REASONED OPINION

Reasoned opinion on the modification of the existing MRLs for difenoconazole in lettuce and other salad plants including Brassicaceae and in basil (mint)[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, Germany, hereafter referred to as the evaluating Member State (EMS), received an application from the Landwirtschaftskammer Nordrhein-Westfalen plant protection service to modify the existing maximum residue limits (MRLs) for the active substance difenoconazole in lettuce and other salad plants including Brassicaceae. Furthermore, Belgium, referred also to as the evaluating Member State (EMS), received an application from the Belgian Federal Public Service Health, Food chain safety and Environment to modify the existing MRL for the active substance difenoconazole in basil (mint). According to EFSA the data are sufficient to derive MRL proposals of 0.7 mg/kg for the proposed uses on lettuce and scarole, 7 mg/kg on lamb's lettuce, 1.5 mg/kg on rucola/rocket and 15 mg/kg on basil (mint). Adequate analytical enforcement methods are available to control the residues of difenoconazole in the commodities under consideration. Based on the risk assessment results, EFSA concludes that the proposed uses of difenoconazole on lettuce, scarole, lamb's lettuce, rucola and mint will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

KEY WORDS

Difenoconazole, leafy vegetables, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, triazole fungicides, triazole derivative metabolites (TDMs)

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[2] Correspondence: pesticides.mrl@efsa.europa.eu

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SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, Germany, hereafter referred to as the evaluating Member State (EMS), received an application from the Landwirtschaftskammer Nordrhein-Westfalen plant protection service to modify the existing maximum residue limits (MRLs) for difenoconazole in lettuce and other salad plants including Brassicaceae. Furthermore, Belgium, referred also to as the EMS, received an application from the Belgian Federal Public Service Health, Food chain safety and Environment to modify the existing MRL for difenoconazole in basil (mint). Germany and Belgium drafted evaluation reports in accordance with Article 8 of Regulation (EC) No 396/2005, which were submitted to the European Commission and forwarded to EFSA on 24/02/2014 and 07/05/2014, respectively.

EFSA bases its assessment on the evaluation reports submitted by the EMS (Germany, 2013; Belgium, 2014), the conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole (EFSA, 2011a), the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) Evaluation reports (FAO, 2008, 2010) as well as the conclusions from previous EFSA reasoned opinions on difenoconazole (EFSA, 2009, 2010, 2011b, 2012, 2013, 2014).

The toxicological profile of difenoconazole was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to propose an acceptable daily intake (ADI) of 0.01 mg/kg bw per day and an acute reference dose (ARfD) of 0.16 mg/kg bw. EFSA defined toxicological reference values also for the triazole derivative metabolites (TDMs).

The metabolism of difenoconazole in primary crops was investigated following foliar applications in fruit crops (tomato, grape), root/tuber crops (potato) and pulse/oilseed crops (rape seed) and following foliar and seed treatments in cereals (wheat). From these studies the peer review established the residue definition for enforcement as difenoconazole (sum of isomers). For risk assessment, considering that the TDMs are toxicologically relevant metabolites present in significant levels, two separate plant residue definitions were proposed: 1) difenoconazole (sum of isomers) and 2) provisionally, TDMs.

EFSA concludes that the submitted residue trials are sufficient to derive MRL proposals of 0.7 mg/kg for the proposed uses on lettuce and scarole (broad-leaf endive), 7 mg/kg for lamb's lettuce, 1.5 mg/kg for rucola/rocket and 15 mg/kg for basil (mint). The MRL proposal of 15 mg/kg for basil (mint) was extrapolated from indoor trials on parsley conducted with three applications instead of two.

However, it should be noted that based on the same dataset (indoor parsley residue trials), an MRL of 10 mg/kg was finally agreed on chervil, parsley and celery leaves following the discussions in the Standing Committee on the Food Chain and Animal Health (SCoFCAH) and published under Regulation (EU) No 459/2010. Therefore, it would be consistent to propose the same MRL value for basil, chervil, parsley and celery leaves (e.g. to align all MRLs to the value of 15 mg/kg proposed in this MRL application, or optionally, to maintain the MRL of 10 mg/kg for chervil, parsley and celery leaves and to adopt a value of 10 mg/kg for basil, considering that the highest level was 5.68 mg/kg only).

Adequate analytical enforcement methods are available to control the residues of difenoconazole in the commodities under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg.

Specific studies to assess the magnitude of difenoconazole residues are not triggered for lettuce, lamb's lettuce, rucola and basil (mint) since these crops are mostly eaten raw. However, processing studies on scarole (cooked) are required.

