Review of the existing maximum residue levels for cyproconazole according to Article 12 of Regulation (EC) No 396/2005

European Food Safety Authority (EFSA), Maria Anastassiadou, Giulia Bellisai, Giovanni Bernasconi, Alba Brancato, Luis Carrasco Cabrera, Lucien Ferreira, Luna Greco, Samira Jarrah, Aija Kazocina, Renata Leuschner, Jose Oriol Magrans, Ileana Miron, Stefanie Nave, Ragnor Pedersen, Hermine Reich, Miguel Santos, Alessia Pia Scarlato, Anne Theobald, Benedicte Vagenende and Alessia Verani

Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance cyproconazole. Considering that no application was received to support the renewal of the approval of cyproconazole and considering the expiry date for its approval on 31 May 2021, and that the import tolerances identified were not supported by sufficient data, and are not forming the basis of any existing EU MRLs, but correspond to existing MRLs established by the Codex Alimentarius Commission (codex maximum residue limits; CXLs), the current assessment is limited to CXLs. To assess the occurrence of cyproconazole residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Commission Regulation (EC) No 33/2008, as well as the MRLs established by the Codex Alimentarius Commission. Based on the assessment of the available data, EFSA assessed the CXLs and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and all MRL proposals derived by EFSA still require further consideration by risk managers.

Keywords: cyproconazole, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, fungicide

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Correspondence: pesticides.mrl@efsaeuropa.eu
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Review of the existing MRLs for cyproconazole

Summary

Cyproconazole was included in Annex I to Directive 91/414/EEC on 1 June 2011 by Commission Implementing Directive 2011/56/EU, and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. Considering that no application was received to support the renewal of the approval of cyproconazole, its approval will expire on 31 May 2021.

As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 18 December 2019 EFSA initiated the collection of data for this active substance. Considering the expiry date for the approval on 31 May 2021, the assessment is limited to uses authorised in third countries and codex maximum residue limits (CXLs). In a first step, Member States and the UK were invited to submit by 24 January 2020 Good Agricultural Practices (GAPs) for the uses authorised in third countries in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State Ireland to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States and the UK were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 24 April 2020. On the basis of all the data submitted by Member States, the UK and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked the rapporteur Member State (RMS) to prepare a supporting evaluation report. The evaluation report, together with Pesticide Residues Intake Model (PRIMO) calculations were provided by the RMS to EFSA on 2 July 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report. During the completeness check, the RMS clarified that the critical GAPs identified in the GAP overview file were not supported by sufficient data and are not forming the basis of any existing EU MRLs, whereas the GAPs were all evaluated by the JMPR and correspond to existing Codex MRLs (CXLs). Therefore, it was concluded that the assessment will focus on the existing CXLs, and thereby also cover GAPs authorised in third countries. Consequently, a Pesticide Residues Overview File (PROFile) was not deemed necessary.

Based on the information provided by the RMS, Member States, the UK and the EURLs, and taking into account the conclusions derived by EFSA in the framework of Commission Regulation (EC) No 33/2008 and the MRLs established by the Codex Alimentarius Commission (CAC), EFSA prepared in December 2020 a draft reasoned opinion, which was circulated to the Member States and the EURLs for consultation via a written procedure. Comments received by 15 January 2021 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

According to the results of the metabolism studies, the residue definition for enforcement in plant can be proposed as cyproconazole (sum of isomers). As regards risk assessment, four residue definitions are set separately: cyproconazole (sum of isomers); triazole alanine (TA) and triazole lactic acid (TLA); triazole acetic acid (TAA); and 1,2,4-triazole (1,2,4-T). These residue definitions are applicable to processed commodities. However, although included in the general residue definition for all triazoles, metabolites TLA and 1,2,4-T are not expected to be relevant for cyproconazole.

An analytical method for the enforcement of the proposed residue definition at the limit of quantification (LOQ) of 0.01 mg/kg in high water, high oil matrices and dry commodities is available. According to the EURLs the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in all four major matrix groups. Two analytical methods for the detection of cyproconazole in coffee and roasted coffee were investigated and found acceptable by JMPR. However, as these methods are not available at EU level, a method for the enforcement of cyproconazole in coffee is still required.

Since the present assessment is limited to CXLs, the investigation of the magnitude of residues in plants and the residues in commodities of animal origin is not required. Nonetheless, the residue definition for enforcement as cyproconazole (sum of isomers) proposed by the peer review is still considered applicable for commodities of animal origin. A fully validated analytical method for the determination of cyproconazole in all animal tissues, milk and eggs, with a LOQ of 0.01 mg/kg is available. The EURLs reported that a multi-residue analytical method with a screening detection limit...
(SDL) of 0.005 mg/kg for the routine analysis of cyproconazole (sum of isomers) is available in muscle, milk, eggs and honey.

The residue definition for risk assessment was proposed as cyproconazole (sum of isomers) and the metabolites M36(Z2), M38(Z1) and M9/M14 (pair of diastereomers), expressed as cyproconazole equivalents. A conversion factor from the residue definition of enforcement to risk assessment was derived for liver.

It is highlighted that residue definitions for monitoring and risk assessment for triazole pesticide active substances in animals have been agreed in the framework of the triazole derivative metabolites (TDM) confirmatory data and these are the same as for plants.

In the framework of this review, the uses previously assessed by the JMPR and adopted by the CAC, were considered. The CXLs, resulting from these assessments by JMPR, are now international recommendations that need to be considered by European risk managers when establishing MRLs. Cyproconazole CXLs are currently set for several plant commodities and for all commodities of animal origin. Only the CXLs for soybeans, and for liver, kidney, edible offal in swine, bovine and sheep were implemented in the EU legislation and are currently in force. Furthermore, it is highlighted that CXLs were derived in most plant commodities from European GAPs (except for soybeans, maize and coffee).

As different toxicological reference values were derived respectively for cyproconazole and for the TDMs, separate consumer risk assessments should be carried out. Therefore, EFSA performed separate consumer risk assessments for cyproconazole, for TA and TAA. The risk assessments for TA and TAA are indicative, as data on the TDMs were only available to derive risk assessment values in soybeans, maize, coffee and animal commodities. In addition, as the data on these plant commodities were not supported by detailed study summaries, EFSA could not verify whether these are from trials compliant with the uses assessed by the JMPR. Therefore, detailed study summaries are still required to confirm the input values considered for the risk assessment of TDMs.

For peas without pods, dry beans, dry peas, rape seed, barley grain, buckwheat grain, millet grain, oats grain, rye grain, wheat grain and sugar beet, data on the levels of TDMs expected according to the most critical GAPs assessed by the JMPR are not available. Therefore, eight trials compliant with the CXL GAPs analysing for TA and TAA are still required. It is noted that all these CXLs were based on European uses.

A separate risk assessment for 1,2,4-T is not needed, since this metabolite is not expected in crops treated with cyproconazole, considering the metabolism of cyproconazole and that the levels were below the LOQ of 0.01 mg/kg in all trials where information was available.

For cyproconazole, the highest chronic exposure was calculated for the Dutch toddler, representing 6% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for bovine liver, representing 56% of the acute reference dose (ARfD). These calculations indicate that the CXLs assessed under this review result in a consumer exposure lower than the toxicological reference values. Therefore, these CXLs are unlikely to pose a risk to consumer's health.

It is underlined that since no application for renewal was submitted, the toxicological reference values were not reviewed recently.

In addition, the potential preferential metabolism of each isomer of cyproconazole in animals and plants was not investigated in the studies submitted and was therefore not considered. However, considering the large margin of safety in the exposure calculations for cyproconazole, the potential change of isomer ratios in the final residues is not expected to be of concern for the uses assessed in this review. In case future uses of cyproconazole would lead to a higher consumer exposure, further information regarding the impact of plant and/or livestock metabolism on the isomer ratio might be required.

For TA, the highest chronic exposure was calculated for the Dutch toddler representing 0.3% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.4% of the ARfD.

For TAA, the highest chronic exposure was calculated for the Dutch toddler representing 0.07% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.1% of the ARfD.

Although for several CXLs residue data for TDMs are not available, considering the large margin of consumer safety, it is not expected that the other CXLs will pose a risk for consumers.

Despite the major uncertainties highlighted above, these calculations indicate that the existing CXLs are unlikely to pose a risk to consumer’s health for what concerns these two metabolites (TA and TAA).

EFSA emphasises that a comprehensive risk assessment including all crops and all pesticides belonging to the class of triazole fungicides has not been performed in the framework of the current review. EFSA recommended to elaborate together with risk managers a strategy to ensure that all required data are made available to finalise the overall risk assessment for triazole fungicides.
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Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as 'the Regulation') establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for that active substance.

Cyproconazole was included in Annex I to Council Directive 91/414/EEC on 1 June 2011 by means of Commission Implementing Directive 2011/56/EU\(^3\) which has been deemed to be approved under Regulation (EC) No 1107/2009\(^4\), in accordance with Commission Implementing Regulation (EU) No 540/2011\(^5\), as amended by Commission Implementing Regulation (EU) No 541/2011\(^6\). Considering that no application was received to support the renewal of the approval of cyproconazole, its approval will expire on 31 May 2021.

By way of background information, upon resubmission in the framework of Commission Regulation (EC) No 33/2008\(^7\) cyproconazole was evaluated by Ireland, designated as rapporteur Member State (RMS). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA scientific output (EFSA, 2010). The approval of cyproconazole is restricted to uses as a fungicide. Furthermore, according to the provisions of the approval regulation, confirmatory information was requested, among others, as regards to residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops and products of animal origin. This data was submitted, however, the peer review of the pesticide risk assessment of the TDMs concluded that the submitted confirmatory data on cyproconazole were not sufficient to fully address the confirmatory data requirements and to finalise the consumer risk assessment, which therefore, was considered as inconclusive (EFSA, 2018b).

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU), and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Regulation (EC) No 1107/2009 is therefore insufficient for the assessment of all existing MRLs for a given active substance.

To gain an overview of the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residues Overview File (PROFile). The PROFile is an inventory of all pesticide residues data relevant to the risk assessment and MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities;
- the analytical methods for enforcement of the proposed MRLs.

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\(^1\) Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

\(^2\) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32. Repealed by Regulation (EC) No 1107/2009.

\(^3\) Commission Implementing Directive 2011/56/EU of 27 April 2011 amending Council Directive 91/414/EEC to include cyproconazole as active substance and amending Commission Decision 2008/934/EC. OJ L 108, 28.4.2011, p. 30–33.

\(^4\) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

\(^5\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

\(^6\) Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.

\(^7\) Commission Regulation (EC) No 33/2008 of 17 January 2008 laying down detailed rules for the application of Council Directive 91/414/EEC as regards a regular and an accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 9(2) of that Directive but have not been included into its Annex I. OJ L 15, 18.1.2008, p. 5–12.
As the basis for the MRL review, on 18 December 2019, EFSA initiated the collection of data for this active substance. Considering that no application was received to support the renewal of the approval of cyproconazole and considering the expiry date for its approval on 31 May 2021, the assessment is limited to uses authorised in third countries and codex maximum residue limits (CXLs). In a first step, Member States and the UK\(^8\) were invited to submit by 24 January 2020 the Good Agricultural Practices (GAPs) for the uses authorised in third countries, in a standardised way, in the format of specific GAP forms. In the framework of this consultation 10 Member States and the UK provided feedback, however, only the United Kingdom reported authorisations of cyproconazole in third countries (Argentina, Bolivia, Brazil, Paraguay, Uruguay and US). Based on the GAP data submitted, the designated RMS Ireland was asked to identify the critical GAPs to be further considered in the assessment, in the format of a specific GAP overview file. Subsequently, in a second step, Member States and the UK were requested to provide residue data supporting the critical GAPs by 25 April 2020.

Only the United Kingdom and the EU Reference Laboratories for Pesticides Residues (EURLs) provided additional data, and on the basis of all the data submitted, EFSA asked Ireland to prepare a supporting evaluation report. The evaluation report, together with the Pesticide Residues Intake Model (PRIMo) calculations, were submitted to EFSA on 2 July 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report. During the completeness check, the RMS clarified that the critical GAPs identified in the GAP overview file were not supported by sufficient data and are not forming the basis of any existing EU MRLs, whereas the GAPs were all evaluated by the JMPR and correspond to existing Codex MRLs (CXLs). Therefore, it was concluded that the assessment will focus on the existing CXLs, and thereby also cover GAPs authorised in third countries. Consequently, a PROFile was not deemed necessary.

