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Modification of the existing maximum residue levels for difenoconazole in wheat and rye

European Food Safety Authority (EFSA),
Giulia Bellisai, Giovanni Bernasconi, Luis Carrasco Cabrera, Irene Castellan, Monica del Aguila, Lucien Ferreira, German Giner Santonja, Luna Greco, Samira Jarrah, Renata Leuschner, Javier Martinez Perez, Ileana Miron, Stefanie Nave, Ragnor Pedersen, Hermine Reich, Silvia Ruocco, Miguel Santos, Alessia Pia Scarlato, Anne Theobald, Manuela Tiramani and Alessia Verani

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Syngenta Crop Protection AG submitted an application to the competent national authority in Germany (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance difenoconazole in wheat and rye grain. The data submitted in support of the request were found sufficient to derive MRL proposals for wheat and rye grain. Adequate analytical methods for enforcement are available to control the residues of difenoconazole in plant matrices under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. The submitted data indicate no need to modify the EU MRLs in animal commodities for the existing enforcement residue definition. EFSA concluded that the dietary exposure to difenoconazole residues from the intake of wheat and rye grain is low, noting that the impact of intended uses on the residues in animal commodities and the consumer exposure could not be properly addressed. Overall, the present risk assessment confirms a very narrow margin of safety for the overall chronic exposure and is considered provisional, pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and the impact of isomerisation on the toxicity of difenoconazole. The assessment is also affected by uncertainties related to the toxicological profile of animal metabolite CGA205375 and, additionally, it does not take into consideration triazole derivative metabolites (TDMs).

Keywords: difenoconazole, wheat, rye, pesticide, TDMs, MRL, consumer risk assessment

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Correspondence: pesticides.mrl@efsa.europa.eu

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta Crop Protection AG submitted an application to the competent national authority in Germany (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance difenoconazole in wheat and rye grain. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 7 February 2023. To accommodate for the intended uses of difenoconazole on wheat and rye in NEU and SEU, the EMS proposed to raise the existing MRLs in wheat and rye grain from 0.1 to 0.3 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified points that needed further clarification, which were requested from the EMS. On 5 April 2023, EFSA received a statement from the applicant requesting to restart the assessment, providing information that confirmatory data on the isomerisation of difenoconazole have been made available for the renewal of the approval of difenoconazole and will not be provided for the present assessment since data requirement related to the isomerisation of difenoconazole according to EFSA guidance on the risk assessments of active substances that have stereoisomers are not applicable for the present MRL application. In response to additional minor data clarification request the EMS submitted a revised evaluation report, which replaced the previously submitted evaluation report.

EFSA emphasises that the present assessment does not take into consideration triazole derivative metabolites (TDMs), which are generated by difenoconazole and by several other pesticides belonging to the group of triazole fungicides. It is noted that in June 2019, the Standing Committee on Plants, Animals, Food and Feed (Pesticide residues) endorsed the EFSA recommendation to perform a separate risk assessment for TDMs and to apply the clock-stop mechanism in case data are missing that are needed to perform a comprehensive assessment for the TDMs. Risk managers agreed that such comprehensive risk assessment should be conducted for applications submitted from September 2019 onwards. As the present application was submitted before September 2019 the risk assessment for TDMs was not performed.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under previous MRL assessments and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of difenoconazole following foliar applications was investigated in crops belonging to the groups of fruit crops, cereals/grass, root crops and pulses/oilseeds. Difenoconazole and TDMs were main metabolites in all plants. In rotational crops, the major residues identified in cereal/grasses, leafy and root crops were the parent compound, difenoconazole alcohol (CGA205375) and triazole metabolites. Studies investigating the effect of processing on the nature of difenoconazole (hydrolysis studies) demonstrated that difenoconazole is hydrolytically stable.

Based on the metabolic pattern identified in metabolism studies and considering the results of hydrolysis studies, the residue definitions for plant products were proposed as difenoconazole for enforcement and risk assessment and, additionally, TDMs for the risk assessment. These residue definitions are applicable to primary crops, rotational crops and processed products.

EFSA concluded that for the crops assessed in this application, the metabolism of difenoconazole in primary and rotational crops, and the possible degradation in processed products have been sufficiently addressed and that the previously derived residue definitions are applicable. During the peer review a data gap on information investigating the possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants was identified and it is still open. The applicant informed that this data gap will be addressed in the framework of the renewal of the approval of difenoconazole.

Sufficiently validated analytical methods based on high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) are available to quantify residues in the crops assessed in this application according to the residue definition for enforcement. The methods enable the quantification of residues at or above the limit of quantification (LOQ) of 0.01 mg/kg in the crops under assessment.

The available residue trials are sufficient to derive an MRL proposal of 0.3 mg/kg for difenoconazole in wheat and rye grain. The applicant has also provided data on the magnitude of TDMs in wheat and rye grain from the intended use of difenoconazole. These data have been compiled in the present assessment for completeness purposes.

Processing studies investigating the effect of processing on the magnitude of difenoconazole residues in processed commodities of wheat and rye were not submitted for the present assessment. Since the individual exposure to residues from the intake of wheat and rye grain is below 1% of the acceptable daily intake (ADI), the submission of processing studies is of low practical relevance. A narrow margin of safety, however, is noted for the overall chronic consumer exposure.

The occurrence of difenoconazole residues in rotational crops was investigated in the framework of the EU pesticides peer review, which noted some limitations of the available studies regarding the magnitude of TDMs in rotational crops. EFSA concludes that for the intended use on wheat and rye, significant residues of difenoconazole and CGA205375 in rotational crops are not expected, provided that the active substance is applied according to the proposed Good Agricultural Practice (GAP). Regarding triazole metabolites, the data are currently not sufficient to conclude on the magnitude of TDMs in rotational crops. These conclusions might be subject to revision following the outcome of the renewal of the approval of difenoconazole.

Wheat and rye grain, straw and various processing by-products might be used as feed products and therefore a potential carry-over of difenoconazole residues into food of animal origin should be assessed. The calculated livestock dietary burden exceeded the trigger value of 0.1 mg/kg dry matter (DM) for all relevant animal species and residues in wheat straw were the main contributors in the diet of poultry, slightly exceeding the dietary burdens calculated by EFSA (2017). Nevertheless, the calculated exposure for all species, except poultry and sheep, is lower than estimated in previous EFSA outputs which did not propose a modification of existing EU MRLs in animal commodities due to divergent residue definitions implemented in the MRL legislation ('difenoconazole') and derived by the EU pesticides peer review ('alcohol (CGA-205375) expressed as difenoconazole'). It is also noted that pending the review of the existing difenoconazole EU MRLs according to Article 12 of Regulation 396/2005, the calculated dietary burdens are only indicative, may be overestimated and not reflecting the existing authorised GAPs. It is also noted that the existing EU MRLs for animal products are based on the implementation of Codex MRLs in the EU legislation from the 2010 JMPR evaluation and these MRLs cover the residue definition 'sum of difenoconazole and CGA205375, expressed as difenoconazole'. Considering the above mentioned, EFSA is of the opinion that, at the current stage, the modification of the existing EU MRLs for difenoconazole on the basis of new intended uses of difenoconazole on wheat and rye cannot be completed. The revision of MRLs in animal commodities will be undertaken under the Article 12 of the Regulation 396/2005, considering the conclusions of the renewal of the approval of difenoconazole which is currently ongoing.

The toxicological profile of difenoconazole was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.01 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.16 mg/kg bw. For the metabolite CGA205375, which is the risk assessment residue definition for commodities of animal origin, no toxicological reference values were derived in the EU pesticides peer review and no conclusions on its toxicity were derived. The toxicological profile of this metabolite is being assessed in the framework of the renewal of the approval process of difenoconazole which is currently ongoing. Depending on the outcome of this assessment, the conclusions derived in the previous and present opinions on the consumer risk assessment might need to be revised.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The short-term exposure assessment was performed only for wheat and rye grain and did not indicate short-term intake concerns.

The most recent long-term consumer exposure was calculated in the previous EFSA output on the modification of the existing MRLs for difenoconazole in leafy brassica: the MRL proposals derived in this reasoned opinion were not implemented in the MRL legislation due to consumer exposure concerns and therefore are not taken into account for the present assessment. The long-term exposure assessment, which was performed by EFSA (2018a,b,c) in the framework of the modification of existing MRLs for difenoconazole in various crops, has been now updated with the risk assessment values derived for wheat and rye from the residue trials submitted in the present assessment. The estimated long-term dietary exposure accounted for a maximum of 98% of the ADI (NL toddler diet). The contribution of residues in wheat and rye accounted for 0.72% and 0.55% of the ADI, respectively.

EFSA concluded that the dietary exposure to difenoconazole residues from the intake of wheat and rye grain is low, noting that the impact of intended uses on the residue levels in animal commodities and the consumer exposure could not be properly addressed. Overall, the present risk assessment confirms a very narrow margin of safety for the overall chronic exposure and is considered provisional

pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and its impact on the toxicity of difenoconazole. The assessment is also affected by uncertainties related to the toxicological profile of animal metabolite CGA205375 and, additionally, it does not take into consideration TDMs.

EFSA proposes to amend the existing MRL as reported in the summary table below.

Full details of all end points and the consumer risk assessment can be found in Appendices B–D.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Difenoconazole				
0500070	Rye	0.1	0.3 (further risk management consideration required)	The submitted data are sufficient to derive an MRL proposal for the intended NEU/SEU use. The dietary exposure to difenoconazole residues from the intended uses on wheat and rye is low, noting that the impact of the intended uses on the residue levels in animal commodities and the consumer exposure could not be properly assessed. A very narrow margin of safety is noted for the overall chronic exposure which is considered provisional pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and the impact of isomerisation on the toxicity of difenoconazole. The consumer exposure assessment is also affected by uncertainties associated with the toxicity of animal metabolite CGA205375 and, additionally, it does not take into consideration triazole derivative metabolites (TDMs).
0500090	Wheat	0.1		

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe; GAP: Good Agricultural Practice.
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

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Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue level (MRL) for difenoconazole in wheat and rye grain. The detailed description of the intended NEU and SEU uses of difenoconazole which are the basis for the current MRL application, is reported in Appendix A.

Difenoconazole is the ISO common name for 3-chloro-4-[(2*RS*,4*RS*;2*RS*,4*SR*)-4-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Difenoconazole was evaluated in the framework of Directive 91/414/EEC[1] with Sweden designated as rapporteur Member State (RMS) for the representative uses as foliar applications on pome fruits and carrots and as seed treatment on cereals. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2011a). Difenoconazole was approved[2] for the use as a fungicide on 1 January 2009. The confirmatory data requirements according to Commission Implementing Regulation (EU) No 1100/2011[3] which are of relevance for the Article 10 MRL applications refer to the submission of data on (a) residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops, processed commodities and commodities of animal origin and (b) the possible impact of the variable isomerisation in the technical material and of the preferential degradation and/or conversion of the mixture of isomers on the worker risk assessment, consumer risk assessment and on the environment.

The process of renewal of the first approval of difenoconazole is currently ongoing.

The EU MRLs for difenoconazole are established in Annex IIIA of Regulation (EC) No 396/2005[4]. The review of the existing EU MRLs of difenoconazole according to Article 12 of Regulation (EC) No 396/2005 is currently ongoing. To date, EFSA has issued several reasoned opinions on the modification of MRLs for difenoconazole. The proposals from these reasoned opinions have been considered in recent MRL regulations,[5] except the last EFSA reasoned opinion on the modification of existing EU MRLs for difenoconazole in leafy brassica (EFSA, 2021). The conclusions of this reasoned opinion will not be taken into consideration for the present assessment. Certain Codex maximum residue limits (CXLs) have been taken over in the EU MRL legislation.[6,7,8,9]

[1] 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.

[2] Commission Directive 2008/69/EC of 1 July 2008 amending Council Directive 91/414/EEC to include clofentezine, dicamba, difenoconazole, diflubenzuron, imazaquin, lenacil, oxadiazon, picloram and pyriproxyfen as active substances OJ L 172, 2.7.2008, p. 9–14.

[3] Commission Implementing Regulation (EU) No 1100/2011 of 31 October 2011 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substances dicamba, difenoconazole and imazaquin. OJ L 285, 1.11.2011, p. 10–14.