It is concluded that residues of parent difenoconazole are not expected in rotational crops, provided that the active substance is applied according to the proposed good agricultural practice (GAP) at a maximum seasonal dose rate of 760 g/ha. In contrast, the possible occurrence of the TDMs in

rotational crops has not been addressed. This point would need to be considered further, when the confirmatory data requested in the framework on the peer review are available and when a global and harmonised approach for the assessment of the triazole chemical class compounds is available

Residues of difenoconazole in commodities of animal origin were not assessed in the framework of this application, since the leafy crops under consideration are normally not fed to livestock.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The total calculated intake accounted for up to 86 % of the ADI (WHO cluster B). For the crops under consideration in this application, the contribution of difenoconazole residues to the total consumer exposure accounted for less than 1 % of the ADI. Acute consumer risk is not expected regarding the MRL proposals for the crops under consideration in this application. The highest acute dietary intake was calculated to be 27 % of the ARfD for scarole (broad-leaf endive).

EFSA concludes that the proposed use of difenoconazole on the crops under consideration in this application will not result in a consumer exposure exceeding the toxicological reference values and, therefore, is unlikely to pose a consumer health risk.

However, EFSA emphasises that the above assessment does not yet take into consideration the TDMs. Since these metabolites may be generated by several pesticides belonging to the triazole fungicides, EFSA recommends that a separate risk assessment should be performed for TDMs when the confirmatory data requested for triazole compounds, in the framework of Regulation (EC) No 1107/2009, have been evaluated and a general methodology on the risk assessment of triazole compounds, and their triazole derivative metabolites, is available. Furthermore, since difenoconazole consists of diastereo isomers, the preferential metabolism/degradation of each enantiomer in plants, as well as the possible impact on the consumer risk assessment, need to be further addressed. Therefore, currently, the overall consumer risk assessment has to be considered provisional.

Thus EFSA proposes to amend the existing MRLs as reported in the summary table.

SUMMARY TABLE

Code number (a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
Enforcement residue definition: difenoconazole (sum of isomers)				
0251010	Lamb's lettuce	0.05*	7	The MRL proposals are sufficiently supported by data and no consumer health risk was identified for the intended NEU outdoor uses of difenoconazole.
0251020	Lettuce	3	0.7	
0251030	Scarole	0.05*	0.7	
0251060	Rocket, rucola	2	1.5	
0256080	Basil (mint)	2	15 (10 optional)	The MRL proposal of 15 mg/kg was extrapolated from indoor trials on parsley conducted with 3 applications instead of 2, as proposed in the GAP reported for mint. This MRL covers the indoor and NEU outdoor uses of difenoconazole on mint. Since based on the same data set (indoor trials on parsley) EFSA would recommend to align the MRLs for basil, chervil, parsley and celery leaves to the value of 15 mg/kg, or optionally, to maintain the MRL of 10 mg/kg for chervil, parsley and celery leaves and to adopt a value of 10 mg/kg for basil, considering that the highest level was only 5.68 mg/kg.

(a): According to Annex I of Regulation (EC) No 396/2005.
(*): Indicates that the MRL is set at the limit of analytical quantification.

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BACKGROUND

Regulation (EC) No 396/2005[3] establishes the rules governing the setting of pesticide maximum residue limits (MRLs) at European Union level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC[4], repealed by Regulation (EC) No 1107/2009[5], shall submit to a Member State, when appropriate, an application to modify an MRL in accordance with the provisions of Article 7 of that Regulation.

Germany, hereafter referred to as the evaluating Member State (EMS), received an application from the Landwirtschaftskammer Nordrhein-Westfalen plant protection service[6] to modify the existing MRLs for the active substance difenoconazole in lettuce and other salad plants including Brassicaceae. Furthermore, Belgium, as an EMS, received an application from the Belgian Federal Public Service Health, Food chain safety and Environment[7] to modify the existing MRLs for the active substance difenoconazole in basil (including mint). These applications were notified to the European Commission and EFSA, and were subsequently evaluated respectively by Germany and Belgium in accordance with Article 8 of the Regulation.

After completion, the evaluation report was submitted to the European Commission who forwarded the applications, the evaluation reports and the supporting dossiers, prepared by Germany and Belgium, to EFSA on 04 February 2014 and 07 May 2014, respectively.

These applications were included in the EFSA Register of Questions with the respective reference numbers EFSA-Q-2014-00136 and EFSA-Q-2014-00395 and the following subject:

Difenoconazole – Application to modify the existing MRLs in lettuce and other salad plants including Brassicaceae

Difenoconazole - Application to modify the existing MRL in basil (including mint)

Germany proposed to raise the existing MRLs from the limit of quantification to 0.6 mg/kg for scarole, to 6 mg/kg for cress, land cress, red mustard, leaves and sprouts of Brassica spp. including turnip greens and other lettuce and salad plants, to raise the value of existing MRL from 0.05 mg/kg to 6 mg/kg for lamb's lettuce, from 2 mg/kg to 6 mg/kg for rocket and rucola and to decrease the existing MRL from 3 mg/kg to 0.6 mg/kg on lettuce. Belgium proposed to raise the value of the existing MRL for basil (mint) from 0.2 mg/kg to 10 mg/kg. EFSA proceeded with the assessment of the application and the evaluation reports as required by Article 10 of the Regulation.