Considering all the available information, and taking into account the MRLs established by the Codex Alimentarius Commission (CAC) (i.e. CXLs), EFSA prepared in December 2020 a draft reasoned opinion, which was circulated to Member States and the EURLs for commenting via a written procedure. All comments received by 15 January 2021 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Ireland, 2020), taking into account also the information provided by the Member States and the UK during the collection of data, and the EURLs report on analytical methods (EURLs, 2020) are considered as main supporting documents to this reasoned opinion and, thus, made publicly available.

In addition, further supporting documents to this reasoned opinion are the completeness check report (EFSA, 2020) and the Member States consultation report (EFSA, 2021). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Furthermore, the exposure calculations for all crops reported in the framework of this review performed using the PRIMo as well as the GAP overview file are key supporting documents and made publicly available as background documents to this reasoned opinion. A screenshot of the report sheet of the PRIMo is presented in Appendix C.

Terms of Reference

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

The active substance and its use pattern

Cyproconazole is the ISO common name for \((2RS,3RS;2RS,3SR)-2-(4-chlorophenyl)-3-cyclopropyl-1-(1H-1,2,4-triazol-1-yl)butan-2-ol\) (IUPAC).

\(^8\) The UK withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the UK from the EU, and with the established transition period, the EU requirements on data reporting also apply to the UK data collected until 31 December 2020.
The chemical structure of the active substance and its main metabolites are reported in Appendix F. It is highlighted that cyproconazole is classified as toxic to reproduction category 1B according to Commission Regulation (EC) No 1272/20089.

The EU MRLs for cyproconazole are established in Annexes IIIA of Regulation (EC) No 396/2005. CXLs were also established by the CAC. An overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

Table 1: Overview of the MRL changes since the entry into force of Regulation (EC) No 396/2005

| Procedure                          | Legal implementation | Remarks |
|------------------------------------|----------------------|---------|
| MRL application                    | Regulation (EU) No 2018/70(a) | Borage seeds (EFSA, 2011a) |
| MRL application                    | Regulation (EU) No 2017/171(b) | Pulses, barley and oats (EFSA, 2016) |
| MRL application                    | Regulation (EU) No 1004/2013(c) | Mustard seeds, gold of pleasure seeds (NEU only) (EFSA, 2013) |
| MRL application                    | Regulation (EU) No 34/2013(d) | Poppy seeds (EFSA, 2012) |
| MRL application                    | Regulation (EU) No 270/2012(e) | Rape seed (EFSA, 2011a) |
| Implementation of CAC 2010         | Regulation (EU) No 441/2012(f) | Soybeans, rape seeds, and liver, kidney, edible offals in swine, bovine and sheep (EFSA, 2011b) |

MRL: maximum residue level; NEU: northern Europe; CAC: Codex Alimentarius Commission.

(a): Commission Regulation (EU) 2018/70 of 16 January 2018 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for ametocetrin, chlorpyrifos-methyl, cyproconazole, difenoconazole, fluazinam, flutriafol, prohexadione and sodium chloride in or on certain products. OJ L 12, 17.1.2018, p. 24–52.

(b): Commission Regulation (EU) 2017/171 of 30 January 2017 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for aminopyralid, azoxystrobin, cytararililproline, cyflufenamid, cyproconazole, diethofencarb, dithiocarbamates, fluazifop-P, flupyradol, haloxyfop, isofetamid, metalaxyl, prohexadione, propaquizafop, pyrimethanil, Trichoderma atroviride strain SCI and zoxamide in or on certain products. OJ L 30, 3.2.2017, p. 45–111.

(c): Commission Regulation (EU) No 1004/2013 of 15 October 2013 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for 8-hydroxyquinoline, cyproconazole, cyprodinil, flupyradol, nicotine, pendimethalin, pencytracetpyrid and trifloxystrobin in or on certain products. OJ L 279, 19.10.2013, p. 10–56.

(d): Commission Regulation (EU) No 34/2013 of 16 January 2013 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for 2-phenylphenol, ametocetrin, Aureobasidium pullulans strains DSM 14940 and DSM 14941, cyproconazole, difenoconazole, dithiocarbamates, folpet, propamocarb, spinosad, spirodiclofen, tebuconazole and tetroconazole in or on certain products. OJ L 89, 27.3.2012, p. 5–63.

(e): Commission Regulation (EU) No 270/2012 of 26 March 2012 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for amidosulfuron, azoxystrobin, bentazone, bifenil, cyproconazole, flupyradol, imazapic, malathion, propiconazole and spinoxad in or on certain products. OJ L 89, 27.3.2012, p. 5–63.

(f): Commission Regulation (EU) No 441/2012 of 24 May 2012 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for bifenthrin, bifenazate, boscalid, cadusafos, chlorantraniliprole, chlorothalonil, clothianidin, cyproconazole, deltamethrin, dicamba, difenoconazole, dinocap, etoxazole, fenpyroximate, flubendiamide, fludioxonil, glyphosate, metalaxyl-M, meptyldinocap, novaluron, thiamethoxam, and triazophos in or on certain products. OJ L 135, 25.5.2012, p. 4–56.

Considering that no application was received to support the renewal of the approval of cyproconazole and the expiry date for its approval is 31 May 2021, the assessment was limited to uses authorised in third countries and CXLs. For the purpose of this MRL review, all the uses of cyproconazole currently authorised in third countries as submitted by the Member States and the UK during the GAP collection, have been reported by the RMS in the GAP overview file. During the completeness check, the RMS clarified that the critical GAPs identified in the GAP overview file were not supported by sufficient data and are not forming the basis of any existing EU MRLs, whereas these GAPs were all evaluated by the JMPR and correspond to existing Codex MRLs (CXLs). Therefore, it was concluded that the assessment will focus on the existing CXLs, and thereby also cover GAPs authorised in third countries.

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

EFSA has based its assessment on the following documents:

- the evaluation report (Ireland, 2020);
- the evaluation report with additional data provided during the data collection (United Kingdom, 2020);
- the draft assessment report (DAR) prepared under Council Directive 91/414/EEC (Ireland, 2006);
- the additional report (AR) and its addenda prepared under Commission Regulation (EC) No 33/2008 (Ireland, 2010a);
- the final addendum to the draft assessment report (DAR) and the additional report (AR) (Ireland, 2010b);
- the conclusion on the peer review of the pesticide risk assessment of the active substance cyproconazole (EFSA, 2010);
- conclusion on the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data (EFSA, 2018b);
- the review report on cyproconazole (European Commission, 2013);
- the Joint Meeting on Pesticide residues (JMPR) Evaluation report (FAO, 2010a,b, 2013);
- the previous reasoned opinions on cyproconazole (EFSA, 2011a, 2012, 2013, 2016).

The assessment is performed in accordance with the legal provisions of the uniform principles for evaluation and authorisation of plant protection products as set out in Commission Regulation (EU) No 546/201110 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1997a–g, 2000, 2010a, 2010b, 2017; OECD, 2011, 2013).

More detailed information on the available data and on the conclusions derived by EFSA can be retrieved from the list of end points reported in Appendix B.

1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of cyproconazole was investigated after foliar or seed treatment in wheat (cereals), sugar beet (root vegetables), apples and grapes (fruit crops), peanuts (pulses/oilseeds) and coffee (Ireland, 2006, 2010a,b) and assessed in the framework of the peer review (EFSA, 2010). Cyproconazole was radiolabelled either on the phenyl ring, the triazole moiety or the alpha carbon position. Studies with the triazole ring label are available in wheat, sugar beet and coffee.

In wheat, three studies with foliar application and one with seed treatment were performed. In the first study, cyproconazole radiolabelled at the phenyl ring was applied at a rate of 100 or 200 g a.s./ha, the major component identified in grain, straw and forage was cyproconazole, representing 16.6% (1.064 mg/kg), 36.6% (0.014 mg/kg) and 60.3% (2.44 mg/kg) of the total radioactive residue (TRR), respectively. Several minor metabolites were also identified but were below 10% TRR. Similarly, in the second study, cyproconazole radiolabelled at the alpha carbon position was applied in two foliar applications of 80 g a.s./ha, the major component identified in grain and leaf/stems was cyproconazole, representing 45.6% and 45.7% TRR. Quantification was not performed in this study. In the third study, cyproconazole radiolabelled at the triazole ring was applied at rates of 100 g a.s./ha or at 160 g a.s./ha. The main component of the residue in straw and forage is parent cyproconazole, representing 51% (2.27 mg/kg) and 0.67% (0.78 mg/kg) of TRR, respectively. In grain, the main component of the residue is triazole alanine (TA) (0.69% of TRR; 0.128 mg/kg), whereas residues of parent cyproconazole are present at low levels (< 0.01 mg/kg). For the seed treatment, cyproconazole labelled in the triazole ring was applied as a seed dressing in 1 g/100 g seed. Residues were determined at 0.001 mg/kg in both grain, forage and straw, therefore no further identification was conducted, and it is not required.

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10 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
In sugar beets, cyproconazole radiolabelled at the triazole ring was applied in four foliar applications of 80 or 120 g a.s./ha, the major component identified in root and tops/leaves was cyproconazole, representing 78.6 (0.017 mg/kg)-80.8% (0.086 mg/kg) and 76.2% (2.25 mg/kg)-76.8% (3.24 mg/kg). Minor metabolites were also identified in roots and tops/leaves but were below 3% TRR.

In apples, after four foliar applications of 40 g a.s./ha, the major component identified in fruits was cyproconazole, representing 76.4% of the TRR while several minor metabolites were also identified but were below 2.5% TRR. Quantification of parent or metabolites was not performed.

In grapes, two studies were available. In both studies, cyproconazole was radiolabelled at the alpha carbon position. In the first study, cyproconazole was applied in four foliar applications of 20 g a.s./ha. Parent was the major component, representing 63.2% of the TRR while several minor metabolites were also identified but were below 4.1% TRR. In the second study, the translocation of cyproconazole in the plant was investigated. Cyproconazole was applied in the leaves of grapevines seedlings (25 mg cyproconazole per plant) and leaf (surface and total residues) and stem/root samples were collected at various sampling points (1; 3; 7; 14; 28; 49); in addition, as to investigate the surface loss, another experiment was conducted where cyproconazole was applied directly in glass plate. A little translocation was observed from the surface into the leaf or stem/root, with the majority of the parent remaining in the surface and degrading through evaporation (25% TRR remaining after 49 days). This is confirmed by the study in treated glass plates (11% TRR remaining after 49 days). The major component identified in the leaves was the parent, representing 63% of the TRR while several metabolites were identified but at levels below 2.5% TRR. Quantification was not performed in either studies.

In peanuts, cyproconazole radiolabelled at the alpha carbon position was applied as a foliar application of 1 x 100 g a.s./ha, 4 x 100 g a.s./ha or 1,000 g a.s./ha. In seeds residues were low (below 0.01% TRR) thus no further identification was conducted. In peanut foliage, the major component identified was cyproconazole, representing 59–98% TRR. Quantification was not performed in this study.

In coffee, cyproconazole radiolabelled at the triazole ring was applied in four foliar applications of 50 or 200 g/ha with samples collected at 30 days preharvest interval (PHI). The major component identified was cyproconazole, representing 42.1–50.1% (0.015–0.1 mg/kg) while metabolite TA was present at 9.2–13% TRR (0.005–0.018 mg/kg). Other minor metabolites identified were below 6.9% TRR (< 0.007 mg/kg).

The metabolic pathway of cyproconazole was similar in all crops assessed. Cyproconazole labelled in the triazole ring was only used in studies in wheat, sugar beet and coffee. These studies indicated that the loss of the triazole molecule with its subsequent conversion to TA occurs to a significant extent in wheat and in coffee but not in sugar beet.

1.1.2. Nature of residues in rotational crops

Since the present assessment is limited to CXLs, the investigation of the nature of cyproconazole in rotational crops is not required. It is noted that the nature of residues in rotational crops was considered during the peer review (EFSA, 2010).

1.1.3. Nature of residues in processed commodities

Studies investigating the nature of residues in processed commodities were assessed in the framework of the peer review. Studies were conducted with radiolabelled cyproconazole on the triazole ring simulating representative hydrolytic conditions for pasteurisation (20 min at 90°C, pH 4), boiling/brewing/baking (60 min at 100°C, pH 5) and sterilisation (20 min at 120°C, pH 6). Cyproconazole was stable to hydrolysis under standard conditions of pasteurisation, baking/brewing/baking and sterilisation (Ireland, 2006, 2010a,b; EFSA, 2010).