[4] Regulation (EC) No 396/2005 of the 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.

[5] For an overview of all MRL Regulations on this active substance, please consult: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN

[6] 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 bifenazate, bifenthrin, 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.

[7] Commission Regulation (EU) 2015/845 of 27 May 2015 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 azoxystrobin, chlorantraniliprole, cyantraniliprole, dicamba, difenoconazole, fenpyroximate, fludioxonil, glufosinate-ammonium, imazapic, imazapyr, indoxacarb, isoxaflutole, mandipropamid, penthiopyrad, propiconazole, pyrimethanil, spirotetramat and trinexapac in or on certain products OJ L 138, 4.6.2015, p. 1–69.

[8] Commission Regulation (EU) 2017/626 of 31 March 2017 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 acetamiprid, cyantraniliprole, cypermethrin, cyprodinil, difenoconazole, ethephon, fluopyram, flutriafol, fluxapyroxad, imazapic, imazapyr, lambda-cyhalothrin, mesotrione, profenofos, propiconazole, pyrimethanil, spirotetramat, tebuconazole, triazophos and trifloxystrobin in or on certain products C/2017/2035 OJ L 96, 7.4.2017, p. 1–43.

[9] Commission Regulation (EU) 2019/552 of 4 April 2019 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 azoxystrobin, bicyclopyrone, chlormequat, cyprodinil, difenoconazole, fenpropimorph, fenpyroximate, fluopyram, fosetyl, isoprothiolane, isopyrazam, oxamyl, prothioconazole, spinetoram, trifloxystrobin and triflumezopyrim in or on certain products C/2019/2496 OJ L 96, 5.4.2019, p. 6–49.

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta Crop Protection AG submitted an application to the competent national authority in Germany (evaluating Member State, EMS) to modify the existing MRLs for the active substance difenoconazole in wheat and rye grain. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 7 February 2023. To accommodate for the intended SEU and NEU uses of difenoconazole, the EMS proposed to raise the existing MRL in wheat and rye from 0.1 to 0.3 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps, which were requested from the EMS. On 5 April 2023, EFSA received a statement from the applicant requesting to restart the assessment, providing a justification on why the data requirement related to the isomerisation of difenoconazole is not applicable for the present MRL application. In response to additional minor data clarification request the EMS submitted a revised evaluation report (Germany, 2022), which replaced the previously submitted evaluation report.

EFSA based its assessment on the evaluation report submitted by the EMS (Germany, 2022), the draft assessment report (DAR) (Sweden, 2006, 2010) prepared under Council Directive 91/414/EEC, the Commission review report on difenoconazole (European Commission, 2013), the conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole (EFSA, 2011a), as well as the conclusions from previous EFSA opinions on difenoconazole (EFSA, 2009, 2010a,b, 2011b, 2012, 2013, 2014a,b, 2017, 2018a, 2021) and the JMPR evaluations (FAO, 2008, 2011, 2013, 2015, 2018).

For this application, the data requirements established in Regulation (EU) No 544/2011[10] and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1996, 1997a–g, 2000, 2010a,b; OECD, 2011, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011[11].

Furthermore, considering the submission date for this MRL application (26/3/2019), the submission and assessment of data on TDMs is not required for MRL applications under Art. 6 of Reg. (EC) No 396/2005 submitted before 1 September 2019. The applicant provided data on TDMs, but these were not assessed by the EMS. EFSA compiled these data for completeness purposes.

As the EU pesticides peer review on the renewal of the approval of the active substance in accordance with Regulation (EC) No 1107/2009 and the review of the existing MRLs under Article 12 of Regulation 396/2005 are not yet finalised, the conclusions reported in this reasoned opinion may need to be reconsidered in the light of the outcome of the EU pesticides peer review and of the MRL review.

A selected list of end points of the studies assessed by EFSA in the framework of this MRL application, including the end points of relevant studies assessed previously, is presented in Appendix B.

The evaluation report submitted by the EMS (Germany, 2022) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.[12]

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 difenoconazole in primary crops has been investigated in the framework of the EU pesticides peer review following foliar applications in fruit crops (tomatoes and grapes), cereals/ grass crops (wheat), root crops (potatoes) and pulses/oilseed crops (rapeseed). Studies in cereals following seed application were also considered (Sweden, 2006; EFSA, 2011a). The metabolism was

[10] Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.

[11] 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.

[12] Background documents to this reasoned opinion are published on OpenEFSA portal and are available at the following link: https://open.efsa.europa.eu/study-inventory/EFSA-Q-2020-00100

found comparable in the four crop groups. Difenoconazole was the major component of the residues in the major plant parts, except for cereal grains, potato tubers and rape seeds, where the major components of the residues were the TDMs: triazole alanine (TA), triazole acetic acid (TAA) and 1,2,4-triazole (1,2,4-T). Metabolites CGA205374 (ketone), CGA205375 (alcohol) and CGA189138 (benzoic acid) were also identified in low proportions (below 5% total radioactive residue (TRR)).

Difenoconazole consists of four stereoisomers. The data have not been provided to conclude on the preferential metabolism/degradation of each enantiomer in plants, as well as the possible impact of isomerisation on the toxicity of difenoconazole. The data gap for these points was set by the EU pesticide peer review but so far has not been addressed. Since the MRL application was submitted before the entry into force of the EFSA guidance on the risk assessments of active substances that have stereoisomers (EFSA, 2019b), the applicant did not address the data gap for the present application. However, the applicant confirmed that the isomerisation of difenoconazole will be subject of assessment in the peer review of the renewal of the approval of difenoconazole. Nevertheless, this remains an additional uncertainty affecting the overall risk assessment of difenoconazole for the present assessment.

The EU pesticides peer review concluded that the metabolism of difenoconazole proceeds in a similar pathway in all crops investigated.

It is concluded that for the intended use of difenoconazole on wheat and rye, the metabolic behaviour of difenoconazole in primary crops is sufficiently addressed, with uncertainties related to the isomerisation of stereoisomers.

1.1.2. Nature of residues in rotational crops

Wheat and rye can be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review, the DT_{90} value of difenoconazole is 879 days (EFSA, 2011a) which exceeds the value of 100 days triggering the need for studies investigating the nature and magnitude of residues in rotational crops.

Metabolism of difenoconazole in rotational crops has been investigated in the framework of the peer review in two studies with ^{14}C-labelled difenoconazole (Sweden, 2006; EFSA, 2011a). In the first study, bare soil was treated with [^{14}C-phenyl-] difenoconazole at 32.4 g/ha and rotational crops belonging to cereal/grasses (wheat), leafy crops (mustard) and root crops (turnip) groups were planted/sown 30–33 days after the soil treatment. In this study, the total TRR was below 0.01 mg eq/kg and was not further characterised.

In the second study, bare soil was treated with [^{14}C-triazole-] and [^{14}C-phenyl-] difenoconazole at 125 g/ha and rotational crops belonging to cereal/grasses (maize and wheat), leafy crop (lettuces) and root crop (sugar beet) groups were planted/sown 98, 126, 342 and 369 days after the soil treatment (Sweden, 2006). In this study, the TRR in mature crops treated with [^{14}C-triazole] difenoconazole accounted for up to 0.02 mg eq/kg in lettuces (at 126 and 151 days after application), 0.34 mg eq/kg wheat grain (at 418 days after application), 0.11 mg eq/kg in straw (at 418 days after application), 0.005 mg eq/kg sugar beet roots (at 488 days after application), 0.03 mg eq/kg in sugar beet tops (at 488 days after application) and 0.21 mg eq/kg in maize grain (at 488 days after application) and was mainly composed of the triazole derivative metabolites.

Extractable residues in mature lettuce, wheat, sugar beet and maize commodities were predominantly aqueous soluble (79.5–90.4% TRR) and were composed of triazole alanine (10.4–66.2% TRR), triazole lactic acid (9.7–54.3% TRR) and triazole acetic acid (2.7–39.4% TRR) (Sweden, 2006).

The TRR in crops treated with [^{14}C-phenyl-] difenoconazole was at levels below 0.01 mg eq/kg and was not further characterised. The EU pesticides peer review concluded that the metabolism of difenoconazole in primary and rotational crops is partially similar (EFSA, 2011a).

An additional rotational crop metabolism study has been made available for the EFSA assessment in the framework of the previous MRL application on leafy brassica (EFSA, 2021). Bare soil was treated with difenoconazole ^{14}C-labelled on the phenyl ring at an application rate of 516 g/ha. The study covers the metabolic pathway of the *p*-chloro-phenoxy ring which has not been elucidated in the previously submitted studies because of the very low TRR in the treated crops. The study was performed on rotational crops belonging to cereal/grasses (wheat and sorghum), leafy crop (lettuces) and root crop (radishes) groups, planted into the treated soil at intervals of 30, 60, 120 and 270 days after treatment.

Very low radioactive residues were found in rotational crops. Parent difenoconazole was the highest residue observed in immature lettuces (42.0–81.5% TRR, from 0.005 mg eq/kg at 270 days after

treatment (DAT) to 0.026 mg eq/kg at 30 DAT), mature lettuces (48.5–68.7% TRR, 0.012 mg eq/kg at 120 DAT to 0.040 mg eq/kg at 30 DAT), radish leaves (27.9–72.0% TRR, from 0.008 mg eq/kg at 30 DAT to 0.060 mg eq/kg at 120 DAT), radish roots (31.1–60.3% TRR, from 0.008 mg eq/kg at 30 and 270 DAT to 0.017 mg eq/kg at 120 DAT) and sorghum forage (9.9% TRR, 0.001 mg eq/kg at 30 DAT). In wheat straw, difenoconazole was a minor residue (6.6–12.3% TRR, from 0.002 mg eq/kg at 270 DAT to 0.006 mg eq/kg at 120 DAT).

Metabolite CGA205375 was also found but in lower levels in radish leaves (7.9–22.6% TRR, from 0.004 mg eq/kg at 270 DAT to 0.007 mg eq/kg at 120 DAT), radish roots (7.6–23.7% TRR, from 0.002 mg eq/kg at DAT 30 DAT to 0.005 mg eq/kg at 60 DAT), immature lettuces (2.8–11.3% TRR, from < 0.001 mg eq/kg at 270 DAT to 0.003 mg eq/kg at 30 DAT), mature lettuces (4.8–6.6% TRR, from 0.001 mg eq/kg at 120 DAT to 0.004 mg eq/kg at 30 DAT) and sorghum forage (2.6% TRR, < 0.001 mg eq/kg at 30 DAT). Metabolite CGA205375 was the main residue in wheat straw (37.9–39.9% TRR, from 0.011 mg eq/kg at 270 DAT to 0.021 mg eq/kg at 60 DAT).

In wheat forage and hay, residues were extracted but not analysed due to the low levels of extractable residues. In sorghum, two components in forage (60.1% TRR) and four in stover (59.2% TRR) remained unidentified. These could be further investigated in the framework of the ongoing renewal of the approval of difenoconazole. In wheat grain, residues were below 0.01 mg eq/kg and in sorghum grain the radioactivity in the plant tissue was also very low, therefore, characterisation of residues in cereal grain was not possible (EFSA, 2021).

The results of the study suggest little uptake of difenoconazole and soil metabolites by cereal grains, leafy and root crops from the treated soil. The study also indicates that apart from parent difenoconazole and TDMs, plant metabolite CGA205375 occurs above 10% of the TRR in several plant matrices but the actual levels of this metabolite in crops were below the trigger values of 0.01 mg/kg in food and 0.05 mg/kg in feed. It is proposed that the toxicological relevance of this metabolite and the possible impact on the risk assessment residue definition in rotational crops will be assessed in the framework of the renewal of the approval process. For the present assessment, considering low levels of this metabolite present in food and feed crops, further assessment is not deemed relevant.

EFSA concludes that the metabolic pathway of difenoconazole in rotational crops is similar to that in primary crops.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of difenoconazole (hydrolysis study) was investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC (Sweden, 2006; EFSA, 2011a). These studies showed that difenoconazole is hydrolytically stable.