TERMS OF REFERENCE

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation reports provided by the evaluating Member States, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more

[3] 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, 16.03.2005, p. 1-16.

[4] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1-32.

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

[6] Landwirtschaftskammer Nordrhein-Westfalen plant protection service, Siebengebirgsstrasse, 200, 53229, Germany

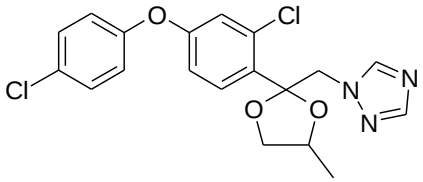
[7] Belgian Federal Public Service Health, Food chain safety and Environment, DG4, Place Victor Horta, 40 box 10, 1060, Brussels, Belgium.

detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

In this particular case the deadlines for providing the reasoned opinions were at the latest, the 04 May and 07 August 2014, respectively.

THE ACTIVE SUBSTANCE AND ITS USE PATTERN

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) and its chemical structure is as follows:



Molecular weight: 406.3 g/mol

Difenoconazole is a systemic triazole fungicide applied by foliar spray or seed treatment that controls broad-spectrum foliar, seed and soilborne diseases, caused by *Ascomycetes*, *Basidiomycetes* and *Deuteromycetes*. Difenoconazole acts by interference with ergosterol biosynthesis in target fungi by inhibition of the C-14-demethylation of sterols.

Difenoconazole was evaluated in the framework of Council Directive 91/414/EEC with Sweden designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Directive 2008/69/EC[8] which entered into force on 01 January 2009 for use as fungicide only. In accordance with Commission Regulation (EU) No 540/2011[9], difenoconazole is approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC. The representative uses evaluated under the peer review were foliar applications on pome fruit and carrots and as a seed treatment on cereals. Further confirmatory data were required under Regulation (EU) No 1100/2011[10] regarding residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops, processed commodities and products of animal origin and the preferential metabolism of each enantiomer in plants, animals and environment and the possible impact on the consumer risk assessment.

The EU MRLs for difenoconazole are established in Annex IIIA of Regulation (EC) No 396/2005. Since the entry into force of this Regulation, EFSA has issued several reasoned opinions on the modification of the existing MRLs for difenoconazole (EFSA, 2009, 2010, 2011b, 2012, 2013) that were implemented in the EU legislation, the last one, by regulation (EU) No 834/2013[11]. In addition, in 2014, EFSA has published a reasoned opinion on the modification of the MRLs for peppers and aubergines (EFSA, 2014), that has not yet been taken over in the EU legislation.

[8] 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, 02.07.2008, p. 9–14.

[9] Commission Regulation (EU) No 540/2011 of 23 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.06.2011, p. 1-186.

[10] 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, 01.11.2011, p. 10-14.

[11] Commission Regulation (EU) No 834/2013 of 30 August 2013 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acequinocyl, bixafen, diazinon, difenoconazole, etoxazole, fenhexamid, fludioxonil, isopyrazam, lambda-cyhalothrin, profenofos and prothioconazole in or on certain products. OJ L 233/11, 31.8.2013, p. 11-42

Codex Alimentarius has established the Codex Maximum Residue Limits (CXLs) for a wide range of commodities, including lettuce (head, leaf) for which a CXL is set at 2 mg/kg.

The details of the intended good agricultural practices **(**GAPs) for difenoconazole are given in Appendix A.

ASSESSMENT

EFSA bases its assessment on the evaluation reports submitted by the EMS (Germany, 2013; Belgium, 2014), the conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole (EFSA, 2011a), the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) Evaluation reports (FAO, 2008, 2010) as well as the conclusions from previous EFSA reasoned opinions on difenoconazole (EFSA, 2009, 2010, 2011b, 2012, 2013, 2014). 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[12] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a-g, 2000, 2010a,b, 2011; OECD, 2011).

1. Method of analysis

1.1. Methods for enforcement of residues in food of plant origin

The analytical methods for the determination of difenoconazole residues in plant commodities were assessed in the framework of the peer review under Directive 91/414/EEC (Sweden, 2006; EFSA, 2011a). The multi-residues DFG S19 method using LC-MS/MS was sufficiently validated at the limit of quantification (LOQ) of 0.02 mg/kg for high water content commodities (apple, lettuce) and at the LOQ of 0.05 mg/kg for dry (wheat grain) and high oil content commodities (rape seed).