Regarding TDMs, no studies were provided in the framework of this review. However, standard hydrolysis studies on TDMs are available and were assessed by EFSA as confirmatory data submitted for the risk assessment of the TDMs (EFSA, 2018b). These studies showed that TA, triazole acetic acid (TAA), triazole lactic acid (TLA) and 1,2,4-triazole (1,2,4-T) remain stable under the standard hydrolysis conditions simulating processing of pasteurisation, baking, brewing and boiling, and sterilisation.

Therefore, it can be concluded that the nature of the residues in processed commodities is sufficiently addressed.
1.1.4. Methods of analysis in plants

During the peer review (EFSA, 2010), an analytical method (DFG Method S19) based on liquid chromatography with tandem mass spectrometry (LC-MS/MS) detection quantifying residues of cyproconazole as sum of its isomers (method not stereoselective) was investigated. The method was validated in high water (apples, melons) and dry commodities (wheat grain), with a limit of quantification (LOQ) of 0.01 mg/kg. One additional selected reaction monitoring (SRM) transition was monitored for confirmation purposes. This primary method is supported by an independent laboratory validation (ILV). For high oil content matrices there was sufficient evidence that the multi-residue QuEChERS method can be used for enforcement purposes (EFSA, 2011b). Two analytical methods for the detection of cyproconazole in coffee and roasted coffee were investigated and found acceptable by JMPR (FAO, 2013). However, as these methods are not available at EU level, a method for the enforcement of cyproconazole in coffee is still required.

During the completeness check, the EURLs provided a multi-residue analytical method (buffered QuEChERS) using LC-MS/MS or gas chromatography with tandem mass spectrometry (GC-MS/MS), with a LOQ of 0.01 mg/kg for the routine analysis of cyproconazole (sum of isomers) in high water, high acid and dry commodities (EURLs, 2020) and an additional single residue analytical method (QuOil) using LC-MS/MS with a LOQ of 0.01 mg/kg in high oil commodities and using GC-MS/MS with a LOQ of 0.05 mg/kg in pepper (EURLs, 2020).

1.1.5. Stability of residues in plants

Since the present assessment is limited to CXLs, the stability of the residue in plants was not investigated. The results of the storage stability studies evaluated in the framework of the peer review of cyproconazole (Ireland, 2006, EFSA, 2010) and of the confirmatory data for the TDMs (EFSA, 2018b) are reported in the list of end points for completeness.

1.1.6. Proposed residue definitions

The metabolism of cyproconazole was similar in all crops assessed and the processing of cyproconazole is not expected to modify the nature of residues. As the parent compound was found to be a sufficient marker, the residue definition for enforcement is proposed as cyproconazole (sum of isomers).

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in high water, high oil matrices and dry commodities is available (EFSA, 2010, 2011b). According to the EURLs the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in all four major matrix groups (EURLs, 2020). A method for the enforcement of cyproconazole in coffee is still required.

The residue definitions proposed for risk assessment for cereals during the peer review were: (1) cyproconazole; (2) TDMs, pending the agreed assessment approach of triazole compounds and TDMs (EFSA, 2010).

In the recently published conclusion on TDMs (EFSA, 2018b), EFSA proposed the following residue definitions for risk assessment for all the triazole active substances, which is considered to replace the previously derived residue definitions:

1) parent compound and any other relevant metabolite exclusively linked to the parent compound;
2) 1,2,4-T;
3) TA and TLA, since these compounds share the same toxicity;
4) TAA.

Considering the metabolism of cyproconazole, other metabolites than the TDMs were found only at very low absolute levels and were not considered relevant (see Section 1.1.1). Therefore, the cyproconazole specific residue definition for risk assessment is proposed to include the parent only.

The abovementioned residue definitions were found appropriate for the current assessment. It should be noted that in the limited metabolism studies available with the triazole ring, only TA was observed at significant levels. The relative contribution of TLA in the residue definition compared to TA is not considered significant, as TLA was not observed in the metabolism studies. Regarding TAA, despite not being present at significant levels in the metabolism studies, it was detected in field trials in wheat conducted according to a GAP less critical than the use under consideration (Ireland, 2020).
In contrast, 1,2,4-T was not observed at significant levels in any of the metabolism study or field trials. Altogether, although included in the general residue definition for all triazoles, metabolites TLA and 1,2,4-T are not expected to be relevant for cyproconazole.

It is highlighted that the risk assessment must be performed separately for each of the relevant residue definitions derived (EFSA, 2018b).

In addition, EFSA emphasises that the above studies do not investigate the possible impact of plant metabolism on the isomer ratio of cyproconazole and further investigation on this matter would in principle be required. However, in view of the large margin of safety in the exposure calculation (see Section 3.1), the potential change in isomer ratios in the final residue is not expected of concern. In case future uses of cyproconazole would lead to a higher consumer exposure, further information regarding the impact of plant and/or livestock metabolism on the isomer ratio might be required (EFSA, 2019b).

1.2. Magnitude of residues in plants

Since the present assessment is limited to CXLs, the investigation of the magnitude of residues in plants is not required.

2. Residues in livestock

Since the present assessment is limited to CXLs, the investigation of the residues in commodities of animal origin is not required. Nonetheless, metabolism studies in lactating goats (three studies) and laying hens (two studies) were provided and assessed in the framework of the peer review (Ireland, 2006, 2010a,b, EFSA, 2010).

In the three available studies in lactating goats, cyproconazole was radio-labelled at the alpha carbon position conducted at a) a dose rate of 1 mg/kg body weight (bw) per day for 12 consecutive days b) a dose rate of 30 mg/kg bw per d for three consecutive days or c) a dose rate of 10 mg/kg bw per day for four consecutive days.

In the two studies on laying hens, cyproconazole was radio-labelled either on the phenyl ring or in the alpha carbon position. In the first study, [phenyl(U)-14C]-cyproconazole was applied at a dose rate of 114 mg/kg bw per day for four consecutive days. In the second study, [α-carbon 14C]-cyproconazole was applied at a dose rate of 1 mg/kg bw per day for three consecutive days.

The peer review concluded that the parent compound is a sufficient marker in livestock commodities, and the residue definition for enforcement was proposed as cyproconazole (sum of isomers).

An analytical method using LC–MS/MS (DFG Method S19) was fully validated for the determination of cyproconazole in all animal tissues, milk and eggs, with a LOQ of 0.01 mg/kg. During the completeness check, the EURLs provided a multi-residue analytical method (buffered QuEChERS) using LC–Q/TOF, with a screening detection limit (SDL) of 0.005 mg/kg for the routine analysis of cyproconazole (sum of isomers) in muscle, milk, eggs and honey (EURLs, 2020).

For risk assessment, the peer review proposed the following residue definition: cyproconazole (sum of isomers) and the metabolites M36(Z2); M38(Z1) and M9/M14 (pair of diastereomers), expressed as cyproconazole equivalents.

A conversion factor from the residue definition of enforcement to risk assessment was derived for liver based on the metabolism studies by the peer review, whereas for other animal commodities it was not relevant (EFSA, 2010).

It is highlighted that residue definitions for risk assessment for triazole pesticide active substances in animals have been agreed in the framework of the TDM confirmatory data (EFSA, 2018b). Accordingly, besides the residue definition for cyproconazole, three other residue definitions for risk assessment were set separately for the TDMs: TA and TLA; TAA; and 1,2,4-T.

3. Consumer risk assessment

In the framework of this review, only the uses previously assessed by the JMPR (FAO, 2010a,b, 2013) were considered. The CXLs, resulting from these assessments by JMPR and adopted by the CAC, are now international recommendations that need to be considered by European risk managers when establishing MRLs.

CXLs are currently set for several plant commodities (peas without pods, beans (dry), peas (dry), rape seeds, soybeans, barley, buckwheat, maize, millet, oat, rye, wheat, coffee and sugar beet roots)
and for all commodities of animal origin. Only the CXLs in soybeans, liver, kidney, edible offals in swine, bovine and sheep were implemented in the EU legislation and are currently in force. Furthermore, it is highlighted that CXLs were derived in most plant commodities from European GAPs (except for soybeans, maize and coffee).

For information, it is noted that the RMS reported additional non-European GAPs in barley (not fully supported by trials) and wheat that are similar or less critical than the existing CXLs (Ireland, 2020). These GAPs were not considered further, as they were not considered by JMPR and detailed study summaries of the trials supporting the uses were not available.

As different toxicological reference values (TRVs) were derived respectively for cyproconazole and for the TDMs, separate consumer risk assessments should be carried out. Regarding TDMs, no residue data were reported by JMPR in plant commodities, as the residue definition for risk assessment agreed by JMPR did not include these metabolites that may arise from multiple triazole fungicides sources.

Nonetheless, an overview of TDM residue levels (TA, TAA and 1,2,4-T) in the trials on soya beans, maize and coffee corresponding to the CXLs derived were reported by the RMS (Ireland, 2020), and were used to perform an indicative consumer risk assessment. However, as these data were not supported by detailed study summaries, EFSA could not verify whether these are from trials compliant with the uses assessed by the JMPR. Therefore, detailed study summaries are still required to confirm the input values considered for the risk assessment of TDMs (TA and TAA).

For peas without pods, dry beans, dry peas, rape seed, barley grain, buckwheat grain, millet grain, oats grain, rye grain, wheat grain and sugar beet, data on the levels of TDMs expected according to the most critical GAPs assessed by the JMPR are not available. Therefore, eight trials compliant with the CXL GAPs analysing for TA and TAA are still required. It is noted that all these CXLs were based on European uses.

While TDM levels were also reported for wheat corresponding to the less critical non-EU GAP mentioned above, the result of the trials could not be used in the consumer risk assessment. Nonetheless, it is noted that both TA and TAA were detected (Ireland, 2020).

Therefore, EFSA performed separate consumer risk assessments for cyproconazole, and indicative risk assessments for TA (TLA not relevant) and TAA based on the available data for this review. A separate risk assessment for 1,2,4-T is not needed, since this metabolite is not expected in the commodities for which CXLs are set, considering the results of the metabolism studies on cyproconazole and the results from the trials reported by the RMS.

In addition, EFSA highlights that the residue definition for dietary risk assessment for animal commodities set by JMPR is limited to ‘cyproconazole, free and conjugated’. In order to circumvent underestimation of the consumer exposure for these commodities, the CF of 3 for liver set by the peer review (EFSA, 2010) was applied.

### 3.1. Consumer risk assessment for cyproconazole

Chronic and acute exposure calculations for all existing CXLs were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018a, 2019a). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. All input values included in the exposure calculations are summarised in Appendix D.

The exposure values calculated were compared with the TRVs for cyproconazole, derived by EFSA in the framework of the peer review for the first approval (EFSA, 2010). The highest chronic exposure was calculated for the Dutch toddler, representing 6% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for bovine liver, representing 56% of the acute reference dose (ARfD). These calculations indicate that the CXLs assessed under this review result in a consumer exposure lower than the toxicological reference values. Therefore, these CXLs are unlikely to pose a risk to consumer’s health.

It is underlined that since no application for renewal was submitted, the TRV were not reviewed recently.

In addition, EFSA emphasises that the above assessment does not consider the possible impact of plant and livestock metabolism on the isomer ratio of cyproconazole and further investigation on this matter would in principle be required. EFSA notes that in the view of the large margin of safety in the exposure calculations, the potential change of isomer ratios in the final residues is not expected to be of concern for the CXLs assessed in the framework of this review. In case future uses of cyproconazole would lead to a higher consumer exposure, further information regarding the impact of plant and/or livestock metabolism on the isomer ratio might be required (EFSA, 2019b).
3.2. Indicative consumer risk assessment for triazole derivative metabolites

Separate calculations were performed for metabolites TA and TAA, and the exposure values calculated were compared with their respective toxicological reference values derived by EFSA (2018b). Chronic and acute exposure calculations using revision 3.1 of the EFSA PRIMo (EFSA, 2018a,b, 2019a,b) could only be performed for soybeans, maize, coffee, and the animal commodities. For all other existing CXLs, in the absence of information on the levels of TDMs, a consumer risk assessment could not be performed. All input values included in the exposure calculations are summarised in Appendix D.