1.1.4. Analytical methods for enforcement purposes in plant commodities

Analytical methods for the determination of difenoconazole residues were assessed in the framework of the EU pesticides peer review (Sweden, 2006; EFSA, 2011a). They are based on liquid chromatography with tandem mass spectrometry (LC–MS/MS) and were validated in high-water content commodities (apples, lettuces) at the LOQ of 0.02 mg/kg, in dry commodities (wheat grain) at the LOQ of 0.05 mg/kg and in high-oil content commodities (rapeseed) at the LOQ of 0.05 mg/kg. A Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) method as reported in the European Standard EN 15662:2008 is also available for the analysis of difenoconazole residues in high water, acidic and dry/high-starch content commodities with an LOQ of 0.01 mg/kg (EFSA, 2017).

Additional validation data for a multiresidue method QuEChERS based on EN15662:2009–02 was submitted in the framework of the assessment of previous EFSA MRL application (EFSA, 2021). The method was evaluated as sufficiently validated for the enforcement purposes for the determination of difenoconazole residues in matrices with high-water content (tomatoes), high-oil content (oilseed rape), high-protein content (dried broad bean), high-starch content (wheat grain), high-acid content (grapes) and herbal infusion (a matrix difficult to analyse) at an LOQ of 0.01 mg/kg (EFSA, 2021).

EFSA concludes that the methods available are sufficiently validated for the determination of residues of difenoconazole in the crops under consideration. The methods allow quantifying residues at or above the LOQ of 0.01 mg/kg in high-starch content/dry commodities.

1.1.5. Storage stability of residues in plants

The storage stability of difenoconazole in plants under frozen conditions was investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC (Sweden, 2006; EFSA, 2011a) and under the previous MRL applications (EFSA, 2017).

In dry/high-starch content commodities the stability of difenoconazole has been demonstrated for 24 months when stored at −20°C (EFSA, 2011a).

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and the capabilities of enforcement analytical methods, the following residue definitions were proposed for primary, rotational crops and processed commodities (EFSA, 2011a, 2018b):

- Residue definition for risk assessment:
  1) difenoconazole;
  2) triazole derivative metabolites (TDM): triazole alanine, 1,2,4- triazole, triazole lactic acid (TLA), triazole acetic acid (TAA). This risk assessment residue definition has been established for triazole active substances by the peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted but not assessed in the present application (EFSA, 2018b).
- Residue definition for enforcement: difenoconazole

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical to the above-mentioned residue definition.

Since difenoconazole consists of four stereo isomers, and since the available analytical methods are not stereo selective, the proposed residue definitions for enforcement and risk assessment are derived for the sum of the *R*- and *S*- isomers. EFSA noted that the data gap identified during the peer review on the possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants is still open (EFSA, 2011a).

EFSA recommends that the existing residue definitions are reconsidered in the renewal of the approval process considering the data of the most recent metabolism study in rotational crops and the EFSA guidance document on stereoisomers (EFSA, 2019b).

For the uses on the crops under consideration, EFSA concludes that the metabolism of difenoconazole is addressed and the residue definitions for enforcement and risk assessment agreed in the peer review (EFSA, 2011a) are applicable.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the intended NEU and SEU uses of difenoconazole on wheat, rye, triticale and spelt, the applicant submitted residue trials on wheat. The samples of wheat grain and straw were analysed for the parent compound difenoconazole and the triazole derivative metabolites (TDM). Since the MRL application was submitted before 1 September 2019, the EMS did not assess the TDM data. EFSA compiled the TDM data for the purpose of completeness for future assessments.

The overview of residue data is provided in Appendix B.1.2.1.

According to the assessment of the EMS, the methods used were sufficiently validated and fit for purpose. The samples of these residue trials were stored under conditions for which the integrity of the samples has been demonstrated for difenoconazole and for the TDMs (Germany, 2022).

NEU GAP: 1 × 125 g/ha, BBCH 30–69, PHI not defined

The applicant submitted in total nine GAP compliant residue trials performed on wheat over the growing seasons of 2010, 2011 and 2021. The applicant proposes to extrapolate residue data from wheat to rye (and consequently to triticale and spelt). Such an extrapolation is acceptable according to the EU Technical Guidelines SANTE/2019/12752 (European Commission, 2020). The residues of difenoconazole in wheat grain were below the LOQ of 0.01 mg/kg with higher levels present in the straw (0.03–0.58 mg/kg). Control samples of grain and straw did not contain residues of difenoconazole. Regarding TDMs, the main residues in grain were triazole acetic acid (TAA;

< 0.01–0.21 mg/kg) and triazole alanine (TA; 0.02–0.53 mg/kg), which were in two cases for TAA and in one case for TA present at higher levels in control samples. In grain, residues of 1,2,4-triazole (1,2,4-T) and triazole lactic acid (TLA) were below the LOQ of 0.01 mg/kg except for one grain sample with residues of TLA quantified at the level of the LOQ.

EFSA concludes that the residue data are sufficient to derive an MRL proposal of 0.01* mg/kg for the residues of difenoconazole in wheat and rye grain.

SEU GAP: 1 × 125 g/ha, BBCH 30–69, PHI not defined

The applicant submitted in total 16 GAP compliant residue trials performed on wheat over the growing seasons of 2009, 2010, 2011 and 2021. The residue trials from three sites in Italy (trials S09-01497-1/2/03) where not considered sufficiently independent and therefore from these trials only one value (the highest) was selected for the residue data set. Residues of difenoconazole in grain were in the range of < 0.01–0.22 mg/kg and in straw of 0.08–4.56 mg/kg. Residues of TDMs in grain were as follows: < 0.01–0.01 mg/kg for 1,2,4 triazole, < 0.01–0.86 mg/kg for triazole acetic acid, 0.02–1.4 mg/kg for triazole alanine and < 0.01–0.01 mg/kg for triazole lactic acid.

The applicant proposes to extrapolate residue data from wheat to rye (and consequently to triticale and spelt). Such an extrapolation is acceptable according to the EU Technical Guidelines SANTE/2019/12752 (European Commission, 2020).

EFSA concludes that the residue data are sufficient to derive an MRL proposal of 0.3 mg/kg for the residues of difenoconazole in wheat and rye grain.

1.2.2. Magnitude of residues in rotational crops

The possible transfer of difenoconazole residues to crops that are grown in rotation has been assessed in the EU pesticides peer review under Directive 91/414/EEC (Sweden, 2006; EFSA, 2011a).

The uptake of difenoconazole and triazole alanine was investigated in carrots and spinaches planted 30–31 days after soil treatment with 750 g difenoconazole/ha (6 N the intended use) (Sweden, 2006). The results showed that in mature crops difenoconazole and triazole alanine residues were below the LOQs of 0.02 mg/kg and 0.05 mg/kg, respectively. Regarding TDM residues, further information on rotational crops was requested by the EU pesticides peer review as the study was limited to two crops only and a single plant back interval (EFSA, 2011a).

In the confined rotational crop study, which investigated the metabolic pathway of triazole labelled difenoconazole (application rate of 125 g a.s./ha, 1 N the intended GAP), residues of difenoconazole were not detected in crops at maturity while the majority of the radioactivity consisted of TDMs, namely triazole alanine, triazole acetic acid, and triazole lactic acid. The quantification was not undertaken to conclude on the actual levels of these compounds in the treated crops. The confined rotational crop study performed with phenyl labelled difenoconazole at an application rate of 516 g a.s./ha (4.1 N intended use) suggests little uptake of difenoconazole in cereal grains, leafy and root/tuber crops from the treated soil (See Section 1.1.2) (EFSA, 2021).

EFSA concludes that since the maximum annual application rate on the crops under consideration is lower than the application rate tested in the limited rotational crop field trials and the more recent confined rotational crop study, it is concluded that significant levels of difenoconazole and CGA205375 in rotational crops are not expected, provided that the active substance is applied according to the proposed GAP. Regarding triazole metabolites, the data are currently not sufficient to conclude on the magnitude of TDMs in rotational crops. These conclusions might be subject to revision following the outcome of the renewal of the approval of difenoconazole.

1.2.3. Magnitude of residues in processed commodities

Processing studies investigating the effect of processing on the magnitude of difenoconazole residues in processed commodities of wheat and rye were not submitted for the present assessment. Since the individual exposure to residues from the intake of wheat and rye grain is below 1% of the ADI, the submission of processing studies is of low practical relevance.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for wheat and rye grain in support of the intended NEU and SEU GAPs. The highest MRL value (0.3 mg/kg) is derived from the SEU GAP. In Section 3 EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumer health risk.

2. Residues in livestock

Wheat and rye grain, straw and various processing by-products can be used as livestock feed. Hence, it was necessary to perform a dietary burden calculation for livestock to estimate whether the intended use of difenoconazole would have an impact on residues expected in food of animal origin. The latest livestock dietary burden has been calculated in the previous EFSA reasoned opinion on the modification of MRLs for difenoconazole in leafy brassica (EFSA, 2021). The MRLs in leafy brassica, however, were not implemented in the MRL legislation and therefore conclusions in this reasoned opinion were not taken into account for the present assessment.

Thus, the previous livestock dietary burden calculated in the EFSA reasoned opinion on the modification of existing EU MRLs for difenoconazole in various crops (EFSA, 2017) was updated with the risk assessment values derived for wheat and rye grain under the present MRL application. For grain the input values derived in the present assessment are lower, whereas input values for straw were higher and these were used in the dietary burden calculation.

The input values for the exposure calculations for livestock are presented in Appendix D.1. The results of the dietary burden calculation are presented in Section B.2 and demonstrated that the trigger value of 0.1 mg/kg DM is exceeded for all livestock species. The residues in wheat straw are the main contributors to the diet of poultry, slightly exceeding the dietary burdens calculated by EFSA (2017).

It is noted that also in 2017, despite dietary burden being triggered, the modification of existing EU MRLs for animal commodities was postponed due to divergent residue definitions derived for difenoconazole: according to metabolism and livestock feeding studies assessed during the EU pesticides peer review, it was concluded that difenoconazole parent is not a sufficient marker for enforcement and a residue definition as difenoconazole alcohol (CGA – 205375) expressed as difenoconazole was proposed for enforcement and risk assessment (EFSA, 2011a). Considering that the proposed residue definition was not implemented in the MRL legislation and that the current residue definition established is difenoconazole only, the modification of the existing MRL in products of animal origin according to this residue definition is not required. Moreover, pending the review of existing difenoconazole EU MRLs according to Article 12 of Regulation (EC) No 396/2005, the calculated dietary burdens are only indicative, may be overestimated and not reflecting the existing authorised GAPs. It is also noted that the existing EU MRLs for animal products are based on the implementation of Codex MRLs in the EU legislation from the 2010 JMPR evaluation (FAO, 2011). These MRLs cover the residue definition 'sum of difenoconazole and CGA205375 (1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethanol), expressed as difenoconazole' and, therefore, take into consideration also metabolite CGA205375. In the meanwhile, these Codex MRLs for animal commodities have been revised by the JMPR in 2014.

It is also noted that no data have been provided to conclude on the preferential metabolism/ degradation of each enantiomer of difenoconazole in animals as well as the possible impact of isomerisation on the toxicity of difenoconazole. The data gap for these points was set by the EU pesticide peer review but so far has not been addressed. Since the MRL application was submitted before the entry into force of the EFSA guidance on the risk assessments of active substances that have stereoisomers (EFSA, 2019b), the applicant did not address the data gap but confirmed that isomerisation of difenoconazole will be subject of assessment in the peer review of the renewal of the approval of difenoconazole. Nevertheless, this remains as an additional uncertainty affecting the overall risk assessment of difenoconazole.

Considering the above mentioned, EFSA is of the opinion that at the current stage, the modification of the existing EU MRLs for difenoconazole on the basis of new intended uses of difenoconazole on wheat and rye cannot be completed. The revision of MRLs in animal commodities will be undertaken in the framework of the Article 12 of the Regulation 396/2005, taking into account the conclusions of the renewal of the approval of difenoconazole which is currently ongoing.

3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo (EFSA, 2018c, 2019a). This exposure assessment model contains food consumption data for different sub-groups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016).