The multi-residue Quick, Easy, Cheap, Effective, Rugged, and Safe (method) (QuEChERS) method using high performance liquid chromatography with tandem mass spectrometry (LC-MS/MS) quantification and described in the European Standard EN 15662:2008 is also applicable. The method analyses difenoconazole residues in high water content, acidic and dry commodities with an LOQ of 0.01 mg/kg (CEN, 2008).

Hence, it can be concluded that difenoconazole can be enforced in food of plant origin with an LOQ of 0.01 mg/kg in high water content, acidic and dry commodities and with an LOQ of 0.05 mg/kg in high oil content commodities. Available methods are, however, not stereoselective.

1.2. Methods for enforcement of residues in food of animal origin

Analytical methods for the determination of residues in food of animal origin are not assessed in the current application, since the crops under consideration are normally not fed to livestock.

2. Mammalian toxicology

The toxicological profile of the active substance difenoconazole was assessed in the framework of the peer review under Directive 91/414/EEC (EFSA, 2011a). The data were sufficient to derive toxicological reference values for difenoconazole which are compiled in Table 2-1.

Toxicological data were submitted for the triazole derivative metabolites (1,2,4-triazole[13], triazole alanine[14], triazole lactic acid[15] and triazole acetic acid[16]) and were considered during the Pesticide Risk Assessment Peer Review (PRAPeR 14) expert meeting (January 2007). Based on these data, specific reference values were agreed for the triazole derivative metabolites and are reported in table 2-1.

[12] 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, 11.06.2011, p. 127-175.
[13] 1,2,4-triazole: 1*H*-[1,2,4]triazole. See Appendix E.
[14] triazole alanine: 2–amino-3-[1,2,4]triazol-1-yl-propionic acid. See Appendix E.
[15] triazole lactic acid: [1,2,4]triazol-1-yl-lactic acid. See Appendix E.
[16] triazole acetic acid: [1,2,4]triazol-1-yl-acetic acid. See Appendix E.

Table 2-1: Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
Difenoconazole					
ADI	EFSA	2011a	0.01 mg/kg bw per day	2-year rat study	100
ARfD	EFSA	2011a	0.16 mg/kg bw	Rat, developmental study	100
1,2,4-triazole, triazole acetic acid and triazole lactic acid[(a)]					
ADI	PRAPeR 14	2007	0.02 mg/kg bw per day	Rat, multigeneration study	1000
ARfD	PRAPeR 14	2007	0.06 mg/kg bw	Rat, developmental study	500
Triazole alanine					
ADI	PRAPeR 14	2007	0.1 mg/kg bw per day	Rat, developmental study	1000
ARfD	PRAPeR 14	2007	0.1 mg/kg bw	Rat, developmental study	1000

(a): EFSA PRAPeR Expert Meeting 14 concluded to apply the same toxicological reference values as for 1,2,4 triazole because of limited database available.

It is noted that JMPR established an ADI of 0.01 mg/kg bw per day and an ARfD of 0.3 mg/kg bw for difenoconazole (FAO, 2008).

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

The metabolism of difenoconazole in primary crops was evaluated in the Draft Assessment Report (DAR) (Sweden, 2006, 2010a, 2010b) and reviewed by EFSA (EFSA, 2011a) in the framework of the peer review under Directive 91/414/EEC. The overview of the metabolism study designs is presented in the table below.

Table 3-1: Summary of available metabolism studies in plants

Crop group	Crop	Application details				
		Method, F or G[(a)]	**Rate kg a.s./ha**	**No/ Interval**	**Sampling**	**Remarks**
Fruits	Tomatoes	G, Foliar	6 × 0.123	-	34 DALA	-
		G, Foliar	6 × 0.123 3 × 0.247	-	7, 16 DALA 40 DALA	-
	Grapes	F, Foliar	5 × 0.247	-	20 DALA	-
Roots/tubers	Potatoes	G, Foliar	6 × 0.123	7 days	11 DALA	
Pulses/oilseeds	Rape seed	F, Foliar	2 × 0.125	14	39 DALA	-
Cereals	Spring wheat	G, Seed treatment	25 & 30 g/100 kg	-	At harvest	
		G, Foliar	4 × 0.247	-	29 DALA	-

(a): Outdoor/field application (F) or glasshouse/protected crops/indoor application (G)

Based on these metabolism data, the residue for enforcement was defined as the parent compound difenoconazole only and is the same as the enforcement residue definition set in regulation (EC) No 396/2005. For risk assessment, considering that TDMs are toxicologically relevant metabolites present in significant proportions in crops, two separate plant residue definitions were proposed: 1) difenoconazole (sum of isomers) and 2) provisionally, TDMs. No final definition can be proposed for the TDMs at this stage, since a global and harmonized approach is needed for all compounds of the triazole chemical class. Meanwhile, since difenoconazole consists of diastereo isomers, and since the available analytical methods are not stereoselective, the proposed residue definitions for enforcement and risk assessment are derived for the sum of the R- and S- isomers.