For TA, the highest chronic exposure was calculated for the Dutch toddler representing 0.3% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.4% of the ARfD. Concerning TAA, the highest chronic exposure was calculated for the Dutch toddler representing 0.07% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.1% of the ARfD.

Although the data gaps highlighted in the previous sections, these calculations indicate that the existing CXLs are unlikely to pose a risk to consumer’s health for what concerns these two metabolites.

EFSA emphasises that a comprehensive risk assessment, including all crops and all pesticides belonging to the class of triazole fungicides, could not be performed in the framework of this MRL review. EFSA recommended to elaborate together with risk managers a strategy to ensure that all required data are made available to finalise the overall risk assessment for triazole fungicides.

Conclusions

Considering that no application was received to support the renewal of the approval of cyproconazole and the expiry date for its approval is 31 May 2021, the assessment was limited to uses authorised in third countries and CXLs. During the completeness check, the RMS clarified that the critical GAPs identified in the GAP overview file were not supported by sufficient data and are not forming the basis of any existing EU MRLs, whereas were all evaluated by the JMPR and correspond to existing CXLs. Therefore, it was concluded that the assessment will focus on the existing CXLs, and thereby also cover GAPs authorised in third countries.

According to the results of the metabolism studies, the residue definition for enforcement in plant can be proposed as cyproconazole (sum of isomers). As regards risk assessment, four residue definitions are set separately: cyproconazole (sum of isomers); TA and TLA; TAA; and 1,2,4-T. These residue definitions are applicable to processed commodities. However, although included in the general residue definition for all triazoles, metabolites TLA and 1,2,4-T are not expected to be relevant for cyproconazole.

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in high water, high oil matrices and dry commodities is available. According to the EURs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in all four major matrix groups. Two analytical methods for the detection of cyproconazole in coffee and roasted coffee were investigated and found acceptable by JMPR. However, as these methods are not available at EU level, a method for the enforcement of cyproconazole in coffee is still required.

Since the present assessment is limited to CXLs, the investigation of the magnitude of residues in plants and the residues in commodities of animal origin is not required. Nonetheless, the residue definition for enforcement as cyproconazole (sum of isomers) proposed by the peer review is still considered applicable for commodities of animal origin. A fully validated analytical method for the determination of cyproconazole in all animal tissues, milk and eggs, with a LOQ of 0.01 mg/kg is available. The EURs reported that a multi-residue analytical method with a SDL of 0.005 mg/kg for the routine analysis of cyproconazole (sum of isomers) is available in muscle, milk, eggs and honey.

The residue definition for risk assessment was proposed as cyproconazole (sum of isomers) and the metabolites M36(Z2), M38(Z1) and M9/M14 (pair of diastereomers), expressed as cyproconazole equivalents. A conversion factor from the residue definition of enforcement to risk assessment was derived for liver.

It is highlighted that residue definitions for monitoring and risk assessment for triazole pesticide active substances in animals have been agreed in the framework of the triazole derivative metabolites (TDM) confirmatory data and these are the same as for plants.

In the framework of this review, the uses previously assessed by the JMPR and adopted by the CAC, were considered. The CXLs, resulting from these assessments by JMPR, are now international.
recommendations that need to be considered by European risk managers when establishing MRLs. Cyproconazole CXLs are currently set for several plant commodities and for all commodities of animal origin. Only the CXLs for soybeans, and for liver, kidney, edible offal in swine, bovine and sheep were implemented in the EU legislation and are currently in force. Furthermore, it is highlighted that CXLs were derived in most plant commodities from European GAPs (except for soybeans, maize, coffee).

As different TRVs were derived, respectively, for cyproconazole and for the TDMs, separate consumer risk assessments should be carried out. Therefore, EFSA performed separate consumer risk assessments for cyproconazole, for TA and TAA. The risk assessments for TA and TAA are indicative, as data on the TDMs were only available to derive risk assessment values in soybeans, maize, coffee and animal commodities. In addition, as the data on these plant commodities were not supported by detailed study summaries, EFSA could not verify whether these are from trials compliant with the uses assessed by the JMPR. Therefore, detailed study summaries are still required to confirm the input values considered for the risk assessment of TDMs.

For peas without pods, dry beans, dry peas, rape seed, barley grain, buckwheat grain, millet grain, oats grain, rye grain, wheat grain and sugar beet, data on the levels of TDMs expected according to the most critical GAPs assessed by the JMPR are not available. Therefore, 8 trials compliant with the CXL GAPs analysing for TA and TAA are still required. It is noted that all these CXLs were based on European uses.

A separate risk assessment for 1,2,4-T is not needed, since this metabolite is not expected in crops treated with cyproconazole, considering the metabolism of cyproconazole and that the levels were below the LOQ of 0.01 mg/kg in all trials where information was available.

For cyproconazole, the highest chronic exposure was calculated for the Dutch toddler, representing 6% of the ADI, and the highest acute exposure was calculated for bovine liver, representing 56% of the ARfD. These calculations indicate that the CXLs assessed under this review result in a consumer exposure lower than the toxicological reference values. Therefore, these CXLs are unlikely to pose a risk to consumer’s health.

It is underlined that since no application for renewal was submitted, the toxicological reference values were not reviewed recently.

In addition, the potential preferential metabolism of each isomer of cyproconazole in animals and plants was not investigated in the studies submitted and was therefore not considered. However, considering the large margin of safety in the exposure calculations for cyproconazole, the potential change of isomer ratios in the final residues is not expected to be of concern for the uses assessed in this review. In case future uses of cyproconazole would lead to a higher consumer exposure, further information regarding the impact of plant and/or livestock metabolism on the isomer ratio might be required.

For TA, the highest chronic exposure was calculated for the Dutch toddler representing 0.3% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.4% of the ARfD.

For TAA, the highest chronic exposure was calculated for the Dutch toddler representing 0.07% of the ADI, and the highest acute exposure was calculated for cattle milk, representing 0.1% of the ARfD.

Although for several CXLs residue data for TDMs are not available, considering the large margin of consumer safety, it is not expected that the other CXLs will pose a risk for consumers.

Despite the major uncertainties highlighted above, these calculations indicate that the existing CXLs are unlikely to pose a risk to consumer’s health for what concerns these two metabolites (TA and TAA).

EFSA emphasises that a comprehensive risk assessment including all crops and all pesticides belonging to the class of triazole fungicides has not been performed in the framework of the current review. EFSA recommended to elaborate together with risk managers a strategy to ensure that all required data are made available to finalise the overall risk assessment for triazole fungicides.

**Recommendations**

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 2). Tentative MRLs, not sufficiently supported by data, need to be confirmed by the following data:

1) Eight residue trials compliant with CXL GAPs investigating the residue levels of TA and TAA in peas without pods, dry beans, dry peas, rape seed, barley grain, buckwheat grain, millet grain, oats grain, rye grain, wheat grain and sugar beet.
2) Study summaries of the trials on soybeans, maize and coffee analysing for TA and TAA.

3) An analytical method for the enforcement of cyproconazole in coffee.

It is noted that the existing CXLs were derived in most plant commodities from European GAPs (except for soybeans, maize, coffee).

To inform further risk management discussions, it is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

It is highlighted that the consumer risk assessment for TDMs was not fully addressed in this review.

Table 2: Summary table

| Code number | Commodity                              | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL<sup>(a)</sup> (mg/kg) | Outcome of the review                  |
|-------------|----------------------------------------|-------------------------|---------------------|---------------------------|---------------------------------------|
| 260040      | Peas (fresh, without pods)             | 0.05*                   | 0.01                | 0.01                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 300010      | Beans (dry)                            | 0.08                    | 0.02*               | 0.02                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 300030      | Peas (dry)                             | 0.08                    | 0.02*               | 0.02                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 401060      | Rape seed                              | 0.4                     | 0.4                 | 0.4                        | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 401070      | Soya bean                              | 0.07                    | 0.07                | 0.07                       | Further consideration needed<sup>(c)</sup> Data gap # 2 |
| 500010      | Barley grain                           | 0.2                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 500020      | Buckwheat grain                        | 0.1                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 500030      | Maize grain                            | 0.1                     | 0.01*               | 0.01*                      | Further consideration needed<sup>(c)</sup> Data gap # 2 |
| 500040      | Millet grain                           | 0.1                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 500050      | Oats grain                             | 0.2                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 500070      | Rye grain                              | 0.1                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 500090      | Wheat grain                            | 0.1                     | 0.08                | 0.08                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |
| 620000      | Coffee beans                           | 0.1                     | 0.07                | 0.07                       | Further consideration needed<sup>(c)</sup> Data gap # 2, 3 |
| 900010      | Sugar beet (root)                      | 0.1                     | 0.05                | 0.05                       | Further consideration needed<sup>(b)</sup> Data gap # 1 |

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| Code number | Commodity                        | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL(a) (mg/kg) | Outcome of the review | Comment                                      |
|-------------|----------------------------------|-------------------------|---------------------|----------------|-----------------------|----------------------------------------------|
| 1016020     | Poultry fat                      | 0.05*                   | 0.01*               | 0.01*          | Further consideration needed(d) |                                             |
| 1016030     | Poultry liver                    | 0.05*                   | 0.01*               | 0.01*          | Further consideration needed(d) |                                             |
| 1020010     | Cattle milk                      | 0.05*                   | 0.01                | 0.01           | Further consideration needed(d) |                                             |
| 1020020     | Sheep milk                       | 0.05*                   | 0.01                | 0.01           | Further consideration needed(d) |                                             |
| 1020030     | Goat milk                        | 0.05*                   | 0.01                | 0.01           | Further consideration needed(d) |                                             |
| 1020040     | Horse milk                       | 0.05*                   | 0.01                | 0.01           | Further consideration needed(d) |                                             |
| 1030000     | Birds’ eggs                      | See Reg. 2018/70        | –                   | –              | Further consideration needed(e) |                                             |
| –           | Other commodities of plant and/or animal origin | –                       | –                   | –              | Further consideration needed(e) |                                             |

MRL: maximum residue level; CXL: codex maximum residue limit; (F): The residue definition is fat soluble.
*: Indicates that the MRL is set at the limit of quantification.
(a): The possible impact of the classification of cyproconazole as toxic for reproduction category 1B, in accordance with Regulation (EC) No 1272/2008 on the validity of the MRL proposal was not considered in the assessment.
(b): MRL is derived from the existing CXL based on an EU GAP, which is not fully supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.
(c): MRL is derived from the existing CXL, which is not fully supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.
(d): MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.
(e): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).

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Abbreviations

| Abbreviation | Meaning |
|--------------|---------|
| a.i.         | active ingredient |
| a.s.         | active substance |
| ADI          | acceptable daily intake |
| AR           | additional report |
| ARfD         | acute reference dose |
| BBCH         | growth stages of mono- and dicotyledonous plants |
| bw           | body weight |
| CAC          | Codex Alimentarius Commission |
| CAS          | Chemical Abstract Service |
| CF           | conversion factor for enforcement residue definition to risk assessment residue definition |
| CXL          | codex maximum residue limit |
| DAR          | draft assessment report |
| DAT          | days after treatment |
| DB           | dietary burden |
| DM           | dry matter |
| EUURLs       | European Union Reference Laboratories for Pesticide Residues (former CRLs) |
| FAO          | Food and Agriculture Organization of the United Nations |
| GAP          | Good Agricultural Practice |
| GC–MS/MS     | gas chromatography with tandem mass spectrometry |
| GLP          | Good Laboratory Practice |
| HPLC–MS/MS   | high-performance liquid chromatography with tandem mass spectrometry |
| HR           | highest residue |
| IEDI         | international estimated daily intake |
| IESTI        | international estimated short-term intake |
| ILV          | independent laboratory validation |
| ISO          | International Organisation for Standardization |
| IUPAC        | International Union of Pure and Applied Chemistry |
| 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) |
| LC–MS/MS     | liquid chromatography with tandem mass spectrometry |
| LOQ          | limit of quantification |
| Mo           | Monitoring |
| MRL          | maximum residue level |
| MS           | Member States |
| NEDI         | national estimated daily intake |
| NESTI        | national estimated short-term intake |
| NTMDI        | national theoretical maximum daily intake |
| OECD         | Organisation for Economic Co-operation and Development |
| PBI          | plant-back interval |
| PF           | processing factor |
| PHI          | preharvest interval |
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| PROFile      | (EFSA) Pesticide Residues Overview File |
| QuEChERS     | Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| RA           | risk assessment |
| RD           | residue definition |
| RMS          | rapporteur Member State |
| Abbreviation | Definition |
|--------------|------------|
| SANCO        | Directorate-General for Health and Consumers |
| SDL          | screening detection limit |
| SMILES       | simplified molecular-input line-entry system |
| SRM          | selected reaction monitoring |
| STMR         | supervised trials median residue |
| 1,2,4-T      | 1,2,4-triazole |
| TA           | triazole alanine |
| TAA          | triazole acetic acid |
| TAR          | total applied radioactivity |
| TLA          | triazole lactic acid |
| TMDI         | theoretical maximum daily intake |
| TRR          | total radioactive residue |
| WHO          | World Health Organization |
Appendix A – Summary of authorised uses considered for the review of MRLs