The toxicological reference values for difenoconazole used in the risk assessment (i.e. ADI of 0.01 mg/kg body weight (bw) and ARfD value of 0.16 mg/kg bw) were derived in the framework of the EU pesticides peer review (EFSA, 2011a). The risk assessment residue definition in plant commodities refers to difenoconazole alone, whereas in animal commodities it refers only to metabolite CGA205375, expressed as difenoconazole. For metabolite CGA205375, no toxicological reference values were derived in the EU pesticides peer review and no conclusion on its toxicity was derived (EFSA, 2011a). The toxicological profile of this metabolite is being assessed in the framework of the renewal of the approval process of difenoconazole which is currently ongoing. Depending on the outcome of this assessment, the conclusions derived in the previous and present opinions on the consumer risk assessment resulting from the intake of animal commodities might need to be revised.

Furthermore, EFSA would like to emphasise that the present assessment does not take into consideration TDMs which may be generated by several pesticides belonging to the group of triazole fungicides. It is noted that in June 2019 the Standing Committee on Plants, Animals, Food and Feed (Pesticide residues)[13] endorsed the EFSA recommendation to perform a separate risk assessment for TDMs, as provided in the peer review of the pesticide risk assessment for TDMs in light of confirmatory data (EFSA, 2018b); and to apply the clock-stop mechanism in case data are missing that are needed in order to perform a comprehensive assessment for the TDMs. Risk managers agreed that such comprehensive risk assessment should be conducted for applications submitted from September 2019 onwards. As the present application was submitted before September 2019 (26 March 2019) the risk assessment for TDMs was not performed.

Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed only for wheat and rye grain and was based on the STMR values derived from the supervised residue field trials on wheat. The complete list of input values can be found in Appendix D.2.

The short-term exposure did not exceed the ARfD for any of the crops assessed in this application (see Appendix B.3).

Long-term (chronic) dietary risk assessment

The most recent long-term exposure was calculated in the previous EFSA output on the modification of the existing MRLs for difenoconazole in leafy brassica (EFSA, 2021). The MRL proposals derived in this reasoned opinion were not implemented in the MRL legislation due to consumer exposure concerns and therefore conclusions of this reasoned opinion are not taken into account for the present assessment. Thus, the long-term exposure assessment, which was performed by EFSA in 2018 in the framework of the modification of existing MRLs for difenoconazole in various crops (EFSA, 2018a), was now updated with the risk assessment values derived for wheat and rye grain from the residue trials submitted in the present assessment.

Additionally, for several plant commodities, the risk assessment values were available from the JMPR assessments supporting the Codex MRLs implemented in Regulation 2019/552[14] (FAO, 2018). Where no risk assessment values were available, the existing EU MRLs set in the Commission Regulation (EU) No 2019/552 were used as input values. For animal commodities, the STMR values were as derived by the JMPR in 2010 (FAO, 2011) and correspond to residues of metabolite CGA205375 expressed as difenoconazole and, therefore, assume that parent and metabolite have a similar toxicological profile. Noting that the toxicological profile of metabolite CGA205375 has not been addressed, the consumer risk assessment resulting from the intake of animal commodities remains indicative and might be subject to revision once the renewal of the approval process for difenoconazole is finalised.

The estimated indicative long-term dietary exposure accounted for a maximum of 98% of the ADI (NL toddler diet). The contribution of residues in wheat and rye grain accounted for 0.72% and 0.55% of the ADI, respectively.

EFSA concluded that the dietary exposure to difenoconazole residues from the intake of wheat and rye grain is low, noting that the impact of intended uses on the residues in animal commodities and

[13] Standing Committee on Plants, Animals, Food and Feed Section Phytopharmaceuticals – Residues, held on 13–14 June 2019. sante.ddg2.g.5(2019)4475145.

[14] Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for azoxystrobin, bicyclopyrone, chlormequat, cyprodinil, difenoconazole, fenpropimorph, fenpyroximate, fluopyram, fosetyl, isoprothiolane, isopyrazam, oxamyl, prothioconazole, spinetoram, trifloxystrobin and triflumezopyrim in or on certain products. OJ L 96, 5.4.2019, p. 6–49.

the consumer exposure could not be properly addressed. Overall, the present risk assessment confirms a very narrow margin of safety for the overall chronic exposure and is considered provisional pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and its impact on the toxicity of difenoconazole. The assessment is also affected by uncertainties related to the toxicological profile of animal metabolite CGA205375 and, additionally, it does not take into consideration TDMs.

The complete list of input values is presented in Appendix D.2. For further details on the exposure calculations, a screenshot of the Report sheet of the PRIMo is presented in Appendix C.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found sufficient to derive an MRL proposal for difenoconazole in wheat and rye grain. The data provided on the magnitude of TDMs in these commodities were presented for reasons of completeness but were not assessed because the dossier was submitted before the date of application of the new strategy for the assessment of TDMs (i.e. September 2019).

EFSA concluded that the dietary exposure to difenoconazole residues from the intake of wheat and rye grain is low, noting that the impact of intended uses on the residues in animal commodities and the consumer exposure could not be properly addressed.

Overall, the present risk assessment confirms a very narrow margin of safety for the overall chronic exposure and is considered provisional pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and its impact on the toxicity of difenoconazole. Additionally, the exposure assessment does not take into consideration TDMs which may be generated by several pesticides belonging to the group of triazole fungicides as this application was submitted before the date of application of the new strategy endorsed by the risk managers for the assessment of TDMs (i.e. September 2019). The consumer exposure to residues from the intake of animal commodities is affected by uncertainties related to the toxicological profile of animal metabolite CGA CGA205375.

The MRL recommendations are summarised in Appendix B.4.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement to risk assessment residue definition
CV	coefficient of variation (relative standard deviation)
CXL	Codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EC	emulsifiable concentrate
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
EURL	EU Reference Laboratory (former Community Reference Laboratory (CRL))
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GC	gas chromatography
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 Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_{oc}	organic carbon adsorption coefficient

LC	liquid chromatography
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry detector
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant back interval
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA	risk assessment
RAC	raw agricultural commodity
RMS	rapporteur Member State
RPF	relative potency factor
SANCO	Directorate-General for Health and Consumers
SEU	southern Europe
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization

Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

Crop and/or situation	NEU, SEU, MS or country	F, G or I[a]	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment				PHI (days)[d]	Remarks
				Type[b]	Conc. a.s. (g/kg)	Method kind	Range of growth stages & season[c]	Number min–max	Interval between application (days) min–max	g a.s./hL min–max	Water (L/ha) min–max	Rate min–max	Unit		
Wheat, rye	NEU	F	*Septoria tritici, Puccinia striiformis, Puccinia recondita*	SC	125	Foliar treatment - broadcast spraying	30–69	1	–	–	100–400	125	g a.s./ha	F[e]	Use in triticale and spelt. MS: Austria, Belgium, Czech Republic, Germany, Denmark, Estonia, Finland, Hungary, Latvia, Lithuania, Netherlands, Poland, Slovakia, Slovenia, Sweden, UK
Wheat, rye	SEU	F	*Septoria tritici, Puccinia striiformis, Puccinia recondita*	SC	125	Foliar treatment - broadcast spraying	31–69	1	–	–	100–400	125	g a.s./ha	F[e]	Use in spelt and triticale. MS: Bulgaria, Croatia, France, reece, Italy, Portugal, Spain

MRL: maximum residue level; GAP: Good Agricultural Practice; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; SC: Suspension concentrate.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3–8263–3152-4), including, where relevant, information on season at time of application.
(d): PHI – minimum pre-harvest interval.
(e): F: defined by the growth stage.

Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and analytical methods for enforcement purposes in plant commodities

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

Primary crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**Sampling (DAT)**	**Comment/Source**
	Fruit crops	Tomato	Foliar, 6 × 123 g a.s./ha	34	Radiolabelled active substance: [phenyl-^{14}C]-difenoconazole, [triazole-^{14}C]-difenoconazole (Sweden, 2006; EFSA, 2011a)
			Foliar, 6 × 123 g a.s./ha	7, 16	
			Foliar, 3 × 247 g a.s./ha	40	
		Grapes	Foliar, 5 × 247 g a.s./ha	20	
	Root crops	Potato	Foliar, 6 × 123 g a.s./ha, 7 days interval	11	
	Leafy crops	Oilseed rape	Foliar: 2 × 125 g a.s./ha, 14 days intervals	39	
	Cereals/grass	Wheat	Foliar: 4 × 247 g a.s./ha	29	
			Seed: 1 × 23 g a.s./100 kg seed	31–34, 48–62, 59–83	
			Seed: 1 × 25 g a.s./100 kg seed	40–72, 236	
	Pulses/oilseeds	Rapeseeds	Foliar, 2 × 125 g a.s./ha, 14 days interval	39	
	Miscellaneous	–	–	–	–
Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/Source**
	Root/tuber crops	Turnip*	Soil, 1 × 32.4 g a.s./ha	30–33	Radiolabelled active substance: [phenyl-^{14}C]- and [triazole-^{14}C]-labelled difenoconazole (Sweden, 2006; EFSA, 2021) * Study performed with [phenyl-^{14}C] difenoconazole only (EFSA, 2021)
		Sugar beet	Soil, 1 × 125 g a.s./ha	98, 126, 342, 369	
		Radishes*	Soil, 1 × 516 g a.s./ha	30, 60, 120, 270	
	Leafy crops	Mustard*	Soil, 1 × 32.4 g a.s./ha	30–33	
		Lettuces	Soil, 1 × 125 g a.s./ha	98, 126, 342, 369	
		Lettuces*	Soil, 1 × 516 g a.s./ha	30, 60, 120, 270	
	Cereal (small grain)	Maize	Soil, 1 × 125 g a.s./ha	98, 126, 342, 369	
		Wheat	Soil, 1 × 125 g a.s./ha		
		Wheat*	Soil, 1 × 32.4 g a.s./ha	30–33	
			Soil, 1 × 516 g a.s./ha	30, 60, 120, 270	
		Sorghum*	Soil, 1 × 516 g a.s./ha	30, 60, 120, 270	
	Other	–	–	–	–
Processed commodities (hydrolysis study)	**Conditions**		**Stable?**		**Comment/Source**
	Pasteurisation (20 min, 90°C, pH 4)		Yes		Hydrolysis studies performed with [triazole-^{14}C]-labelled difenoconazole identify no degradation of difenoconazole (Sweden, 2006; EFSA, 2011a)
	Baking, brewing and boiling (60 min, 100°C, pH 5)		Yes		
	Sterilisation (20 min, 120°C, pH 6)		Yes		
	Other processing conditions				

Can a general residue definition be proposed for primary crops?	Yes	EFSA (2011a)
Rotational crop and primary crop metabolism similar?	Yes	Residues in rotational and primary crops mainly consist of parent difenoconazole and TDMs (EFSA, 2011a, 2021). The relevance of metabolite CGA205375 in plants shall be investigated in the framework of the renewal of the approval process of difenoconazole.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes	EFSA (2021)
Plant residue definition for monitoring (RD-Mo)	Difenoconazole	
Plant residue definition for risk assessment (RD-RA)	Difenoconazole Triazole derivative metabolites (TDM) (new RD, EFSA, 2018b)*: - 1,2,4-triazole - triazole alanine - triazole acetic acid - triazole lactic acid *Not considered in the present assessment as dossier submitted before the date of application of the new strategy for the assessment of TDMs (i.e. September 2019).	

Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	LC–MS/MS: - high water content, LOQ: 0.02 mg/kg (lettuces, apples) - high oil content, LOQ: 0.05 mg/kg (oilseed rape) - high starch content, LOQ: 0.05 mg/kg (wheat). ILV available for all matrices (EFSA, 2011a) HPLC–MS/MS (QuEChERS): - high acid content, LOQ: 0.01 mg/kg - high water content, LOQ: 0.01 mg/kg - high starch content (cereals), LOQ: 0.01 mg/kg (EFSA, 2017) HPLC–MS/MS (QuEChERS): - high water content, LOQ: 0.01 mg/kg - high acid content, LOQ: 0.01 mg/kg - high oil content, LOQ: 0.01 mg/kg - high starch content, LOQ: 0.01 mg/kg - high protein content, LOQ: 0.01 mg/kg - dry commodities, LOQ: 0.01 mg/kg - difficult matrices (herbal infusion), LOQ: 0.01 mg/kg. ILV available in high water, high oil, high protein content commodities and herbal infusions (EFSA, 2021)

DAT: days after treatment; PBI: plant-back interval; a.s.: active substance; LC–MS/MS: liquid chromatography with tandem mass spectrometry; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; ILV: independent laboratory validation.