For the uses on lettuce and other salad plants including Brassicacea and mint, EFSA concludes that the metabolism of difenoconazole is sufficiently addressed and the residue definitions for enforcement and risk assessment agreed in the peer review are applicable.

3.1.1.2. Magnitude of residues

In support of the MRL application, the EMS provided sufficient GAP-compliant residue trials for difenoconazole on lettuce (open leaf varieties), on lamb's lettuce, on rucola and on parsley with a possible extrapolation to basil (mint). No residue data on TDMs are available.

a. Lettuce

Fifteen residue trials on open leaf lettuce varieties, and compliant with the northern outdoor GAP (2 × 125 g/ha, PHI 14 days), were submitted. All trials were considered valid for deriving a MRL proposal of 0.7 mg/kg on lettuce.

According to the current guidance documents, an extrapolation to the whole lettuce and other salad plants group is possible. However, since a sufficient number of residue trials conducted on lamb's lettuce and rucola were submitted (see below), specific MRLs were derived on these crops and the extrapolation from the residue dataset on lettuce is proposed for scarole only.

b. Lamb's lettuce

Four outdoor residue trials on lamb's lettuce and compliant with the northern outdoor GAP (2 × 125 g/ha, PHI 14 days) were provided and are considered sufficient to derive an MRL proposal of 7 mg/kg, as lamb's lettuce is a minor crop in the northern outdoor zone.

c. Rucola, rocket

Four outdoor residue trials on rucola compliant with the northern outdoor GAP (2 × 125 g/ha, PHI 14 days) were provided and are considered sufficient to derive an MRL proposal of 1.5 mg/kg, as rucola is a minor crop in northern EU.

d. Mint (covered by the MRL on Basil (Code 0256080) in Annex I of Reg. (EC) No 396/2005)

Four indoor residue trials, conducted on parsley, were provided in support to an extrapolation to the basil group commodity, covering the MRL for mint. These trials have already been submitted to EFSA in 2009 in support of an MRL proposal of 12 mg/kg in parsley, chervil and celery leaves (EFSA, 2009), that was finally transposed in the EU legislation at a level of 10 mg/kg by Regulation (EU) No 459/2010[17].

[17] Commission Regulation (EU) No 459/2010 of 27 May 2010 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for certain pesticides in or on certain products. OJ L 129, 28.5/2010, p. 3-49.

The residue trials conducted on parsley with a total of three applications at 125 g/ha, are not in compliance with the indoor GAP proposed for mint with a total of two treatments only. However, having regard to the low contribution of the basil group commodities to the consumer diets, and since no consumer health risk was identified (see section 4), EFSA proposes to consider these residue trials as acceptable for extrapolation, bearing in mind that the MRL proposal might be slightly higher than necessary.

Based on the OECD MRL calculator (see Table 3-2), EFSA proposed an MRL of 15 mg/kg for the basil group, including mint.

However, it should be noted that based on the same dataset (indoor parsley residue trials), an MRL of 10 mg/kg was finally agreed for chervil, parsley and celery leaves following the discussions in the Standing Committee on the Food Chain and Animal Health **(**SCoFCAH) and published under Regulation (EU) No 459/2010. Therefore, it would be consistent to propose the same MRL value for basil, chervil, parsley and celery leaves (e.g. to align all MRLs to the value of 15 mg/kg proposed in this MRL application, or optionally, to maintain the MRL of 10 mg/kg for chervil, parsley and celery leaves and to adopt a value of 10 mg/kg for basil, considering that the highest residue (HR) is 5.68 mg/kg only).

In addition, three overdosed residue trials on parsley were provided to cover the northern outdoor use, conducted with two applications at 600 g/ha and resulting in residue levels of 0.17 to 0.54 mg/kg at 14 day pre-harvest interval (PHI). Since these overdosed outdoor trials result in significantly lower residue levels than the indoor trials, EFSA is of the opinion that no further northern European Union (NEU) GAP-compliant trials are required as a more critical residue situation is anticipated under the indoor conditions.

The results of the residue trials, the related risk assessment input values (highest residue, median residue) and the MRL proposals are summarised in Table 3-2.

The storage stability of difenoconazole in primary crops was investigated in the DAR under Directive 91/414/EEC (Sweden, 2006). Residues of difenoconazole were found to be stable at ≤ -20°C for up to 2 years in high water content (tomatoes, potatoes), high oil content (cotton) and dry matrices (wheat grain). Since the storage time intervals of the lettuce, lamb's lettuce and rucola residue trials samples were covered by the storage stability data, degradation of the difenoconazole residues during frozen storage of the trial samples is therefore not expected. Although the storage conditions for the reported residue trials on parsley were not reported by the EMS, it is assumed that storage periods longer than 24 months are not expected in practice.