Considering that no application was received to support the renewal of the approval of cyproconazole and considering the expiry date for its approval on 31 May 2021, the assessment was limited to uses authorised in third countries and CXLs. During the completeness check, the RMS clarified that the critical GAPs identified in the GAP overview file were not supported by sufficient data and are not forming the basis of any existing EU MRLs, whereas these GAPs were all evaluated by the JMPR and correspond to existing Codex MRLs (CXLs). Therefore, it was concluded that the assessment will focus on the existing CXLs, and thereby also cover GAPs authorised in third countries.
Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups       | Crop(s)       | Application(s)          | Sampling (DAT) | Comment/Source                                                                 |
|-----------------------------------|-------------------|---------------|-------------------------|----------------|--------------------------------------------------------------------------------|
| Fruit crops                       | Apples            | Foliar, 4 × 40 g/ha | 28                      | 14C alpha carbon; pre-GLP (EFSA, 2010) |
|                                   | Grapes            | Foliar, 4 × 20 g/ha | 29                      | 14C alpha carbon; pre-GLP (EFSA, 2010) |
|                                   | Grapevine seedlings| Foliar, 25 mg/plant | 1; 3; 7; 14; 28; 49    | 14C alpha carbon; (EFSA, 2010)          |
| Root crops                        | Sugar beet        | Foliar, 4 × 80 or 120 g/ha | 28                      | 14C triazole moiety (EFSA, 2010)          |
| Leafy crops                       |                   |               |                         |                                            |
| Cereals/grass                     | Wheat             | Foliar, 2 × 80 g/ha | 34 11(a); 41 11(a); 42 BBCH 51, maturity | 14C alpha carbon; pre-GLP 14C-phenyl ring 14C triazole moiety 14C triazole moiety (EFSA, 2010) |
|       | 100 or 200 g/ha | Foliar, 2 × 100 or 160 g/ha |                  |                                    |
|       | Seed, 1 g/100 g seed |                         |                      |                                    |
| Pulses/oilseeds                  | Peanuts           | Foliar, 1 × 100 or 4 × 100 g/ha | 0, 6 weeks prior to maturity | 14C alpha carbon (EFSA, 2010)          |
|       |                   | Foliar, 1000 g/ha | 21                      | 14C alpha carbon (EFSA, 2010)          |
| Miscellaneous                     | Coffee            | Foliar, 3 × 50 or 200 g/ha | 30                      | 14C triazole moiety (EFSA, 2010)          |
| Rotational crops (available studies) | Crop groups       | Crop(s)       | Application(s)          | PBI (DAT) | Comment/Source                                                                 |
| Root/tuber crops                  | Sugar beer        | Soil application, 0.1 kg a.s./ha | 10 cm in length | 14C alpha carbon Soil ageing intervals (DAT): 30, 90 Soil, leaves and roots were analysed (EFSA, 2010) |
| Leafy crops                       | Lettuce           | Soil application, 0.1 kg a.s./ha | At maturity (42-48) | 14C alpha carbon Soil ageing intervals (DAT): 30, 90 Soils, lettuce foliage and root were analysed (EFSA, 2010) |
| Cereal (small grain)              | Wheat             | Soil application, 0.1 kg a.s./ha | At maturity           | 14C alpha carbon Soil ageing intervals (DAT): 30, 90 Soil, straw and grain were analysed (EFSA, 2010) |
### Processed Commodities (Hydrolysis Study)

| Conditions                                    | Stable? | Comment/Source                  |
|-----------------------------------------------|---------|---------------------------------|
| Pasteurisation (20 min, 90°C, pH 4)           | Yes     | $^{14}C$ triazole moiety (EFSA, 2010) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes     | $^{14}C$ triazole moiety (EFSA, 2010) |
| Sterilisation (20 min, 120°C, pH 6)           | Yes     | $^{14}C$ triazole moiety (EFSA, 2010) |
| Other processing conditions                   | –       | –                               |

(a): Days after first treatment.
Can a general residue definition be proposed for primary crops? **Yes**

Rotational crop and primary crop metabolism similar? **Yes**

Residue pattern in processed commodities similar to residue pattern in raw commodities? **Yes**

Residues of cyproconazole and TDMs are both stable following processing (EFSA, 2010, 2018b)

| Plant residue definition for monitoring (RD-Mo) | Cyproconazole (sum of isomers) |
|-----------------------------------------------|-------------------------------|
| Plant residue definition for risk assessment (RD-RA) | Cyproconazole (sum of isomers) |

For all triazole active substances (EFSA, 2018b)

- TA and TLA;
- TAA;
- 1,2,4-T

TA: triazole alanine; TLA: triazole lactic acid; TAA: triazole acetic acid; 1,2,4-T: 1,2,4-triazole

The previously derived provisional residue definitions (1. cyproconazole, 2. TDMs; EFSA, 2010) have been replaced by the abovementioned residue definitions derived during the peer review of the pesticide risk assessment of the TDMs (EFSA, 2018b). Although included in the general residue definition for all triazoles, metabolites TLA and 1,2,4-T are not expected to be relevant for cyproconazole.

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

| High water, high oil, dry commodities (Ireland, 2006; EFSA, 2010, 2011b): |
| DFG Method S19 (LC–MS/MS), LOQ 0.01 mg/kg; ILV for barley grain and straw. |
| LOQ achievable during routine analysis (EURL, 2020): |
| High water, high acid, and dry commodities, QuEChERS (LC–MS/MS or GC–MS/MS), LOQ of 0.01 mg/kg; high oil commodities, QuOil (LC–MS/MS), LOQ of 0.01 mg/kg; pepper, QuOil (GC–MS/MS), LOQ of 0.05 mg/kg. |

DAT: days after treatment; PBI: plant-back interval; BBCH: growth stages of mono- and dicotyledonous plants; a.s.: active substance; TA: triazole alanine; TLA: triazole lactic acid; TAA: triazole acetic acid; 1,2,4-T: 1,2,4-triazole; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method).
### B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category       | Commodity                      | T (°C) | Stability period (Value, Unit) | Compounds covered | Comment/Source |
|-----------------------------------|----------------|--------------------------------|--------|-------------------------------|-------------------|----------------|
|                                   | High water content | Apples                         | -18    | Months 12                      | Cyproconazole     | Apple residues were very low and bordered on the limit of determination. Thus, the results for apples are inconclusive based on the data presented (Ireland, 2006). |
|                                   | Peanut forage     | -12                            | 38     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Wheat forage      | -12                            | 39     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Peaches           | -18                            | 12     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Peaches, nectarines | -12                            | 42     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Sugar beet (roots and tops) | -18                            | 12     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Bananas (whole fruit and pulp) | -16                            | 12     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Wheat forage (a)  | -20                            | 53     | Months                        | TA                | EFSA et al. (2018b) |
|                                   | Wheat forage      | -20                            | 53     | Months                        | TAA               | EFSA et al. (2018b) |
|                                   | Wheat forage      | -20                            | 6      | Months                        | 1,2,4-T           | EFSA et al. (2018b) |
|                                   | Lettuce           | -20                            | 48     | Months                        | TLA               | EFSA et al. (2018b) |
|                                   | High oil content  | Peanuts (nutmeat)              | -12    | 40 Months                      | Cyproconazole     | EFSA (2010)     |
|                                   | High protein content | --                            | --     | --                            | --                | --             |
|                                   | High starch content | Wheat grain                    | -18    | 36 Months                      | Cyproconazole     | EFSA (2010)     |
|                                   | Wheat grain       | -20                            | 26     | Months                        | TA                | EFSA et al. (2018b) |
|                                   | Barley grain      | -20                            | 26     | Months                        | TAA               | EFSA et al. (2018b) |
|                                   | Grapes            | -18                            | 36     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Peanut (oil, soap stock and pressed cake) | -12                            | 27     | Months                        | Cyproconazole     | EFSA (2010)     |
|                                   | Raisins           | -12                            | 42     |                               |                   |                |
### Plant products

| Category          | Commodity                   | T (°C) | Stability period | Compounds covered | Comment/Source       |
|-------------------|-----------------------------|--------|------------------|--------------------|----------------------|
| Others            | Peanut hay, wheat hay       | –12    | 41 Months        | Cyproconazole      | EFSA (2010)          |
|                   | Peanut hulls                | –12    | 39 Months        | Cyproconazole      | EFSA (2010)          |
|                   | Wheat straw                 | –20    | 53 Months        | TAA                | EFSA et al. (2018b)  |
|                   | Barley straw                | –20    | 40 Months        | TA                 | EFSA et al. (2018b)  |
|                   |                              | –20    | 12 Months        | 1,2,4-T            | EFSA et al. (2018b)  |

TA: triazole alanine; TLA: triazole lactic acid; TAA: triazole acetic acid; 1,2,4-T: 1,2,4-triazole.

(а): Stability of residues TA, TAA and 1,2,4-T was investigated in 8 other high-water content commodities, however not relevant in the framework of the current review: apples, tomatoes, mustard leaves, radishes tops/roots, turnips roots, sugar beet roots, cabbage, lettuces (EFSA et al., 2018b).

### B.1.2. Magnitude of residues in plants

Since the present assessment is limited to CXLs, the investigation of the magnitude of residues in plants is not required.

### B.2. Residues in livestock

#### B.2.1. Nature of residues and methods of analysis in livestock

#### B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

| Livestock (available studies) | Animal               | Dose (mg/kg bw/d) | Duration (days) | Comment/Source                                      |
|-------------------------------|----------------------|-------------------|-----------------|------------------------------------------------------|
|                               | Laying hen           | 1                 | 3               | [α-carbon 14C]-cyproconazole (EFSA, 2010)             |
|                               |                      | 114               | 4               | 14C-phenyl ring (EFSA, 2010)                         |
|                               | Lactating ruminants  | 1                 | 12              | [α-carbon 14C]-cyproconazole (EFSA, 2010)             |
|                               | (goat)               | 30                | 3               |                                                      |
|                               |                      | 10                | 4               |                                                      |
|                               | Pig                  | –                 | –               |                                                      |
|                               | Fish                 | –                 | –               |                                                      |
**Review of the existing MRLs for cyproconazole**

| Time needed to reach a plateau concentration in milk and eggs (days) | Milk: 7 days | EFSA (2010) |
|---|---|---|
| Eggs: | Feeding study not available and not required |
| Metabolism in rat and ruminant similar | Yes | EFSA (2010) |
| Can a general residue definition be proposed for animals? | Yes | EFSA (2010) |
| Animal residue definition for monitoring (RD-Mo) | Cyproconazole (sum of isomers) |
| Animal residue definition for risk assessment (RD-RA) | For all animal commodities (EFSA, 2010, 2018b): Cyproconazole (sum of isomers) and the metabolites M36(Z2), M38(Z1) and M9/M14 (pair of diastereomers), expressed as cyproconazole equivalents. For all triazole active substances: • TA and TLA; • TAA; • 1,2,4-T. TA: triazole alanine; TLA: triazole lactic acid; TAA: triazole acetic acid; 1,2,4-T: 1,2,4-triazole |
| Fat soluble residues | Yes |
| LogP_{ow} = 3.09 (EFSA, 2010) |
| Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs) | Milk, eggs, muscle, fat, liver, kidney: HPLC–MS/MS, LOQ 0.01 mg/kg. Confirmatory method available. ILV available (EFSA, 2010) EURLs: multi-residue analytical method with a Screening detection limit (SDL) of 0.005 mg/kg for the routine analysis of cyproconazole (sum of isomers) is available in muscle, milk, eggs and honey (EURLs, 2020). |

bw: body weight; HPLC-MS/MS: high performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification.
B.3. Consumer risk assessment