B.1.1.2. Stability of residues in plants

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/Source
				Value	Unit		
	High-water content	Tomatoes	–20	24	Months	Difenoconazole	In all studies, the demonstrated storage stability period of parent difenoconazole is equal with the overall duration of the study. All studies assessed in the DAR (Sweden, 2006; EFSA, 2017)
		Lettuces	–20	12	Months	Difenoconazole	
		Banana	–20	12	Months	Difenoconazole	
		Sugar beet	–18	12	Months	Difenoconazole, difenoconazole alcohol	
	High-oil content	Soybean	–20	12	Months	Difenoconazole	
		Cotton seed	–20	24	Months	Difenoconazole	
		Rapeseeds	–18	18	Months	Difenoconazole, difenoconazole alcohol	
	High-protein content	–	–	–	–		–
	Dry / High starch	Potatoes	–20	24	Months	Difenoconazole	
		Wheat grain	–20	24	Months	Difenoconazole, difenoconazole alcohol	
	High-acid content	Grapes	–18	18	Months	Difenoconazole, difenoconazole alcohol	
	Processed products	–	–	–	–	–	–
	Others	–	–	–	–	–	–

B.1.2. Magnitude of residues in plants

B.1.2.1. Summary of residues data from the supervised residue trials

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)	CF[d]
Wheat grain	NEU	**Difenoconazole** 9 × < 0.01 **Triazole derivative metabolites** 1,2,4-triazole: 9 × < 0.01 Triazole alanine: 0.02; 2 × 0.05; 2 × 0.11; 0.13; 0.15; 0.16; 0.53[c] Triazole acetic acid: < 0.01; 0.01; 0.04[c]; 2 × 0.07; 0.08; 0.11[c]; 0.12; 0.21 Triazole lactic acid: 8 × < 0.01; 0.01	Residue trials on wheat compliant with the intended NEU GAP. Extrapolation to rye is applicable.	0.01*	0.01 1,2,4-T: 0.01 TA: 0.53 TAA: 0.21 TLA: 0.01	0.01 1,2,4-T: 0.01 TA: 0.11 TAA: 0.07 TLA: 0.01	N/A
Wheat grain	SEU	**Difenoconazole** Grain: 10 × < 0.01; 0.04; 0.06; 0.08; 0.22 **Triazole derivative metabolites** 1,2,4-triazole: 11 × < 0.01; 2 × 0.01 Triazole alanine: 2 × 0.02; 2 × 0.03; 4 × 0.06; 0.14; 0.67; 0.78; 0.8; 1.4 Triazole acetic acid: 3 × < 0.01; 2 × 0.02; 0.04; 0.05; 2x 0.07; 0.27; 0.29; 0.6[c]; 0.86 Triazole lactic acid: 11 × < 0.01; 0.01[c]; 0.01	Residue trials on wheat compliant with the intended SEU GAP. Extrapolation to rye is applicable.	0.3	0.22 1,2,4-T: 0.01 TA: 1.4 TAA: 0.86 TLA: 0.01	0.01 1,2,4-T: 0.01 TA: 0.06 TAA: 0.05 TLA: 0.01	N/A
Wheat straw	NEU	**Difenoconazole** 0.03; 0.14; 0.18; 0.19; 0.21; 0.22; 0.34; 0.44; 0.58 **Triazole derivative metabolites** 1,2,4-triazole: 9 × < 0.01 Triazole alanine: 7 × < 0.01; 0.01; 0.02 Triazole acetic acid: 2 × < 0.01; 0.02; 0.04; 2 × 0.05; 0.08; 2 × 0.09 Triazole lactic acid: 4 × < 0.01; 0.02[c]; 0.03[c]; 0.04; 0.07; 0.21[c]	Residue trials on wheat compliant with the intended NEU GAP. Extrapolation to rye is applicable.	–	0.58 1,2,4-T: 0.01 TA: 0.02 TAA: 0.09 TLA: 0.21	0.21 1,2,4-T: 0.01 TA: 0.01 TAA: 0.05 TLA: 0.02	N/A

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)	CF[d]
Wheat straw	SEU	**Difenoconazole** 0.08; 0.10; 0.13; 0.23; 0.34; 0.38; 0.41; 0.92; 1.6; 1.63; 2.83; 3.33; 3.85; 4.56 **Triazole derivative metabolites** 1,2,4-triazole: 12 × < 0.01; 0.01 Triazole alanine: 6 × < 0.01; 0.01[c]; 0.01; 2× 0.02; 0.03[c]; 0.06; 0.11[c] Triazole acetic acid: 2 × < 0.01; 2 × 0.01; 3 × 0.02; 0.03; 2 × 0.05; 0.17; 0.18[c]; 0.41 Triazole lactic acid: 3 × < 0.01; 0.01[c]; 2 × 0.01; 2 × 0.02; 2 × 0.03; 0.13; 0.27; 0.49[c]	Residue trials on wheat compliant with the intended SEU GAP. Extrapolation to rye is applicable.	–	4.56 1,2,4-T: 0.01 TA: 0.11 TAA: 0.41 TLA: 0.49	0.67 1,2,4-T: 0.01 TA: 0.01 TAA: 0.02 TLA: 0.02	N/A

MRL: maximum residue level; GAP: Good Agricultural Practice; Mo: monitoring; RA: risk assessment; c: control sample; N/A: not applicable.
*: Indicates that the MRL is proposed at the limit of quantification.
(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, EU: indoor EU trials or Country code: if non-EU trials.
(b): Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.
(d): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	Yes	In studies with [^{14}C-phenyl] difenoconazole (appl. of 32.4 g/ha and 125 g/ha), the TRR was too low to be characterised (Sweden, 2006). In a new study submitted under a previous EFSA assessment with [^{14}C-phenyl] difenoconazole (appl. of 516 g/ha) in lettuces, radishes and wheat, the TRR accounted for up to 0.04 mg eq/kg in lettuces and 0.06 mg eq/kg in radishes. In wheat grain, residues were below 0.01 mg eq/kg and, therefore, too low to be characterised (EFSA, 2021). In a study with [^{14}C-triazole] difenoconazole (appl. 125 g/ha), the TRR in mature crops accounted for up to 0.02 mg eq/kg in lettuces, 0.34 mg eq/kg in wheat grain, 0.11 mg eq/kg in straw, 0.005 mg eq/kg in sugar beet roots, 0.03 mg eq/kg in sugar beet tops and 0.21 mg eq/kg in maize grain (Sweden, 2006).
Residues in rotational and succeeding crops expected based on field rotational crop study?	Inconclusive	Field study available with difenoconazole applied on bare soil at a rate of 750 g/ha (Sweden, 2006). Mature rotational crops carrots and spinaches, planted at 30 and 31-day PBI, did not contain difenoconazole and triazole alanine residues above the respective LOQs (Sweden, 2006). Regarding TDM residues, further information in rotational crops was requested by the EU pesticides peer review as the study was limited to two crops only and a single plant back interval (EFSA, 2011a).

TRR: total radioactive residue; PBI: plant-back interval; LOQ: limit of quantification; TDM: triazole derivative metabolite.

B.1.2.3. Processing factors

No processing studies were submitted in the framework of the present MRL application.

B.2. Residues in livestock

Dietary burden calculation according to OECD (2013).

Relevant groups	Dietary burden expressed in				Most critical diet[(a)]	Most critical commodity[(b)]	Trigger exceeded (Yes/No) 0.10 mg/kg DM	Previous assessment (EFSA, 2017) Max burden mg/kg DM
	mg/kg bw per day		mg/kg DM					
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0.301	0.317	9.65	10.45	Dairy cattle	Potato process waste	Yes	10.45 (beef)
Cattle (dairy only)	0.301	0.317	7.83	8.23	Dairy cattle	Potato process waste	Yes	8.25 (dairy)
Sheep (all diets)	0.275	0.310	8.24	9.30	Ram/Ewe	Potato process waste	Yes	8.86

Relevant groups	Dietary burden expressed in				Most critical diet[a]	Most critical commodity[b]	Trigger exceeded (Yes/No) 0.10 mg/kg DM	Previous assessment (EFSA, 2017) Max burden mg/kg DM
	mg/kg bw per day		mg/kg DM					
	Median	Maximum	Median	Maximum				
Sheep (ewe only)	0.275	0.310	8.24	9.30	Ram/Ewe	Potato process waste	Yes	8.86
Swine (all diets)	0.115	0.134	4.99	5.79	Swine (breeding)	Potato process waste	Yes	5.81
Poultry (all diets)	0.076	0.100	1.08	1.46	Poultry layer	Wheat straw	Yes	1.28 (broiler)
Poultry (layer only)	0.076	0.100	0.82	1.46	Poultry layer	Wheat straw	Yes	1.10

bw: body weight; DM: dry matter.

(a): When several diets are relevant (e.g. cattle, sheep and poultry "all diets"), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day".

(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

B.3. Consumer risk assessment

ARfD	0.16 mg/kg bw (European Commission, 2013)
Highest IESTI, according to EFSA PRIMo	Wheat grain: 0.09% of ARfD Rye grain: 0.04% of ARfD
Assumptions made for the calculations	Calculations were performed with PRIMo revision 3.1. The calculation is based on the STMR levels expected in wheat and rye grain according to the submitted residue trials.

ADI	0.01 mg/kg bw per day (European Commission, 2013)
Highest IEDI, according to EFSA PRIMo	98% ADI (NL Toddler) Contribution of crops assessed: Wheat: 0.72% of ADI (GEMS/Food G06) Rye: 0.55% of ADI (DK child diet)
Assumptions made for the calculations	Calculations were performed with PRIMo revision 3.1. The consumer exposure calculated by EFSA in 2018 (EFSA, 2018a) was updated using the STMR values in wheat and rye grain as derived from the submitted residue trials. For a number of plant commodities, the risk assessment values as derived in previous EFSA assessments or by the JMPR were used to further refine the exposure. Where no risk assessment values were available, the existing EU MRLs set in the Commission Regulation (EU) No 2019/552 were used as input values. For animal commodities the STMR values as derived by the JMPR in 2010 were used as input values, highlighting that these values correspond to residues of metabolite CGA205375 expressed as difenoconazole and, therefore, assume that parent and metabolite have a similar toxicological profile. Noting that the toxicological profile of metabolite CGA205375 has not been addressed, the consumer risk assessment resulting from the intake of animal commodities remains indicative and might be subject to revision once the renewal of the approval process for difenoconazole is finalised.