According to the EMS, the analytical methods used to analyse the supervised residue trial samples has been sufficiently validated and was proven to be fit for the purpose (section 1.1).

EFSA concludes that the data are sufficient to derive a MRL proposal of 0.7 mg/kg on lettuce and scarole, 7 mg/kg on lamb's lettuce and 1.5 mg/kg on rucola/rocket to cover the proposed NEU outdoor GAP on these crops and a MRL proposal of 15 mg/kg on basil (mint) to cover the proposed NEU outdoor and indoor GAPs.

Table 3-2: Overview of the available residues trials data

Commodity	Residue region (a)	Outdoor /Indoor	Individual trial results (mg/kg) Enforcement & Risk assessment Difenoconazole (sum of isomers)	Median residue (mg/kg) (b)	Highest residue (mg/kg) (c)	MRL proposal (mg/kg)	Comments (e)
Lettuce → scarole (broad-leaf endive)	NEU	Outdoor	<0.01, 0.01, 0.060, 0.090, 0.13, 0.14, 0.16, 0.18, 0.22, 0.25, 0.26, 0.28, 0.29, 0.30, 0.49	0.18	0.49	0.7	R_{ber}=0.56 R_{max}=0.52 MRL_{OECD} = 0.7/0.7
Lamb's lettuce	NEU	Outdoor	0.49, 1.3, 1.6, 3.4	1.45	3.40	7	R_{ber}=5.9 R_{max}=8.0 MRL_{OECD} = 6.6/7.0
Rucola, rocket	NEU	Outdoor	0.026, 0.38, 0.50, 0.70	0.44	0.70	1.5	R_{ber}=1.3 R_{max}=1.9 MRL_{OECD} = 1.5/1.5
Parsley→ basil (mint)	NEU	Outdoor	GAP-compliant trials not available.	-	-	-	Possible extrapolation from the parsley residue trials conducted with 3 instead of 2 applications. R_{ber}=11.3 R_{max}=14.9 MRL_{OECD} = 12.6/15.0
	NEU	Indoor	1.17, 3.67, 5.63, 5.68	4.65	5.68	15 (optional 10)	

(a): NEU (Northern and Central Europe), SEU (Southern Europe and Mediterranean), EU (i.e. indoor use) or Import (country code) (EC, 2011).
(b): Median value of the individual trial results according to the enforcement residue definition.
(c): Highest value of the individual trial results according to the enforcement residue definition.
(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residue trial.
(e): Statistical estimation of MRLs according to the EU methodology (R_{ber}, R_{max}; EC, 1997g) and unrounded/rounded values according to the OECD methodology (OECD, 2011).
(*): Indicates that the MRL is set at the limit of analytical quantification.
n.a.: Not applicable.

3.1.1.3. Effect of industrial processing and/or household preparation

Difenoconazole was found to be stable under the standard hydrolysis conditions simulating pasteurisation, baking and sterilisation. Therefore, the same residue definition as for the primary crops also applies to processed commodities (EFSA, 2011a).

Specific studies to assess the magnitude of difenoconazole residues are not triggered for lettuce, lamb's lettuce, rucola and basil (mint) since these crops are mostly eaten raw. However, processing studies on scarole (cooked) are required (EC, 1997d).

3.1.2. Rotational crops

3.1.2.1. Preliminary considerations

Lettuce, scarole, lamb's lettuce, rucola and basil (mint) can be grown in rotation with other plants and therefore the possible occurrence of residues in succeeding crops resulting from the use on primary crops has to be assessed. The soil degradation studies demonstrated that difenoconazole has a moderate to high persistence (maximum DT_{50}: 242 days; DT_{90}: 879 days) (EFSA, 2011a) and further studies investigating the nature and magnitude of the compound uptake in rotational crops are therefore required (EC, 1997c).

3.1.2.2. Nature of residues

The metabolism of difenoconazole in rotational crops was peer reviewed (EFSA, 2011a). The parent difenoconazole was never detected whilst the triazole derivative metabolites (triazole alanine, triazole acetic acid and triazole lactic acid) were found to be the major compounds of the total residues in the edible parts of the rotational crops. EFSA derived the same residue definition for enforcement and risk assessment as established for the primary crops.

3.1.2.3. Magnitude of residues

Rotational field trials conducted on leafy crops (spinach) and root/tuber crops (carrots) following application of parent difenoconazole to bare soil at a rate of 750 g/ha one month prior to sowing, confirmed that residues of difenoconazole are not expected in rotational crop (EFSA, 2011a). In contrast, a data gap was set for further information on the TDMs residues since the reported field trials were limited to a single plant back interval and to two crop categories only.

