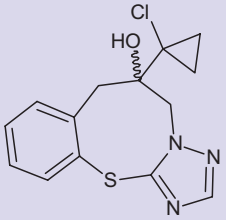
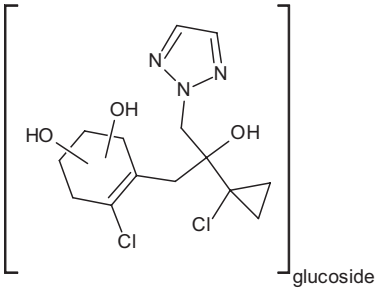
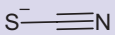
Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b,d]	Structural formula[c,e]
Prothioconazole-desthio-3-hydroxy-glucoside, JAU 6476-desthio-3-hydroxy-glucoside M21[b,c]	2-chloro-3-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenyl β-D-glucopyranoside OC(Cn1ncnc1)(Cc1cccc(O[C@@H]2O[C@H](CO)[C@@H](O)[C@H](O)[C@H]2O)c1Cl)C1(Cl)CC1 QICURFZZBUGFKB-QZFWYPLZSA-N	
Prothioconazole-desthio-4-hydroxy-glucoside, JAU 6476-desthio-4-hydroxy-glucoside M22[b,c]	3-chloro-4-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenyl β-D-glucopyranoside OC(Cn1ncnc1)(Cc1ccc(cc1Cl)O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O)C1(Cl)CC1 UOSFBRWNUDUTNU-WMJZPAMESA-N	
Prothioconazole-desthio-6-hydroxy-glucoside, JAU 6476-desthio-6-hydroxy-glucoside M23[b,c]	3-chloro-2-[2-(1-chlorocyclopropyl)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propyl]phenyl β-D-glucopyranoside OC(Cn1ncnc1)(Cc1c(O[C@@H]2O[C@H](CO)[C@@H](O)[C@H](O)[C@H]2O)cccc1Cl)C1(Cl)CC1 VUADZGIYEZJOBR-WMJZPAMESA-N	
triazole alanine (TA)[b,c]	3-(1*H*-1,2,4-triazol-1-yl)alanine NC(Cn1ncnc1)C(O)=O XVWFTOJHOHJIMQ-UHFFFAOYSA-N	
Triazole lactic acid (TLA), THP Triazolylhydroxypropi nic acid, M30[b,c]	2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid OC(Cn1ncnc1)C(O)=O KJRGHGWETVMENC-UHFFFAOYSA-N	
1,2,4-triazole; 1,2,4-T, M13[b,c]	1*H*-1,2,4-triazole [NH]1ncnc1 NSPMIYGKQJPBQR-UHFFFAOYSA-N	
Prothioconazole-S-methyl, JAU 6476-S-methyl, M01[b,c]	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-[5-(methylsulfanyl)-1*H*-1,2,4-triazol-1-yl]propan-2-ol OC(Cn1ncnc1SC)(Cc1ccccc1Cl)C1(Cl)CC1 ZXMXTEOZDXZOBF-UHFFFAOYSA-N	
Prothioconazole-triazolylketone, JAU 6476-triazolylketone, M42[b,c]	1-(1-chlorocyclopropyl)-2-(1*H*-1,2,4-triazol-1-yl)ethenone ClC1(CC1)C(=O)Cn1cncn1 OFBGUOXVCAKOPV-UHFFFAOYSA-N	

(Continues)

(Continued)

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b,d]	Structural formula[c,e]
Prothioconazole-thiazocine, JAU 6476-thiazocine, M12[b,c]	6-(1-chlorocyclopropyl)-6,7-dihydro-5*H*-[1,2,4]triazolo[5,1-*b*][1,3]benzothiazocin-6-ol OC1(Cn2ncnc2Sc2ccccc2C1)C1(Cl)CC1 OCGPTHWHDHELMC-UHFFFAOYSA-N	
Prothioconazole-desthio-dihydroxy-olefin-glucoside, JAU 6476-desthio-dihydroxy-olefin-glucoside, M64[b,c]	Not applicable as structure contains Markush bonds	
Thiocyanate[d,e]	Thiocyanate [S-]C#N ZMZDMBWJUHKJPS-UHFFFAOYSA-M	

[a]The metabolite name in bold is the name used in the conclusion.

[b]ACD/ChemSketch 2023.2.4 ACD/Labs 2023.2.4 (File Version C45H41, Build 137017, 18 Jan 2024).

[c]ACD/Name 2023.2.4 ACD/Labs 2023.2.4 (File Version N25E41, Build 137185, 31 Jan 2024).

[d]ACD/ChemSketch 2024.2.3 ACD/Labs 2024.2.3 (File Version C45H41, Build 142855, 23 Jan 2025).

[e]ACD/Name 2024.2.3 ACD/Labs 2024.2.3 (File Version N25E41, Build 142837, 21 Jan 2025).