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level; STMR: supervised trials median residue

B.4. Recommended MRLs

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Difenoconazole				
0500070	Rye	0.1	0.3 (further risk management consideration required)	The submitted data are sufficient to derive an MRL proposal for the intended NEU/SEU use. The dietary exposure to difenoconazole residues from the intended uses on wheat and rye is low, noting that the impact of the intended uses on the residue levels in animal commodities and the consumer exposure could not be properly assessed. A very narrow margin of safety is noted for the overall chronic exposure which is considered provisional pending the submission of confirmatory data on possible preferential metabolism/degradation of the four stereo isomers of difenoconazole in plants and animals and the impact of isomerisation on the toxicity of difenoconazole. The consumer exposure assessment is also affected by uncertainties associated with the toxicity of animal metabolite CGA205375 and, additionally, it does not take into consideration triazole derivative metabolites (TDMs).
0500090	Wheat	0.1		

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe; GAP: Good Agricultural Practice.
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

Appendix C – Pesticide Residue Intake Model (PRIMo)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Difenoconazole

LOQs (mg/kg) range from: 0.005 to: 0.05

Toxicological reference values

ADI (mg/kg bw per day):	0.01	ARfD (mg/kg bw):	0.16
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	2013	Year of evaluation:	2013

Input values

Details – chronic risk assessment | Supplementary results – chronic risk assessment

Details – acute risk assessment/children | Details – acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	98%	NL toddler	9.78	17%	Apples	8%	Beans (with pods)	8%	Table grapes	5%	
	74%	DE child	7.36	20%	Apples	7%	Tomatoes	7%	Table grapes	1%	
	71%	GEMS/Food G06	7.07	26%	Tomatoes	14%	Rice	5%	Table grapes	2%	
	55%	IE adult	5.50	7%	Wine grapes	4%	Other leafy brassica	4%	Sweet potatoes	1%	
	54%	GEMS/Food G10	5.42	11%	Rice	10%	Tomatoes	3%	Chinese cabbages/pe-tsai	2%	
	54%	GEMS/Food G11	5.39	7%	Tomatoes	6%	Celeriacs/turnip rooted celeries	5%	Wine grapes	2%	
	53%	GEMS/Food G07	5.25	8%	Tomatoes	8%	Wine grapes	4%	Potatoes	2%	
	51%	NL child	5.11	9%	Apples	5%	Table grapes	4%	Tomatoes	2%	
	50%	PT general	5.02	13%	Wine grapes	7%	Rice	6%	Tomatoes	0.4%	
	48%	GEMS/Food G08	4.82	8%	Tomatoes	5%	Wine grapes	4%	Potatoes	2%	
	45%	GEMS/Food G15	4.51	9%	Tomatoes	5%	Wine grapes	4%	Potatoes	2%	
	44%	FR child 3 15 yr	4.39	6%	Tomatoes	5%	Oranges	5%	Beans (with pods)	2%	
	42%	RO general	4.20	14%	Tomatoes	9%	Wine grapes	4%	Potatoes	1%	
	41%	FR toddler 2 3 yr	4.08	8%	Beans (with pods)	5%	Rice	5%	Apples	0.9%	
	37%	SE general	3.69	6%	Tomatoes	4%	Potatoes	4%	Chinese cabbages/pe-tsai	0.6%	
	35%	ES child	3.54	7%	Tomatoes	4%	Rice	3%	Oranges	0.9%	
	34%	DE women 14-50 yr	3.43	5%	Tomatoes	4%	Wine grapes	4%	Apples	0.8%	
	32%	FR adult	3.16	12%	Wine grapes	3%	Tomatoes	2%	Beans (with pods)	0.8%	
	32%	UK infant	3.16	6%	Peas (without pods)	6%	Rice	3%	Potatoes	1%	
	31%	DE general	3.15	5%	Tomatoes	4%	Wine grapes	4%	Apples	0.7%	
	31%	UK toddler	3.11	5%	Rice	4%	Tomatoes	3%	Potatoes	0.6%	
	31%	NL general	3.07	3%	Wine grapes	3%	Tomatoes	2%	Beans (with pods)	1%	
	28%	IT toddler	2.84	10%	Tomatoes	2%	Rice	2%	Lettuces	0.9%	
	28%	ES adult	2.83	6%	Tomatoes	3%	Lettuces	2%	Beans (with pods)	0.5%	
	27%	IT adult	2.66	8%	Tomatoes	2%	Lettuces	2%	Florence fennels	0.4%	
	25%	FI 3 yr	2.53	5%	Rice	5%	Potatoes	4%	Tomatoes	0.5%	
	24%	DK child	2.40	4%	Tomatoes	4%	Apples	3%	Rice	0.7%	
	23%	UK vegetarian	2.29	4%	Tomatoes	4%	Wine grapes	3%	Rice	0.4%	
	21%	UK adult	2.07	6%	Wine grapes	3%	Rice	3%	Tomatoes	0.3%	
	20%	PL general	2.01	6%	Tomatoes	3%	Potatoes	3%	Apples	0.1%	
	20%	FI 6 yr	1.99	4%	Potatoes	4%	Rice	3%	Tomatoes	0.4%	
	20%	FR infant	1.99	5%	Beans (with pods)	3%	Apples	2%	Potatoes	0.2%	
	19%	DK adult	1.93	5%	Wine grapes	4%	Tomatoes	2%	Apples	0.2%	
	17%	FI adult	1.66	4%	Tomatoes	3%	Coffee beans	2%	Wine grapes	3%	
	16%	LT adult	1.60	4%	Tomatoes	3%	Potatoes	3%	Apples	0.4%	
	7%	IE child	0.72	3%	Rice	0.9%	Beans (without pods)	0.6%	Potatoes	0.1%	

Conclusion:

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of Difenoconazole is unlikely to present a public health concern.

Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

Feed commodity	Median dietary burden		Maximum dietary burden	
	Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Risk assessment residue definition in plants: difenoconazole				
Wheat, rye straw	**0.67**	**STMR (Table B.1.2.1)**	**4.56**	**HR (Table B.1.2.1)**
Wheat, rye grain	**0.01**	**STMR (Table B.1.2.1)**	**0.01**	**STMR (Table B.1.2.1)**
Barley straw	0.71	HR (EFSA, 2017)	0.31	STMR (EFSA, 2017)
Barley grain	0.02	STMR (EFSA, 2017)	0.02	STMR (EFSA, 2017)
Peas	0.028	STMR (FAO, 2018)	0.028	STMR (FAO, 2018)
Beans, Lupin seed	0.02	STMR (EFSA, 2017)	0.02	STMR (EFSA, 2017)
Sugar beet tops	0.25	STMR (EFSA, 2017)	0.62	HR (EFSA, 2017)
Head cabbage leaves	0.02	STMR (EFSA, 2017)	0.19	HR (EFSA, 2017)
Kale	2.00	EU MRL	2.00	EU MRL
Carrot, culls	0.10	STMR (EFSA, 2017)	0.28	HR (EFSA, 2017)
Cassava/tapioca, roots	0.10	EU MRL	0.10	EU MRL
Potato, culls	0.10	EU MRL	0.10	EU MRL
Turnips, Swedes roots	0.08	STMR (EFSA, 2010a)	0.28	HR (EFSA, 2010a)
Soybean seed	0.01	STMR (EFSA, 2017)	0.01	STMR (EFSA, 2017)
Apple pomace, wet	0.69	STMR × PF (4.3) (EFSA, 2017)	0.69	STMR × PF (4.3) (EFSA, 2017)
Sugar beet, dried pulp	0.20	STMR × PF (10) (EFSA, 2017)	0.20	STMR × PF (10) (EFSA, 2017)
Sugar beet, ensiled pulp	0.06	STMR × PF 3[(b)] (EFSA, 2017)	0.06	STMR × PF 3[(b)] (EFSA, 2017)
Sugar beet, molasses	0.58	STMR × PF (29) (EFSA, 2017)	0.58	STMR × PF (29) (EFSA, 2017)
Rape seed meal	0.08	STMR × PF (2[(b)]) (EFSA, 2017)	0.08	STMR × PF (2[(b)]) (EFSA, 2017)
Citrus, dried pulp	0.64	STMR × PF (4) (EFSA, 2017)	0.64	STMR × PF (4) (EFSA, 2017)
Distiller's grain, brewer's grain, dried	0.03	STMR (wheat grain, Table B.1.2.1) × PF (3.3[(b)])	0.03	STMR (wheat grain, Table B.1.2.1) × PF (3.3[(b)])
Flaxseed/Linseed, meal	0.40	EU MRL × PF (2[(b)])	0.40	EU MRL × PF (2[(b)])
Lupin seed meal	0.02	STMR × PF (1.1[(b)]) (EFSA, 2017)	0.02	STMR × PF (1.1[(b)]) (EFSA, 2017)
Potato process waste	2.00	EU MRL × PF (20[(b)])	2.00	EU MRL × PF (20[(b)])
Potato dried pulp	3.80	EU MRL × PF (38[(b)])	3.80	EU MRL × PF (38[(b)])
Rape seed/Canola meal	0.08	STMR × PF (0.04 × 2[(b)]) (EFSA, 2017)	0.08	STMR × PF (0.04 × 2[(b)]) (EFSA, 2017)
Rice bran	8.80	STMR × PF (10[(b)]) (EFSA, 2017)	8.80	STMR × PF (10[(b)]) (EFSA, 2017)
Soybean hulls	0.02	STMR × PF (2) (EFSA, 2017)	0.02	STMR × PF (2) (EFSA, 2017)
Soybean meal	0.004	STMR × PF (0.38) (EFSA, 2017)	0.004	STMR × PF (0.38) (EFSA, 2017)
Wheat gluten, meal	0.02	STMR (Table B.1.2.1) × PF (1.8[(b)])	0.02	STMR (Table B.1.2.1) × PF (1.8[(b)])
Wheat, milled by-products	0.07	STMR (Table B.1.2.1) × PF (7[(b)])	0.07	STMR (Table B.1.2.1) × PF (7[(b)])

STMR: supervised trials median residue; HR: highest residue; PF: processing factor.

(a): Figures in the table are rounded to 2 digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce dietary burden calculations, the unrounded values need to be used.

(b): In the absence of processing factors supported by data, default processing factors (in bracket) were respectively included in the calculation to consider the potential concentration of residues in these commodities.