Considering that the maximum seasonal application rate for the crops under consideration in this MRL application is 760 g/ha, EFSA concludes that significant residues of parent difenoconazole (> LOQ) are not expected in rotational crops.

However, the possible occurrence of the TDMs in rotational crops has not been addressed. This point would need to be considered further, when the confirmatory data requested in the framework on the peer review are available and when a global and harmonized approach for the assessment of the triazole chemical class compounds is available.

4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population[18] (EFSA, 2007).

[18] The calculation of the long-term exposure (chronic exposure) is based on the mean consumption data representative for 22 national diets collected from MS surveys plus one regional and four cluster diets from the WHO GEMS Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

For the calculation of chronic exposure, EFSA used the median residue values as derived from the residue trials on lettuce, scarole, lamb's lettuce, rucola and basil (mint) (see Table 3-2), the median residue values reported in previously issued EFSA reasoned opinions (EFSA, 2009, 2010, 2011b, 2012, 2013, 2014) and in the JMPR Evaluation Report (FAO, 2008, 2010). For the remaining commodities of plant and animal origin, the existing MRLs as established in Regulation (EC) No 396/2005 were used as input values.

The model assumptions for the long-term exposure assessment are considered to be sufficiently conservative for a first tier exposure assessment, assuming that all food items consumed have been treated with the active substance under consideration. In reality, it is not likely that all food consumed will contain residues at the MRL or at levels of the median residue values identified in supervised field trials. However, if this first tier exposure assessment does not exceed the toxicological reference value for long-term exposure (i.e. the ADI), a consumer health risk can be excluded with a high probability.

The acute exposure assessment was performed only with regard to the commodities under consideration assuming the consumption of a large portion of the food items as reported in the national food surveys and that these items contained residues at the highest level as observed in supervised field trials. A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation, when required (EFSA, 2007).

The input values used for the dietary exposure calculation are summarised in Table 4-1.

Table 4-1: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: difenoconazole (sum of isomers)				
Lettuce	0.18	Median residue	0.49	Highest residue
Scarole	0.18	Median residue	0.49	Highest residue
Lamb's lettuce	1.45	Median residue	3.40	Highest residue
Rucola, rocket	0.44	Median residue	0.70	Highest residue
Basil (mint)	4.65	Median residue	5.68	Highest residue
Peppers	0.17	Median residue (EFSA, 2014)	Acute risk assessment was undertaken only with regard to the crops under consideration.	
Aubergines	0.18	Median residue (EFSA, 2014)		
Quince	0.11	Median residue (EFSA, 2013)		
Papaya	0.07	Median residue (EFSA 2013)		
Carrot	0.1	Median residue (EFSA 2013)		
Beetroot	0.1	Median residue (EFSA 2013)		
Horseradish	0.1	Median residue (EFSA 2013)		
Jerusalem artichoke	0.1	Median residue (EFSA 2013)		
Parsnip	0.1	Median residue (EFSA 2013)		
Parsley root	0.1	Median residue (EFSA 2013)		
Salsify	0.1	Median residue (EFSA 2013)		

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Radish	0.1	Median residue (EFSA 2013)		
Garlic	0.01	Median residue (EFSA 2013)		
Onion (bulb)	0.01	Median residue (EFSA 2013)		
Shallot	0.01	Median residue (EFSA 2013)		
Spring onion	0.43	Median residue (EFSA 2013)		
Melon	0.05	Median residue (EFSA 2013)		
Pumpkin, watermelon	0.05	Median residue (EFSA 2013)		
Witloof	0.01	Median residue (EFSA 2013)		
Globe artichoke	0.36	Median residue (EFSA 2013)		
Rice	0.88	Median residue (EFSA 2013)		
Chicory roots	0.2	Median residue (EFSA 2013)		
Raspberries	0.04	Median residue (EFSA 2012)		
Blackberries	0.04	Median residue (EFSA 2012)		
Cucumbers, gherkins, courgettes	0.01	Median residue (EFSA 2012)		
Beet leaves	0.04	Median residue (EFSA 2011b)		
Broccoli	0.13	Median residue (EFSA 2011b)		
Cardoons	0.83	Median residue (EFSA 2011b)		
Strawberry	0.14	Median residue (EFSA 2011b)		
Swedes, turnips	0.08	Median residue (EFSA 2010)		
Fennel	1.66	Median residue (EFSA 2009)		
Parsley, chervil, celery	4.65	Median residue (EFSA 2009)		
Apples, pears	0.11	Median residue (EFSA, 2013)		
Olives (table and oil)	0.47	Median residue (FAO, 2008)		
Sugar beet	0.02	Median residue (FAO, 2008)		
Peaches	0.15	Median residue (FAO, 2008)		
Apricots	0.14	Median residue (EC, 2008)		
Tomatoes	0.72	Median residue (EC, 2008)		
Celery	0.94	Median residue (EC, 2008)		
Ruminant muscle[(b)]	0.0104	0.8 × Median muscle + 0.2 × Median fat (FAO, 2010)		
Ruminant fat	0.012	Median residue (FAO, 2010)		

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Ruminant liver, kidney	0.041	Median residue (FAO, 2010)		
Other commodities of food and animal origin	EU MRLS	See Reg. (EU) No 834/2013		

(b): Consumption figures in the EFSA PRIMo are expressed as muscle, therefore the median and highest residue values were calculated considering 80 % of the residue derived for muscle and 20 % of the residue derived for fat (FAO, 2009).