B.3.1. Consumer risk assessment considering the existing CXLs

| ARfD                                                                 |
|----------------------------------------------------------------------|
| **Cyproconazole:** 0.02 mg/kg bw (European Commission, 2013)         |
| **TA (triazole alanine) and TLA (triazole lactic acid):** 0.3 mg/kg bw (EFSA, 2018b) |
| **TAA (triazole acetic acid):** 1 mg/kg bw (EFSA, 2018b)              |
| **1,2,4-triazole:** 0.1 mg/kg bw (EFSA, 2018b)                        |

Highest IESTI, according to EFSA PRIMO (rev.3.1)

| Cyproconazole: Bovine liver: 56% of ARfD |
|-----------------------------------------|
| **TA and TLA:**                         |
| Milk, cattle: 0.4% of ARfD              |
| Indicative, as residue data available only for maize, soybeans, coffee (for which no study summaries are available) and for animal commodities. |
| **TAA:**                                |
| Milk, cattle: 0.1% of ARfD              |
| Indicative, as residue data available only for maize, soybeans, coffee (for which no study summaries are available) and for animal commodities. |
| **1,2,4-triazole:** no risk assessment performed, and not required. |

NESTI (% ARfD)

| Not assessed in this review. |

Assumptions made for the calculations

**Cyproconazole:**
The calculation is based on the highest residue levels expected in raw agricultural commodities, except for bulk commodities for which the median residue (STMR) was used. The following CF for risk assessment was also applied:
3 – liver (EFSA, 2010)

**TA and TLA, TAA:**
Residue data for metabolite TLA were not available and not required, since residues of TLA are not expected following the metabolism studies.
Residue data for TA and TAA were only available for soybeans, maize and coffee. For animal commodities, residue levels were derived based on feeding studies (JMPR, 2010b). In the absence of residue data for all commodities, and the lack of study summaries, the calculations are considered indicative only. Altogether, the calculation is based on the median residue levels expected in soybeans, maize and coffee and the highest residue levels in animal commodities.

The input values are derived considering the residues of TA and TAA reported in the residue trials following the use of cyproconazole only, noting that residues of TA and TAA could arise from the use of other triazole fungicides not considered in this assessment.
No residue data were available for this metabolite and not required, since according to the metabolic pathway of cyproconazole 1,2,4-T is not relevant. Therefore, the risk assessment to this metabolite was not needed.

It is underlined that a comprehensive risk assessment, including all crops and all pesticides belonging to the class of triazole fungicides has not yet been performed.

| Metabolite       | ADI               | TMDI according to EFSA PRIMo | NTMDI, according to (to be specified) | Highest IEDI, according to EFSA PRIMo (rev.3.1) | NEDI (% ADI) | Assumptions made for the calculations |
|------------------|-------------------|------------------------------|---------------------------------------|-----------------------------------------------|--------------|--------------------------------------|
| Cyproconazole    | 0.02 mg/kg bw per day (European Commission, 2013) | Not assessed in this review. | Not assessed in this review. | Cyproconazole: 6% ADI (Dutch toddler) | Not assessed in this review. | The calculation is based on the median residue levels expected in raw agricultural commodities. The following CF for risk assessment was also applied: 3 – liver (EFSA, 2010) |
| TA and TLA       | 0.3 mg/kg bw per day (EFSA, 2018b) | 0.3% ADI (Dutch toddler) | Indicative, as residue data available only for maize, soybeans, coffee (for which no study summaries are available) and for animal commodities. | TA and TLA: 0.3% ADI (Dutch toddler) | 0.07% ADI (Dutch toddler) | Indicative, as residue data available only for maize, soybeans, coffee (for which no study summaries are available) and for animal commodities. |
| TAA              | 1 mg/kg bw per day (EFSA, 2018b) | 0.07% ADI (Dutch toddler) | | TAA: 0.07% ADI (Dutch toddler) | | |
| 1,2,4-triazole   | 0.023 mg/kg bw per day (EFSA, 2018b) | Not assessed in this review. | Not assessed in this review. | 1,2,4-triazole: no risk assessment performed, and not required. | | |

1,2,4-triazole:
No residue data were available for this metabolite and not required, since according to the metabolic pathway of cyproconazole 1,2,4-T is not relevant. Therefore, the risk assessment to this metabolite was not needed.

ARfD: acute reference dose; bw: body weight; NESTI: national estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; IESTI: international estimated short-term intake; TA: triazole alanine; TLA: triazole lactic acid; TAA: triazole acetic acid; 1,2,4-T: 1,2,4-triazole.
The calculation is based on the median residue levels expected in soybeans, maize, coffee and in animal commodities.

The input values are derived considering the residues of TA and TAA reported in the residue trials following the use of cyproconazole only, noting that residues of TA and TAA could arise from the use of other triazole fungicides not considered in this assessment.

1,2,4-triazole:
No residue data were available for this metabolite and not required, since according to the metabolic pathway of cyproconazole 1,2,4-T is not relevant. Therefore, the risk assessment to this metabolite was not needed.

It is underlined that a comprehensive risk assessment, including all crops and all pesticides belonging to the class of triazole fungicides has not yet been performed.

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003)

Metabolite(s) ................................................................. Not assessed in this review.
ADI (mg/kg bw per day) .................................................. Not assessed in this review.
Intake of groundwater metabolites (% ADI) ..................... Not assessed in this review.

B.4. Proposed MRLs

| Code number | Commodity                  | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL(a) (mg/kg) | Outcome of the review | Comment |
|-------------|----------------------------|-------------------------|---------------------|----------------|-----------------------|---------|
| 260040      | Peas (fresh, without pods) | 0.05*                   | 0.01                | 0.01           | Further consideration needed(b) Data gap # 1 |
| 300010      | Beans (dry)                | 0.08                    | 0.02*               | 0.02           | Further consideration needed(b) Data gap # 1 |
| 300030      | Peas (dry)                 | 0.08                    | 0.02*               | 0.02           | Further consideration needed(b) Data gap # 1 |
| 401060      | Rape seed                  | 0.4                     | 0.4                 | 0.4            | Further consideration needed(b) Data gap # 1 |
| 401070      | Soya bean                  | 0.07                    | 0.07                | 0.07           | Further consideration needed(c) Data gap # 2 |
| 500010      | Barley grain               | 0.2                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 500020      | Buckwheat grain            | 0.1                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 500030      | Maize grain                | 0.1                     | 0.01*               | 0.01*          | Further consideration needed(c) Data gap # 2 |
| 500040      | Millet grain               | 0.1                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 500050      | Oats grain                 | 0.2                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 500070      | Rye grain                  | 0.1                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 500090      | Wheat grain                | 0.1                     | 0.08                | 0.08           | Further consideration needed(b) Data gap # 1 |
| 620000      | Coffee beans               | 0.1                     | 0.07                | 0.07           | Further consideration needed(c) Data gap # 2, 3 |
| 900010      | Sugar beet (root)          | 0.1                     | 0.05                | 0.05           | Further consideration needed(b) Data gap # 1 |

ADI: acceptable daily intake; bw: body weight; NEDI: national estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; TMDI: theoretical maximum daily intake; NTMDI: national theoretical maximum daily intake.
| Code number | Commodity                      | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL<sup>(a)</sup> (mg/kg) | Outcome of the review | Comment |
|-------------|--------------------------------|-------------------------|----------------------|-----------------------------|-----------------------|---------|
| 1011010     | Swine meat                     | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1011020     | Swine fat (free of lean meat)  | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1011030     | Swine liver                    | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1011040     | Swine kidney                   | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1012010     | Bovine meat                    | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1012020     | Bovine fat                     | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1012030     | Bovine liver                   | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1012040     | Bovine kidney                  | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1013010     | Sheep meat                     | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1013020     | Sheep fat                      | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1013030     | Sheep liver                    | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1013040     | Sheep kidney                   | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1014010     | Goat meat                      | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1014020     | Goat fat                       | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1014030     | Goat liver                     | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1014040     | Goat kidney                    | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1015010     | Horse meat                     | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1015020     | Horse fat                      | 0.05*                   | 0.02                 | 0.02                        | Further consideration needed<sup>(d)</sup> |         |
| 1015030     | Horse liver                    | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1015040     | Horse kidney                   | 0.5                     | 0.5                  | 0.5                         | Further consideration needed<sup>(d)</sup> |         |
| 1016010     | Poultry meat                   | 0.05*                   | 0.01*                | 0.01*                       | Further consideration needed<sup>(d)</sup> |         |
| 1016020     | Poultry fat                    | 0.05*                   | 0.01*                | 0.01*                       | Further consideration needed<sup>(d)</sup> |         |
| 1016030     | Poultry liver                  | 0.05*                   | 0.01*                | 0.01*                       | Further consideration needed<sup>(d)</sup> |         |
| 1020010     | Cattle milk                    | 0.05*                   | 0.01                 | 0.01                        | Further consideration needed<sup>(d)</sup> |         |
| 1020020     | Sheep milk                     | 0.05*                   | 0.01                 | 0.01                        | Further consideration needed<sup>(d)</sup> |         |
| 1020030     | Goat milk                      | 0.05*                   | 0.01                 | 0.01                        | Further consideration needed<sup>(d)</sup> |         |
| 1020040     | Horse milk                     | 0.05*                   | 0.01                 | 0.01                        | Further consideration needed<sup>(d)</sup> |         |
| 1030000     | Birds’ eggs                    | 0.05*                   | 0.01*                | 0.01*                       | Further consideration needed<sup>(d)</sup> |         |
| –           | Other commodities of plant and/or animal origin |       |                     |                             | Further consideration needed<sup>(e)</sup> |         |

MRL: maximum residue level; CXL: codex maximum residue limit; (F): The residue definition is fat soluble.

*: Indicates that the MRL is set at the limit of quantification.

(a): The possible impact of the classification of cyproconazole as toxic for reproduction category 1B, in accordance with Regulation (EC) No 1272/2008 on the validity of the MRL proposal was not considered in the assessment.

(b): MRL is derived from the existing CXL based on an EU GAP, which is not fully supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

(c): MRL is derived from the existing CXL, which is not fully supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

(d): MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E). It is noted that cyproconazole is classified as toxic for reproduction category 1B in accordance with Regulation (EC) No 1272/2008.

(e): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
### Appendix C – Pesticide Residue Intake Model (PRIMo)

- **PRIMo cyproconazole**

| Toxicological reference values | ADI (mg/kg bw per day) | ARfD (mg/kg bw) |
|--------------------------------|------------------------|-----------------|
| Source                          | EC                     | EC              |

**LOQs (mg/kg) range from:** 0.01 to 0.02

**MS Diet**

| Exposure resulting from ADI (%) | Highest contributor to MS diet (in % of ADI) | 2nd contributor to MS diet (in % of ADI) | 3rd contributor to MS diet (in % of ADI) |
|---------------------------------|---------------------------------------------|-----------------------------------------|-----------------------------------------|
| Sugar beet roots                | 6%                                          | 3%                                       | 0.7%                                     |
| Wheat                           | 3%                                          | 3%                                       | 0.3%                                     |
| Bovine: Liver                   | 3%                                          | 3%                                       | 0.2%                                     |
| Sugar beet roots                | 2%                                          | 2%                                       | 0.4%                                     |
| Sugar beet roots                | 2%                                          | 2%                                       | 0.4%                                     |
| Wheat                           | 2%                                          | 2%                                       | 0.6%                                     |
| Milk: Cattle                    | 2%                                          | 2%                                       | 0.6%                                     |
| Rye                             | 2%                                          | 2%                                       | 0.4%                                     |
| Beans                           | 2%                                          | 2%                                       | 0.3%                                     |
| Maize/corn                      | 1%                                          | 1%                                       | 0.6%                                     |
| Soyabeans                       | 1%                                          | 1%                                       | 0.6%                                     |
| Swine: Liver                    | 1%                                          | 1%                                       | 0.4%                                     |
| Bovine: Muscle/meat             | 0.8%                                        | 0.8%                                     | 0.2%                                     |
| Sugar beet roots                | 0.7%                                        | 0.7%                                     | 0.0%                                     |
| Barley                          | 0.7%                                        | 0.7%                                     | 0.0%                                     |
| Wheat                           | 0.7%                                        | 0.7%                                     | 0.0%                                     |
| Peas (without pods)             | 0.6%                                        | 0.6%                                     | 0.0%                                     |
| Swine: Liver                    | 0.5%                                        | 0.5%                                     | 0.0%                                     |
| Soyabeans                       | 0.5%                                        | 0.5%                                     | 0.0%                                     |
| Sugar beet roots                | 0.5%                                        | 0.5%                                     | 0.0%                                     |
| Sugar beet roots                | 0.4%                                        | 0.4%                                     | 0.0%                                     |
| Oat                             | 0.3%                                        | 0.3%                                     | 0.0%                                     |
| Sheep                           | 0.0%                                        | 0.0%                                     | 0.0%                                     |

**Chronic risk assessment:**

- **JMPR methodology (IEDI/TMDI)**

**Conclusion:**

- UK vegetarian
- UK adult
- IE child
- FR toddler 2-3 yr
- FR child 3-15 yr
- DK child
- NL toddler
- UK infant
- FR adult
- SE general
- FI adult
- IT toddler
- DK adult
- LT adult
- PT general
- GEMS/Food G07
- GEMS/Food G10
- GEMS/Food G11

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Cyproconazole is unlikely to present a public health concern.
The acute risk assessment is based on the ARfD.
The calculation is based on the large portion of the most critical consumer group.