D.2. Consumer risk assessment

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Risk assessment residue definition: Difenoconazole						
Grapefruits	0.6	FAO (2013)	0.16	STMR-RAC	Acute exposure assessment performed only for the crops under consideration.	
Oranges	0.6	FAO (2013)	0.16	STMR-RAC		
Lemons	0.6	FAO (2013)	0.16	STMR-RAC		
Limes	0.6	FAO (2013)	0.16	STMR-RAC		
Mandarins	0.6	FAO (2013)	0.16	STMR-RAC		
Other citrus fruit	0.6	FAO (2013)	0016	STMR-RAC		
Almonds	0.05	Existing MRL	0.05	LOQ		
Brazil nuts	0.05	Existing MRL	0.05	LOQ		
Cashew nuts	0.05	Existing MRL	0.05	LOQ		
Chestnuts	0.05	Existing MRL	0.05	LOQ		
Coconuts	0.05	Existing MRL	0.05	LOQ		
Hazelnuts/cobnuts	0.05	Existing MRL	0.05	LOQ		
Macadamia	0.05	Existing MRL	0.05	LOQ		
Pecans	0.05	Existing MRL	0.05	LOQ		
Pine nut kernels	0.05	Existing MRL	0.05	LOQ		
Pistachios	0.05	Existing MRL	0.05	LOQ		
Walnuts	0.05	Existing MRL	0.05	LOQ		
Other tree nuts	0.05	Existing MRL	0.05	LOQ		
Apples	0.8	FAO (2013)	0.16	STMR-RAC		
Pears	0.8	FAO (2013)	0.16	STMR-RAC		
Quinces	0.8	FAO (2013)	0.16	STMR-RAC		
Medlar	0.8	FAO (2013)	0.16	STMR-RAC		
Loquats/Japanese medlars	0.8	FAO (2013)	0.16	STMR-RAC		
Other pome fruit	0.8	FAO (2013)	0.16	STMR-RAC		
Apricots	0.7	EFSA (2017)	0.17	STMR-RAC		
Cherries (sweet)	0.3	Existing MRL	0.3	MRL		
Peaches	0.5	European Commission (2008)	0.15	STMR-RAC		
Plums	0.5	Existing MRL	0.5	MRL		
Other stone fruit	0.1	Existing MRL	0.1	MRL		
Table grapes	3	FAO (2013)	0.52	STMR-RAC		
Wine grapes	3	FAO (2013)	0.52	STMR-RAC		
Strawberries	2	FAO (2018)	0.42	STMR-RAC		
Blackberries	1.5	EFSA (2012)	0.04	STMR-RAC		
Dewberries	0.1	Existing MRL	0.1	MRL		
Raspberries (red and yellow)	1.5	EFSA (2012)	0.04	STMR-RAC		
Other cane fruit	0.1	Existing MRL	0.1	MRL		
Blueberries	4	FAO (2018)	1	STMR-RAC		
Cranberries	0.1	Existing MRL	0.1	MRL		
Currants (red, black and white)	0.2	Existing MRL	0.2	MRL		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Gooseberries (green, red and yellow)	0.1	Existing MRL	0.1	MRL		
Rose hips	0.1	Existing MRL	0.1	MRL		
Mulberries (black and white)	0.1	Existing MRL	0.1	MRL		
Azarole/ Mediteranean medlar	0.8	FAO (2013)	0.16	STMR-RAC		
Elderberries	0.1	Existing MRL	0.1	MRL		
Other other small fruit & berries	0.1	Existing MRL	0.1	MRL		
Dates	0.1	Existing MRL	0.1	MRL		
Figs	0.1	Existing MRL	0.1	MRL		
Table olives	2	European Commission (2008)	0.47	STMR-RAC		
Kumquats	0.6	FAO (2013)	0.16	STMR-RAC		
Carambolas	0.1	Existing MRL	0.1	MRL		
Kaki/Japanese persimmons	0.8	FAO (2013)	0.16	STMR-RAC		
Jambuls/ jambolans	0.1	Existing MRL	0.1	MRL		
Other miscellaneous fruit (edible peel)	0.1	Existing MRL	0.1	MRL		
Kiwi fruits (green, red, yellow)	0.1	Existing MRL	0.1	MRL		
Litchis/lychees	0.1	Existing MRL	0.1	MRL		
Passionfruits/ maracujas	0.1	Existing MRL	0.1	MRL		
Prickly pears/ cactus fruits	0.15	FAO (2018)	0.034	STMR-RAC		
Star apples/ cainitos	0.1	Existing MRL	0.1	MRL		
American persimmon/ Virginia kaki	0.1	Existing MRL	0.1	MRL		
Other miscellaneous fruit (inedible peel, small)	0.1	Existing MRL	0.1	MRL		
Avocados	0.6	FAO (2015)	0.05	STMR-RAC		
Bananas	0.1	FAO (2008)	0.02	STMR-RAC		
Mangoes	0.1	Existing MRL	0.1	MRL		
Papayas	0.2	EFSA (2013)	0.01	STMR-RAC		
Granate apples/ pomegranates	0.1	Existing MRL	0.1	MRL		
Cherimoyas	0.1	Existing MRL	0.1	MRL		
Guavas	0.1	Existing MRL	0.1	MRL		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Pineapples	0.1	Existing MRL	0.1	MRL		
Breadfruits	0.1	Existing MRL	0.1	MRL		
Durians	0.1	Existing MRL	0.1	MRL		
Soursops/ guanabanas	0.1	Existing MRL	0.1	MRL		
Other miscallaneous fruit (inedible peel, large)	0.1	Existing MRL	0.1	MRL		
Potatoes	0.1	Existing MRL	0.1	MRL		
Cassava roots/ manioc	0.1	Existing MRL	0.1	MRL		
Sweet potatoes	0.1	Existing MRL	0.1	MRL		
Yams	0.1	Existing MRL	0.1	MRL		
Arrowroots	0.1	Existing MRL	0.1	MRL		
Other tropical root and tuber vegetables	0.1	Existing MRL	0.1	MRL		
Beetroots	0.4	EFSA (2013)	0.08	STMR-RAC		
Carrots	0.4	EFSA (2013)	0.08	STMR-RAC		
Celeriacs/turnip rooted celeries	2	Existing MRL	2	MRL		
Horseradishes	0.4	EFSA (2013)	0.08	STMR-RAC		
Jerusalem artichokes	0.4	EFSA (2013)	0.08	STMR-RAC		
Parsnips	0.4	EFSA (2013)	0.08	STMR-RAC		
Parsley roots/ Hamburg roots parsley	0.4	EFSA (2013)	0.08	STMR-RAC		
Radishes	0.4	EFSA (2013)	0.08	STMR-RAC		
Salsifies	0.4	EFSA (2013)	0.08	STMR-RAC		
Swedes/rutabagas	0.4	EFSA (2013)	0.08	STMR-RAC		
Turnips	0.4	EFSA (2013)	0.08	STMR-RAC		
Other root and tuber vegetables	0.4	EFSA (2013)	0.08	STMR-RAC		
Garlic	0.5	EFSA (2013)	0.01	STMR-RAC		
Onions	0.5	EFSA (2013)	0.01	STMR-RAC		
Shallots	0.5	EFSA (2013)	0.01	STMR-RAC		
Spring onions/ green onions and Welsh onions	9	FAO (2013)	2.8	STMR-RAC		
Other bulb vegetables	0.5	EFSA (2013)	0.01	STMR-RAC		
Tomatoes	2	European Commission (2008)	0.72	STMR-RAC		
Sweet peppers/ bell peppers	0.9	FAO (2017)	0.24	STMR-RAC		
Aubergines/egg plants	0.6	EFSA (2014a)	0.18	STMR-RAC		
Okra/lady's fingers	0.6	FAO (2018)	0.18	STMR-RAC		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Other solanaceae	0.6	FAO (2018)	0.18	STMR-RAC		
Cucumbers	0.3	EFSA (2012)	0.01	STMR-RAC		
Gherkins	0.3	EFSA (2012)	0.01	STMR-RAC		
Courgettes	0.3	EFSA (2012)	0.01	STMR-RAC		
Other cucurbits - edible peel	0.3	Existing MRL	0.3	MRL		
Melons	0.2	EFSA (2013)	0.01	STMR-RAC		
Pumpkins	0.2	EFSA (2013)	0.01	STMR-RAC		
Watermelons	0.2	EFSA (2013)	0.01	STMR-RAC		
Other cucurbits - inedible peel	0.2	EFSA (2013)	0.01	STMR-RAC		
Sweet corn	0.05	Existing MRL	0.05	LOQ		
Other fruiting vegetables	0.6					
Broccoli	1	EFSA (2011)	0.13	STMR-RAC		
Cauliflowers	0.2	FAO (2008)	0.02	STMR-RAC		
Other flowering brassica	0.08	EFSA (2018)	0.01	STMR-RAC		
Head brassica						
Brussels sprouts	0.4	EFSA (2018)	0.07	STMR-RAC		
Head cabbages	0.3	EFSA (2017)	0.02	STMR-RAC		
Other head brassica	0.3	Existing MRL	0.3	MRL		
Leafy brassica	2					
Chinese cabbages/pe-tsai	2	Existing MRL	2	MRL		
Kales	2	Existing MRL	2	MRL		
Other leafy brassica	2	Existing MRL	2	MRL		
Kohlrabies	0.05	Existing MRL	0.05	LOQ		
Lamb's lettuce/ corn salads	7	EFSA (2014)	1.45	STMR-RAC		
Lettuces	4	EFSA (2017)	0.52	STMR-RAC		
Escaroles/broad-leaved endives	3	EFSA (2018)	0.33	STMR-RAC		
Cress and other sprouts and shoots	4	EFSA (2017)	0.52	STMR-RAC		
Land cress	4	EFSA (2017)	0.52	STMR-RAC		
Roman rocket/ rucola	3	EFSA (2018)	0.33	STMR-RAC		
Red mustards	4	EFSA (2017)	0.52	STMR-RAC		
Baby leaf crops (including brassica species)	4	EFSA (2017)	0.52	STMR-RAC		
Other lettuce and other salad plants	4	EFSA (2017)	0.52	STMR-RAC		
Spinaches	3	EFSA (2018)	0.33	STMR-RAC		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Purslanes	3	EFSA (2018)	0.33	STMR-RAC		
Chards/beet leaves	4	EFSA (2017)	0.52	STMR-RAC		
Other spinach and similar	3	EFSA (2018)	0.33	STMR-RAC		
Grape leaves and similar species	0.05	Existing MRL	0.05	LOQ		
Watercress	0.5	Existing MRL	0.5	MRL		
Witloofs/Belgian endives	4	EFSA (2018)	1.3	STMR-RAC		
Chervil	10	EFSA (2009)	4.65	STMR-RAC		
Chives	4	EFSA (2017)	0.52	STMR-RAC		
Celery leaves	10	EFSA (2009)	4.65	STMR-RAC		
Parsley	10	EFSA (2009)	4.65	STMR-RAC		
Sage	4	EFSA (2017)	0.52	STMR-RAC		
Rosemary	4	EFSA (2017)	0.52	STMR-RAC		
Thyme	4	EFSA (2017)	0.52	STMR-RAC		
Basil and edible flowers	10	EFSA (2009)	4.65	STMR-RAC		
Laurel/bay leaves	4	EFSA (2017)	0.52	STMR-RAC		
Tarragon	4	EFSA (2017)	0.52	STMR-RAC		
Other herbs	4	EFSA (2017)	0.52	STMR-RAC		
Beans (with pods)	1	Existing MRL	1	MRL		
Beans (without pods)	1	Existing MRL	1	MRL		
Peas (with pods)	1	Existing MRL	1	MRL		
Peas (without pods)	1	Existing MRL	1	MRL		
Lentils (fresh)	0.05	Existing MRL	0.05	LOQ		
Other legume vegetables (fresh)	0.05	Existing MRL	0.05	LOQ		
Asparagus	0.05	Existing MRL	0.05	LOQ		
Cardoons	7	EFSA (2017)	1.22	STMR-RAC		
Celeries	7	EFSA (2017)	1.22	STMR-RAC		
Florence fennels	5	EFSA (2009)	1.66	STMR-RAC		
Globe artichokes	1.5	FAO (2018)	0.51	STMR-RAC		
Leeks	0.6	EFSA (2017)	0.13	STMR-RAC		
Rhubarbs	5	EFSA (2018)	0.7	STMR-RAC		
Bamboo shoots	0.05	Existing MRL	0.05	LOQ		
Palm hearts	0.05	Existing MRL	0.05	LOQ		
Other stem vegetables	0.05	Existing MRL	0.05	LOQ		
Cultivated fungi	0.05	Existing MRL	0.05	LOQ		
Wild fungi	0.05	Existing MRL	0.05	LOQ		
Mosses and lichens	0.05	Existing MRL	0.05	LOQ		
Algae and prokaryotes organisms	0.05	Existing MRL	0.05	LOQ		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Beans	0.06	EFSA (2017)	0.02	STMR-RAC		
Lentils	0.06	EFSA (2017)	0.02	STMR-RAC		
Peas	0.15	FAO (2018)	0.028	STMR-RAC		
Lupins/lupini beans	0.06	EFSA (2017)	0.02	STMR-RAC		
Other pulses	0.06	EFSA (2017)	0.02	STMR-RAC		
Linseeds	0.2	Existing MRL	0.2	MRL		
Peanuts/ groundnuts	0.05	Existing MRL	0.05	LOQ		
Poppy seeds	0.05	Existing MRL	0.05	LOQ		
Sesame seeds	0.05	Existing MRL	0.05	LOQ		
Sunflower seeds	0.05	Existing MRL	0.05	LOQ		
Rapeseeds/canola seeds	0.5	Existing MRL	0.5	MRL		
Soyabeans	0.1	FAO (2015)	0.01	STMR-RAC		
Mustard seeds	0.2	Existing MRL	0.2	MRL		
Cotton seeds	0.05	Existing MRL	0.05	LOQ		
Pumpkin seeds	0.05	Existing MRL	0.05	LOQ		
Safflower seeds	0.05	Existing MRL	0.05	LOQ		
Borage seeds	0.05	Existing MRL	0.05	LOQ		
Gold of pleasure seeds	0.05	Existing MRL	0.05	LOQ		
Hemp seeds	0.05	Existing MRL	0.05	LOQ		
Castor beans	0.05	Existing MRL	0.05	LOQ		
Other oilseeds	0.05	Existing MRL	0.05	LOQ		
Olives for oil production	2	European Commission (2008)	0.47	STMR-RAC		
Oil palm kernels	0.05	Existing MRL	0.05	LOQ		
Oil palm fruits	0.05	Existing MRL	0.05	LOQ		
Kapok	0.05	Existing MRL	0.05	LOQ		
Other oilfruit	0.05	Existing MRL	0.05	LOQ		
Barley	0.3	EFSA (2017)	0.02	STMR-RAC		
Buckwheat and other pseudo-cereals	0.05	Existing MRL	0.05	LOQ		
Maize/corn	0.05	Existing MRL	0.05	LOQ		
Common millet/ proso millet	0.05	Existing MRL	0.05	LOQ		
Oat	0.05	Existing MRL	0.05	LOQ		
Rice	3	FAO (2018)	0.88	STMR-RAC		
Rye	**0.3**	**MRL proposal**	**0.01**	**STMR-RAC (Table B.1.2.1)**	**0.01**	**STMR-RAC (Table B.1.2.1)**
Sorghum	0.05	Existing MRL	0.05	LOQ		
Wheat	**0.3**	**MRL proposal**	**0.01**	**STMR-RAC (Table B.1.2.1)**	**0.01**	**STMR-RAC (Table B.1.2.1)**