### Results for Children

| Commodity | MRL/input (mg/kg) | Exposure (µg/kg bw) | Percentage of ARfD/ADI |
|-----------|-------------------|---------------------|------------------------|
| Bovine: Liver | 0.5/1.38 | 1.38 | 28% |
| Bovine: Kidney | 0.5/1.38 | 1.38 | 19% |
| Sheep: Liver | 0.5/1.38 | 1.38 | 8% |
| Bovine: Edible offals (other than liver and kidney) | 0.5/0.46 | 0.46 | 7% |
| Swine: Kidney | 0.5/1.38 | 1.38 | 5% |
| Bovine: Edible offals (other than liver and kidney) | 0.5/0.46 | 0.46 | 4% |
| Milk: Cow | 0.01/0.01 | 0.01 | 1% |
| Bovine: Edible offals (other than liver and kidney) | 0.5/0.46 | 0.46 | 0.6% |
| Milk: Cattle | 0.01/0.01 | 0.01 | 0.4% |
| Sugar beets (root)/sugar | 0.05/0.24 | 0.24 | 11% |
| Maize/oil | 0.01/0.5 | 0.5 | 2% |
| Wheat/milling (flour) | 0.08/0.02 | 0.02 | 1% |
| Peas/canned | 0.02/0.01 | 0.01 | 0.7% |
| Wheat/milling (wholemeal)–baking | 0.08/0.02 | 0.02 | 0.3% |
| Buckwheat/bulgur and grits | 0.08/0.02 | 0.02 | 0.3% |
| Barley/cooked | 0.08/0.02 | 0.02 | 0.3% |
| Rye/milling (wholemeal)–baking | 0.08/0.02 | 0.02 | 0.3% |
| Oat/milling (flakes) | 0.08/0.02 | 0.02 | 0.3% |

### Results for Adults

| Commodity | MRL/input (mg/kg) | Exposure (µg/kg bw) | Percentage of ARfD/ADI |
|-----------|-------------------|---------------------|------------------------|
| Sheep: Liver | 0.5/1.38 | 1.38 | 28% |
| Swine: Liver | 0.5/1.38 | 1.38 | 19% |
| Sheep: Edible offals (other than liver and kidney) | 0.5/1.38 | 1.38 | 8% |
| Swine: Kidney | 0.5/1.38 | 1.38 | 5% |
| Sheep: Edible offals (other than liver and kidney) | 0.5/1.38 | 1.38 | 4% |
| Milk: Goat | 0.01/0.01 | 0.01 | 1% |
| Poultry: Muscle/meat | 0.01/0.01 | 0.01 | 0.6% |
| Maize/oil | 0.01/0.5 | 0.5 | 2% |
| Wheat/milling (flour) | 0.08/0.02 | 0.02 | 1% |
| Peas/canned | 0.02/0.01 | 0.01 | 0.3% |
| Poultry: Muscle/meat | 0.01/0.01 | 0.01 | 0.3% |
| Thoughts | 0.02/0.02 | 0.02 | 0.4% |
| Poultry: Muscle/meat | 0.01/0.01 | 0.01 | 0.3% |

### Conclusion

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of Cyproconazole is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
Review of the existing MRLs for cyproconazole

**TA (cyproconazole)**

| Commodity | Group | Diet | LOQs (mg/kg) range from: to: |
|-----------|-------|------|-----------------------------|
| Bovine: Muscle/meat | 0.1% | 0.0% | oily fish 
| Bovine: Muscle/meat | 0.1% | 0.0% | olive oil 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: Cattle 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: goat 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: Sheep 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: goat 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: Sheep 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: camel 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: buffalo 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: yak 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: camel 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: buffalo 
| Bovine: Muscle/meat | 0.1% | 0.0% | milk: yak 
| Bovine: Liver | 0.1% | 0.0% | oily fish 
| Bovine: Liver | 0.1% | 0.0% | olive oil 
| Bovine: Liver | 0.1% | 0.0% | milk: Cattle 
| Bovine: Liver | 0.1% | 0.0% | milk: goat 
| Bovine: Liver | 0.1% | 0.0% | milk: Sheep 
| Bovine: Liver | 0.1% | 0.0% | milk: goat 
| Bovine: Liver | 0.1% | 0.0% | milk: Sheep 
| Bovine: Liver | 0.1% | 0.0% | milk: camel 
| Bovine: Liver | 0.1% | 0.0% | milk: buffalo 
| Bovine: Liver | 0.1% | 0.0% | milk: yak 
| Bovine: Liver | 0.1% | 0.0% | milk: camel 
| Bovine: Liver | 0.1% | 0.0% | milk: buffalo 
| Bovine: Liver | 0.1% | 0.0% | milk: yak 
| Sheep: Liver | 0.1% | 0.0% | oily fish 
| Sheep: Liver | 0.1% | 0.0% | olive oil 
| Sheep: Liver | 0.1% | 0.0% | milk: Cattle 
| Sheep: Liver | 0.1% | 0.0% | milk: goat 
| Sheep: Liver | 0.1% | 0.0% | milk: Sheep 
| Sheep: Liver | 0.1% | 0.0% | milk: goat 
| Sheep: Liver | 0.1% | 0.0% | milk: Sheep 
| Sheep: Liver | 0.1% | 0.0% | milk: camel 
| Sheep: Liver | 0.1% | 0.0% | milk: buffalo 
| Sheep: Liver | 0.1% | 0.0% | milk: yak 
| Sheep: Liver | 0.1% | 0.0% | milk: camel 
| Sheep: Liver | 0.1% | 0.0% | milk: buffalo 
| Sheep: Liver | 0.1% | 0.0% | milk: yak 
| Bovine: Muscle/meat | 0.0% | 0.0% | oily fish 
| Bovine: Muscle/meat | 0.0% | 0.0% | olive oil 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: Cattle 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: goat 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: Sheep 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: goat 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: Sheep 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: camel 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: buffalo 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: yak 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: camel 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: buffalo 
| Bovine: Muscle/meat | 0.0% | 0.0% | milk: yak 
| Sheep: Liver | 0.0% | 0.0% | oily fish 
| Sheep: Liver | 0.0% | 0.0% | olive oil 
| Sheep: Liver | 0.0% | 0.0% | milk: Cattle 
| Sheep: Liver | 0.0% | 0.0% | milk: goat 
| Sheep: Liver | 0.0% | 0.0% | milk: Sheep 
| Sheep: Liver | 0.0% | 0.0% | milk: goat 
| Sheep: Liver | 0.0% | 0.0% | milk: Sheep 
| Sheep: Liver | 0.0% | 0.0% | milk: camel 
| Sheep: Liver | 0.0% | 0.0% | milk: buffalo 
| Sheep: Liver | 0.0% | 0.0% | milk: yak 
| Sheep: Liver | 0.0% | 0.0% | milk: camel 
| Sheep: Liver | 0.0% | 0.0% | milk: buffalo 
| Sheep: Liver | 0.0% | 0.0% | milk: yak 

**Conclusion:**

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of TA (cyproconazole) is unlikely to present a public health concern.
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Show results for all crops

| Commodity | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodity | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI |
|-----------|--------------------------|---------------------|-----------------------|-----------|--------------------------|---------------------|-----------------------|
| 0.1% Milk: Cattle | 0.04 | 0.32 | 0.1% Milk: Goat | 0.01 | 0.18 |
| 0.10% Bovine: Edible offals (other than liver and kidney) | 0.04 | 0.29 | 0.05% Bovine: Liver | 0.06 | 0.16 |
| 0.08% Maize/corn | 0.04 | 0.27 | 0.05% Milk: Sheep | 0.01 | 0.15 |
| 0.09% Bovine: Kidney | 0.01 | 0.24 | 0.04% Bovine: Edible offals (other than liver and kidney) | 0.06 | 0.13 |
| 0.05% Swine: Edible offals (other than liver and kidney) | 0.04 | 0.13 | 0.04% Swine: Liver | 0.04 | 0.11 |
| 0.05% Bovine: Muscle/meat | 0.01 | 0.07 | 0.03% Swine: Edible offals (other than liver and kidney) | 0.04 | 0.10 |
| 0.05% Other farmed animals: Muscle/meat | 0.01 | 0.07 | 0.02% Maize/corn | 0.06 | 0.09 |
| 0.05% Equine: Muscle/meat | 0.01 | 0.06 | 0.02% Maize | 0.04 | 0.08 |
| 0.05% Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.05 | 0.02% Swine: Liver | 0.04 | 0.06 |
| 0.02% Swine: Edible offals (other than liver and kidney) | 0.01 | 0.04 | 0.02% Other farmed animals: Muscle/meat | 0.01 | 0.06 |
| 0.01% Bovine: Muscle/meat | 0.01 | 0.04 | 0.02% Maize | 0.04 | 0.05 |
| 0.01% Milk: Sheep | 0.01 | 0.04 | 0.02% Sheep | 0.05 | 0.05 |

### Results for children

- **No exceedance of the toxicological reference value was identified for any unprocessed commodity.**
- A short term intake of residues of TA (cyproconazole) is unlikely to present a public health risk.
- **For processed commodities, no exceedance of the ARfD/ADI was identified.**

### Results for adults

- **No exceedance of the toxicological reference value was identified for any unprocessed commodity.**
- **For processed commodities, no exceedance of the ARfD/ADI was identified.**

### Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

| Commodity | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI |
|-----------|--------------------------|---------------------|-----------------------|
| 0.3% Maize | 0.01 | 0.53 | 0.2% Maize | 0.01 | 0.51 |
| 0.0% Maize (processed, not specified) | 0.04 | 0.09 | 0.06% Coffee/infusions | 0.06 | 0.19 |
| 0.0% Soybean/wine | 0.02 | 0.06 | 0.03% Coffee | 0.01 | 0.03 |
| 0.0% Soybean/beer | 0.01 | 0.03 | 0.02% Coffee/boiled | 0.01 | 0.01 |

### Conclusion

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of TA (cyproconazole) is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
### Input values

#### TAA (cyproconazole)

- **LOQs (mg/kg)** range from: to:

### Toxicological values

- **ADI (mg/kg bw per day):**
- **ARfD (mg/kg bw):**

### Toxicological reference values

- **Toxicological reference values assessment:**
- **Chronic risk assessment:**
- **Acute risk assessment**

#### Source of ADI:

- **Source of ARfD:**

#### Year of evaluation:

- **EFSA PRIMo revision 3.1; 2019/03/19**

### Comments

- **Normal mode**

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### Chronic risk assessment: JMPR methodology (IEDI/TMDI)

| Commodity/group of commodities | Calculated exposure calculated (in % of ADI) | Chronic risk assessment: JMPR methodology (IEDI/TMDI) |
|-------------------------------|---------------------------------------------|-------------------------------------------------------|
| Maize/corn                    | 0.069%                                      | No of diets exceeding the ADI: –––                  |
| Coffee beans                  | 0.00%                                      | Exposure resulting from commodities not under assessment |
| Maize/corn                    | 0.32%                                      | Highest contributor to MS diet (in % of ADI)          |
| Coffee beans                  | 0.27%                                      | 2nd contributor to MS diet (in % of ADI)              |
| Maize/corn                    | 0.21%                                      | 3rd contributor to MS diet (in % of ADI)              |
| Coffee beans                  | 0.18%                                      | Calculated exposure |
The acute risk assessment is based on the ARfD. The calculation is based on the large portion of the most critical consumer group.

### Show results for all crops

| Commodity | MRL/Input (mg/kg) | Exposure (µg/kg bw) | Commodity | MRL/Input (mg/kg) | Exposure (µg/kg bw) |
|-----------|-------------------|---------------------|-----------|-------------------|---------------------|
| Milk: Goat | 0.01 | 0.24 | Milk: Cow | 0.00 | 0.18 |
| Swine: Muscle/meat | 0.01 | 0.12 | Bovine: Muscle | 0.00 | 0.06 |
| Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.07 | Sheep: Liver | 0.00 | 0.06 |
| Bovine: Muscle/meat | 0.01 | 0.07 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.06 |
| Milk: Sheep | 0.01 | 0.04 | Bovine: Kidney | 0.00 | 0.04 |
| Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.03 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.03 |
| Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.02 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.02 |
| Bovine: Muscle/meat | 0.01 | 0.02 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.02 |
| Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.02 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.02 |
| Bovine: Edible offals (other than liver and kidney) | 0.01 | 0.02 | Sheep: Edible offals (other than liver and kidney) | 0.00 | 0.02 |

No exceedance of the toxicological reference value was identified for any unprocessed commodity.

A short term intake of residues of TAA (cyproconazole) is unlikely to present a public health risk.

For processed commodities, no exceedance of the ARfD/ADI was identified.

### Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of TAA (cyproconazole) is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
Appendix D – Input values for the exposure calculations

D.1. Consumer risk assessment considering the existing CXLs

| Commodity | Chronic risk assessment | Acute risk assessment |
|-----------|-------------------------|-----------------------|
|           | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
|           |                         |                       |                     |                       |
| Risk assessment residue definition 1 (plants): cyproconazole | | | | |
| Peas (without pods) | 0.01 STMR (CXL) | 0.01 HR (CXL) | | |
| Beans (dry) | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Peas (dry) | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Rape seeds/canola seeds | 0.065 STMR (CXL) | 0.065 STMR (CXL) | | |
| Soybeans | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Barley | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Buckwheat and other pseudo-cereals | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Maize/corn | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Common millet/proso millet | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Oat | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Rye | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Wheat | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Coffee beans | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Sugar beet roots | 0.02 STMR (CXL) | 0.02 STMR (CXL) | | |
| Risk assessment residue definition 2 (animals): cyproconazole (sum of isomers), metabolites M36(Z2), M38(Z1) and M9/M14 (pair of diastereomers), expressed as cyproconazole | | | | |
| Swine, bovine, equine, sheep and goat meat | 0.003 \(0.8 \times \text{STMR (CXL)}\) muscle + 0.2 \(\times \text{STMR (CXL)}\) fat | 0.003 \(0.8 \times \text{HR (CXL)}\) muscle + 0.2 \(\times \text{HR (CXL)}\) fat | | |
| Swine, bovine, equine, sheep and goat fat | 0.003 STMR (CXL) | 0.02 HR (CXL) | | |
| Swine, bovine, equine, sheep and goat liver | 0.42 STMR_{90\%} (CXL) \times CF (3) | 1.38 HR_{90\%} (CXL) \times CF (3) | | |
| Swine, bovine, equine, sheep and goat kidney | 0.14 STMR (CXL) | 0.46 HR (CXL) | | |
| Poultry meat | 0.01* \(0.9 \times \text{STMR (CXL)}\) muscle + 0.1 \(\times \text{STMR (CXL)}\) fat | 0.01* \(0.9 \times \text{HR (CXL)}\) muscle + 0.1 \(\times \text{HR (CXL)}\) fat | | |
| Poultry fat | 0.01* STMR (CXL) | 0.01* HR (CXL) | | |
| Poultry liver | 0.01* STMR (CXL) | 0.01* HR (CXL) | | |
| Milk | 0.01* STMR (CXL) | 0.01* STMR (CXL) | | |
| Commodity | Chronic risk assessment | Acute risk assessment |
|-----------|------------------------|----------------------|
|           | Input value (mg/kg)    | Comment              | Input value (mg/kg) | Comment |
| Birds eggs| 0.01*                  | STMR (CXL)           | 0.01*              | HR (CXL) |
| Soybeans  | 0.02                   | STMR (CXL) (Ireland, 2020) | 0.02          | STMR (CXL) (Ireland, 2020) |
| Maize     | 0.04                   | STMR (CXL) (Ireland, 2020) | 0.04          | STMR (CXL) (Ireland, 2020) |
| Coffee    | 0.04                   | STMR (CXL) (Ireland, 2020) | 0.04          | STMR (CXL) (Ireland, 2020) |
| Peas (without pods), beans (dry), pea(dry), rape seeds, barley, buckwheat, millet, oat, rye, wheat, sugar beet roots | – | CXL, TDMs not reported | – | CXL, TDMs not reported |
| Swine, bovine, equine, sheep and goat liver | 0.03 | STMR (CXL) (JMPR, 2010b) | 0.04 | HR (CXL) (JMPR, 2010b) |
| Swine, bovine, equine, sheep and goat meat, fat, kidney, milk | 0.01* | LOQ (CXL) (JMPR, 2010b) | 0.01* | LOQ (CXL) (JMPR, 2010b) |
| Soybeans  | 0.01*                  | STMR (CXL) (Ireland, 2020) | 0.01*          | STMR (CXL) (Ireland, 2020) |
| Maize     | 0.01*                  | STMR (CXL) (Ireland, 2020) | 0.01*          | STMR (CXL) (Ireland, 2020) |
| Coffee    | 0.01*                  | STMR (CXL) (Ireland, 2020) | 0.01*          | STMR (CXL) (Ireland, 2020) |
| Peas (without pods), beans (dry), pea(dry), rape seeds, barley, buckwheat, millet, oat, rye, wheat, sugar beet roots | – | CXL, TDMs not reported | – | CXL, TDMs not reported |
| Swine, bovine, equine, sheep and goat meat, fat, liver, kidney, milk | 0.01* | LOQ (CXL) (FAO, 2010b) | 0.01* | LOQ (CXL) (FAO, 2010b) |

Risk assessment residue definition 3: triazole alanine (TA)

Risk assessment residue definition 4: triazole acetic acid (TAA)

STMR: supervised trials median residue; CXL: codex maximum residue limit; HR: highest residue; LOQ: limit of quantification; TDMs: triazole derivative metabolites.

*: Indicates that the input value is proposed at the limit of quantification.
Appendix E – Decision tree for deriving MRL recommendations

1. **Result EU assessment**
   - **CXL available?**
     - Yes
       - **RD comparable?**
         - Yes
           - **CXL higher?**
             - Yes
               - **CXL is recommended; EU recommendation is covered as well.**
             - No
               - **CXL is included in the RA.**
                 - **Risk identified?**
                   - Yes
                     - **Codex median/highest residues are included in the RA.**
                   - No
                     - **CXL supported by data?**
                       - Yes
                         - **CXL is recommended; EU recommendation is covered as well.**
                       - No
                         - **Input values for the RA remain unchanged.**
                   - **No**
                     - **Input values for the RA remain unchanged.**
2. **Input values for the RA remain unchanged.**
   - **Yes**
     - **CXL higher?**
       - Yes
         - **Maintain EU recommendation; higher CXL is not safe for consumer.**
       - No
         - **Input values for the RA remain unchanged.**
   - **No**
     - **Input values for the RA remain unchanged.**
3. **CXL supported by data?**
   - Yes
     - **CXL is included in the RA.**
       - **Risk identified?**
         - Yes
           - **Codex median/highest residues are included in the RA.**
         - No
           - **CXL is recommended; EU recommendation is covered as well.**
     - **No**
       - **CXL supported by data?**
         - Yes
           - **CXL is included in the RA.**
             - **Risk identified?**
               - Yes
                 - **Codex median/highest residues are included in the RA.**
               - No
                 - **CXL is recommended; EU recommendation is covered as well.**
             - **No**
               - **CXL higher?**
                 - Yes
                   - **Maintain EU recommendation; higher CXL is not safe for consumer.**
                 - No
                   - **Maintain EU recommendation; higher CXL is not safe for consumer.**
               - No
                 - **Maintain EU recommendation; higher CXL is not safe for consumer.**
4. **Input values for the RA remain unchanged.**
   - **Yes**
     - **CXL higher?**
       - Yes
         - **Maintain EU recommendation; higher CXL is not safe for consumer.**
       - No
         - **Input values for the RA remain unchanged.**
   - **No**
     - **Input values for the RA remain unchanged.**

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*References:*
- EFSA Journal 2021;19(3):6483
Review of the existing MRLs for cyproconazole

Evaluation of the GAPs and available residues data at EU level

- GAP or QM > 0.1 mg/kg in EU?
  - Yes
  - No
  - MRL and RA derived in Section 3?
    - Yes
    - No
    - MRL fully supported by data?
      - Yes
      - No

Consumer risk assessment for GAPs evaluated at EU level – EU scenarios

- Not considered for the RA?
  - Yes
  - No

- Current EU MRL is included in the RA?
  - Yes
  - No

- Tentative median/highest values are included in the RA?
  - Yes
  - No

- Median/highest values are included in the RA?
  - Yes
  - No

- Risk identified?
  - Yes
  - No

- Fall-back MRL available?
  - Yes
  - No

Recommendations resulting from EU authorisations and import tolerances

- Specific LOQ or default MRL?
  - Yes
  - No

(A) Specific LOQ or default MRL?
(B) Specific LOQ or default MRL?
(C) Maintain current EU MRL?
(D) Specific LOQ or default MRL?
(E) Establish tentative EU MRL?
(F) Specific LOQ or default MRL?
(G) Specific LOQ or default MRL?
(H) MRL is recommended.
# Appendix F – Used compound codes

| Code/Trivial name(a) | Chemical name(b) | Structural formula(c) |
|----------------------|------------------|-----------------------|
| Cyproconazole        | (2RS,3RS;2RS,3SR)-2-[(4-chlorophenyl)-3-cyclopropyl-1-(1H-1,2,4-triazol-1-yl)]butan-2-ol | ![Structural formula](image1) |
|                      | OC(C)n1cncn1)(C)(C)C1CC1)c1cccc(Cl)cc1 | UFNOUKDBUJZYDE-UHFFFAOYSA-N |
|                      | MW: 291.8 g/mol |                       |
| M9/M14, pair of diastereoisomers (NOA 421153) | 2-[(4-chlorophenyl)-3-cyclopropyl-1-(1H-1,2,4-triazol-1-yl)-2,3-butanediol | ![Structural formula](image2) |
|                      | OC(C)n1cncn1)(C1cccc(Cl)cc1)C(C)(O)C1CC1 | NUFIGFDCSFQXRE-UHFFFAOYSA-N |
| M36(Z2) (NOA 405872) | 5-[(4-chlorophenyl)-3,5-dihydroxy-4-methyl-6-[1,2,4]triazol-1-yl-hexanoic acid | ![Structural formula](image3) |
|                      | OC(C)n1cncn1)(C)(C)C(O)CC(=O)O)c1cccc(Cl)cc1 | ALRYPOALP0JWSE-UHFFFAOYSA-N |
| M38(Z1) (NOA 421155) | 1-[(E)-2-[(4-chlorophenyl)-3-cyclopropyl-but-1-enyl]-1H-[1,2,4]triazole | ![Structural formula](image4) |
|                      | Clc1cccc(cc1)(C(-C/n1cncn1)/C(C)C1CC1 | YLJOHDOQKIQZGS-OVCLIPMQSA-N |

## Triazole derivative metabolites

| Metabolite                | IUPAC Name | Structure |
|---------------------------|------------|-----------|
| 1,2,4-triazole            | 1H-1,2,4-triazole | ![Structure](image5) |
| 1,2,4-T                   | c1ncnn1    | NSPMIYGKQ1PBQR-UHFFFAOYSA-N |
| Triazole alanine TA       | 3-(1H-1,2,4-triazol-1-yl)-D,L-alanine | ![Structure](image6) |
| Triazole acetic acid TAA  | 1H-1,2,4-triazol-1-ylacetic acid | ![Structure](image7) |
| Triazole lactic acid      | 1H-1,2,4-triazol-1-ylactic acid | ![Structure](image8) |
| Triazole hydroxy propionic acid | (2RS)-2-hydroxy-3-(1H-1,2,4-triazol-1-yl)propanoic acid | ![Structure](image9) |

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(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).
(c): ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version C05H41, Build 111302, 27 August 2019).