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Other cereals	0.05	Existing MRL	0.05	LOQ	Acute exposure assessment performed only for the crops under consideration.	
Tea (dried leaves of Camellia sinensis)	0.05	Existing MRL	0.05	LOQ		
Coffee beans	0.05	Existing MRL	0.05	LOQ		
Chamomille	20	Existing MRL	20	MRL		
Hybiscus/roselle	20	Existing MRL	20	MRL		
Rose	20	Existing MRL	20	MRL		
Jasmine	20	Existing MRL	20	MRL		
Lime/linden	20	Existing MRL	20	MRL		
Other herbal infusions (dried flowers)	20	Existing MRL	20	MRL		
Strawberry leaves	20	Existing MRL	20	MRL		
Rooibos	20	Existing MRL	20	MRL		
Mate/maté	20	Existing MRL	20	MRL		
Other herbal infusions (dried leaves)	20	Existing MRL	20	MRL		
Valerian root	20	Existing MRL	20	MRL		
Ginseng root	20	Existing MRL	20	MRL		
Other herbal infusions (dried roots)	20	Existing MRL	20	MRL		
Cocoa beans	0.05	Existing MRL	0.05	LOQ		
Carobs/Staint John's bread	0.05	Existing MRL	0.05	LOQ		
HOPS (dried)	0.05	Existing MRL	0.05	LOQ		
Anise/aniseed	0.3	Existing MRL	0.3	MRL		
Black caraway/ black cumin	0.3	Existing MRL	0.3	MRL		
Celery seed	0.3	Existing MRL	0.3	MRL		
Coriander seed	0.3	Existing MRL	0.3	MRL		
Cumin seed	0.3	Existing MRL	0.3	MRL		
Dill seed	0.3	Existing MRL	0.3	MRL		
Fennel seed	0.3	Existing MRL	0.3	MRL		
Fenugreek	0.3	Existing MRL	0.3	MRL		
Nutmeg	0.3	Existing MRL	0.3	MRL		
Other spices (seeds)	0.3	Existing MRL	0.3	MRL		
Allspice/pimento	0.3	Existing MRL	0.3	MRL		
Sichuan pepper	0.3	Existing MRL	0.3	MRL		
Caraway	0.3	Existing MRL	0.3	MRL		
Cardamom	0.3	Existing MRL	0.3	MRL		
Juniper berry	0.3	Existing MRL	0.3	MRL		
Peppercorn (black, green and white)	0.3	Existing MRL	0.3	MRL		
Vanilla pods	0.3	Existing MRL	0.3	MRL		

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Tamarind	0.3	Existing MRL	0.3	MRL		
Other spices (fruits)	0.3	Existing MRL	0.3	MRL		
Cinnamon	0.3	Existing MRL	0.3	MRL		
Other spices (bark)	0.3	Existing MRL	0.3	MRL		
Liquorice	3	EFSA (2017)	0.64	STMR-RAC		
Ginger	3	EFSA (2017)	0.64	STMR-RAC		
Turmeric/curcuma	3	EFSA (2017)	0.64	STMR-RAC		
Horseradish, root spices	2.8	EFSA (2017)	0.64	STMR-RAC		
Other spices (roots)	3	EFSA (2017)	0.64	STMR-RAC		
Cloves	0.3	Existing MRL	0.3	MRL		
Capers	0.3	Existing MRL	0.3	MRL		
Other spices (buds)	0.3	Existing MRL	0.3	MRL		
Saffron	0.3	Existing MRL	0.3	MRL		
Other spices (flower stigma)	0.3	Existing MRL	0.3	MRL		
Mace	0.3	Existing MRL	0.3	MRL		
Other spices (aril)	0.3	Existing MRL	0.3	MRL		
Sugar beet roots	0.2	EFSA (2013), FAO (2008)	0.02	STMR-RAC		
Sugar canes	0.05	Existing MRL	0.05	LOQ		
Chicory roots	0.6	EFSA (2013)	0.2	STMR-RAC		
Other sugar plants	0.05	Existing MRL	0.05	LOQ		
Risk assessment residue definition: Difenoconazole alcohol (CGA-205375), expressed as difenoconazole						
Swine: Muscle/ meat	0.05	FAO (2011)	0.01	STMR-RAC	Acute exposure assessment performed only for the crops under consideration (wheat and rye grain). As no modification of the existing EU MRLs for difenoconazole in animal commodities on the basis of new intended uses of difenoconazole on wheat and rye was proposed, the acute exposure assessment for these commodities was not performed in the present opinion.	
Swine: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Swine: Liver	0.2	FAO (2011)	0.041	STMR-RAC		
Swine: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Swine: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		
Swine: Other products	0.1	Existing MRL	0.1	MRL		
Bovine: Muscle/ meat	0.05	FAO (2011)	0.01	STMR-RAC		
Bovine: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Bovine: Liver	0.2	FAO (2011)	0.041	STMR-RAC		
Bovine: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Bovine: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		

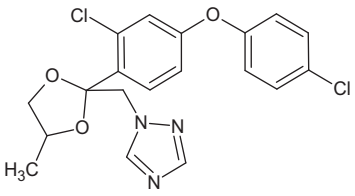
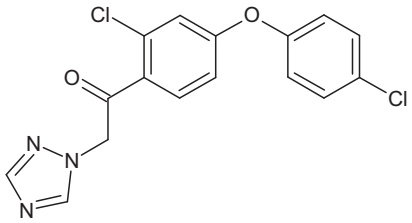
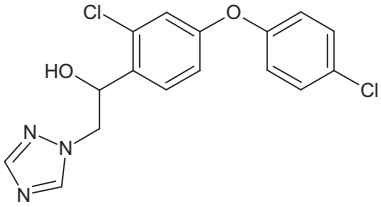
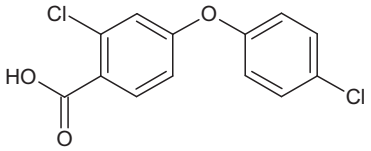
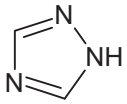
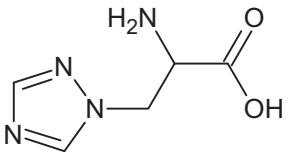
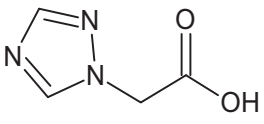
Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Bovine: Other products	0.1	Existing MRL	0.1	MRL		
Sheep: Muscle/ meat	0.05	FAO (2011)	0.01	STMR-RAC		
Sheep: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Sheep: Liver	0.2	FAO (2011)	0.041	STMR-RAC		
Sheep: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Sheep: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		
Sheep: other products	0.1	Existing MRL	0.1	MRL		
Goat: Muscle/ meat	0.05	FAO (2011)	0.01	STMR-RAC		
Goat: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Goat: Liver	0.2	FAO (2011)	0.041	STMR-RAC		
Goat: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Goat: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		
Goat: other products	0.1	Existing MRL	0.1	MRL		
Equine: Muscle/ meat	0.05	FAO (2011)	0.01	STMR-RAC		
Equine: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Equine: Liver	0.2	FAO (2011)	0.041	STMR-RAC		
Equine: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Equine: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		
Equine: Other products	0.1	Existing MRL	0.1	MRL		
Poultry: Muscle/ meat	0.1	Existing MRL	0.1	MRL		
Poultry: Fat tissue	0.1	Existing MRL	0.1	MRL		
Poultry: Liver	0.1	Existing MRL	0.1	MRL		
Poultry: Kidney	0.1	Existing MRL	0.1	MRL		
Poultry: Edible offals (other than liver and kidney)	0.1	Existing MRL	0.1	MRL		
Poultry: Other products	0.1	Existing MRL	0.1	MRL		
Other farmed animals: Muscle/ meat	0.05	FAO (2011)	0.012	STMR-RAC		
Other farmed animals: Fat tissue	0.05	FAO (2011)	0.012	STMR-RAC		
Other farmed animals: Liver	0.2	FAO (2011)	0.041	STMR-RAC		

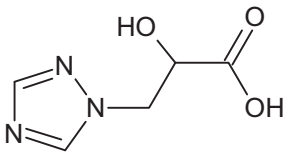
Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[(a)] (mg/kg)	Comment	Input value[(a)] (mg/kg)	Comment
Other farmed animals: Kidney	0.2	FAO (2011)	0.041	STMR-RAC		
Other farmed animals: Edible offals (other than liver and kidney)	0.2	FAO (2011)	0.041	STMR-RAC		
Other farmed animals: Other products	0.1	Existing MRL	0.1	MRL		
Milk: Cattle	0.005	FAO (2011)	0.005	STMR-RAC		
Milk: Sheep	0.005	FAO (2011)	0.005	STMR-RAC		
Milk: Goat	0.005	FAO (2011)	0.005	STMR-RAC		
Milk: Horse	0.005	FAO (2011)	0.005	STMR-RAC		
Milk: Others	0.005	FAO (2011)	0.005	STMR-RAC		
Eggs: Chicken	0.05	Existing MRL	0.05	LOQ		
Eggs: Duck	0.05	Existing MRL	0.05	LOQ		
Eggs: Goose	0.05	Existing MRL	0.05	LOQ		
Eggs: Quail	0.05	Existing MRL	0.05	LOQ		
Eggs: Others	0.05	Existing MRL	0.05	LOQ		
Honey and other apiculture products	0.05		0.05	LOQ		
Amphibians and reptiles	0.05		0.05	LOQ		
Terrestrial invertebrate animals	0.05		0.05	LOQ		
Wild terrestrial vertebrate animals	0.05		0.05	LOQ		

STMR-RAC: supervised trials median residue in raw agricultural commodity; HR-RAC: highest residue in raw agricultural commodity; PeF: Peeling factor.

(a): Figures in the table are rounded to two digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce dietary burden calculations, the unrounded values need to be used.

Appendix E – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Difenoconazole	3-chloro-4-[(2*RS*,4*RS*;2*RS*,4*SR*)-4-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether BQYJATMQXGBDHF-UHFFFAOYSA-N Clc1ccc(cc1)Oc1ccc(c(Cl)c1)C1(Cn2ncnc2)OCC(C)O1	
Difenoconazole-ketone CGA205374	1-[2-chloro-4-(4-chlorophenoxy)-phenyl]-2-[1,2,4] triazol-1-yl-ethanone HCYKJGWQCCFTNV-UHFFFAOYSA-N O=C(Cn1cncn1)c1ccc(Oc2ccc(Cl)cc2)cc1Cl	
Difenoconazole alcohol CGA205375	1-[2-chloro-4-(4-chlorophenoxy)phenyl]-2-(1*H*-1,2,4-triazol-1-yl)ethanol OC(Cn1cncn1)c1ccc(Oc2ccc(Cl)cc2)cc1Cl NBYSKMWDHCZSIP-UHFFFAOYSA-N	
Difenoconazole benzoic acid CGA189138	2-chloro-4-(4-chloro-phenoxy)-benzoic acid OC(=O)c1ccc(cc1Cl)Oc1ccc(Cl)cc1 PQYCPVXNIJXBCU-UHFFFAOYSA-N	
Triazole derivative metabolites		
1,2,4-triazole 1,2,4-T	1*H*-1,2,4-triazole c1ncnn1 NSPMIYGKQJPBQR-UHFFFAOYSA-N	
Triazole alanine TA	3-(1*H*-1,2,4-triazol-1-yl)-D,L-alanine NC(Cn1cncn1)C(=O)O XVWFTOJHOHJIMQ-UHFFFAOYSA-N	
Triazole acetic acid TAA	1*H*-1,2,4-triazol-1-ylacetic acid O=C(O)Cn1cncn1 RXDBSQXFIWBJSR-UHFFFAOYSA-N	

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Triazole lactic acid or Triazole hydroxy propionic acid TLA	(2*RS*)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl) propanoic acid OC(Cn1cncn1)C(=O)O KJRGHGWETVMENC-UHFFFAOYSA-N	

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.
(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 7 July 2021).
(c): ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021).