The estimated exposure was then compared with the toxicological reference values derived for difenoconazole (see Table 2-1). The results of the intake calculation are presented in Appendix B to this reasoned opinion.

The total calculated intake accounted for up to 86 % of the ADI (WHO Cluster B). The contribution of residues in lettuce, scarole, lamb's lettuce, rocket/rucola and basil (mint) to the total consumer exposure accounted for less than 1 % of the ADI (lettuce, Spanish adult).

Acute consumer risk is not expected in relation to the MRL proposals for lettuce, scarole, lamb's lettuce, rocket/rucola and basil (mint). The calculated maximum exposure in percentage of the ARfD was 27 % for scarole (broad-leaf endive) (Dutch child).

EFSA concludes that the intended uses of difenoconazole on lettuce, scarole, lamb's lettuce, rocket/rucola and basil (mint) will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a public health concern.

It is, however, highlighted that the consumer risk assessment has to be considered provisional since the possible contribution of TDM metabolites present in primary crops, rotational crops and in processed commodities to the overall consumer exposure was not considered. Furthermore, since difenoconazole consists of diastereo isomers, the preferential metabolism/degradation of each enantiomer in plants as well as the possible impact on the consumer risk assessment need to be further addressed. Therefore currently, the overall consumer risk assessment has to be considered provisional.

CONCLUSIONS AND RECOMMENDATIONS

The toxicological profile of difenoconazole was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to propose an ADI of 0.01 mg/kg bw per day and an ARfD of 0.16 mg/kg bw. EFSA defined toxicological reference values also for the TDMs.

The metabolism of difenoconazole in primary crops was investigated following foliar applications in fruit crops (tomato, grape), root/tuber crops (potato) and pulse/oilseed crops (rape seed) and following foliar and seed treatments in cereals (wheat). From these studies the peer review established the residue definition for enforcement as difenoconazole (sum of isomers). For risk assessment, considering that TDMs are toxicologically relevant metabolites present in significant levels, two separate plant residue definitions were proposed: 1) difenoconazole (sum of isomers) and 2) provisionally, TDMs.

EFSA concludes that the submitted residue trials are sufficient to derive MRL proposals of 0.7 mg/kg for the proposed uses on lettuce and scarole (broad-leaf endive), 7 mg/kg for lamb's lettuce, 1.5 mg/kg for rucola/rocket and 15 mg/kg for basil (mint). The MRL proposal of 15 mg/kg for basil (mint) was extrapolated from indoor trials on parsley conducted with three applications instead of two.

However, it should be noted that based on the same dataset (indoor parsley residue trials), an MRL of 10 mg/kg was finally agreed on chervil, parsley and celery leaves following the discussions in the SCoFCAH and published under Regulation (EU) No 459/2010. Therefore, it would be consistent to

propose the same MRL value for basil, chervil, parsley and celery leaves (e.g. to align all MRLs to the value of 15 mg/kg proposed in this MRL application, or optionally, to maintain the MRL of 10 mg/kg for chervil, parsley and celery leaves and to adopt a value of 10 mg/kg for basil, considering that the highest level was 5.68 mg/kg only).

Adequate analytical enforcement methods are available to control the residues of difenoconazole in the commodities under consideration at the validated LOQ of 0.01 mg/kg.

Specific studies to assess the magnitude of difenoconazole residues are not triggered for lettuce, lamb's lettuce, rucola and basil (mint) since these crops are mostly eaten raw. However, processing studies on scarole (cooked) are required.

It is concluded that residues of parent difenoconazole are not expected in rotational crops, provided that the active substance is applied according to the proposed GAP at a maximum seasonal dose rate of 760 g/ha. In contrast, the possible occurrence of the TDMs in rotational crops has not been addressed. This point would need to be considered further, when the confirmatory data requested in the framework on the peer review are available and when a global and harmonized approach for the assessment of the triazole chemical class compounds is available.

Residues of difenoconazole in commodities of animal origin were not assessed in the framework of this application, since the leafy crops under consideration are normally not fed to livestock.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The total calculated intake accounted for up to 86 % of the ADI (WHO cluster B). For the crops under consideration in this application, the contribution of difenoconazole residues to the total consumer exposure accounted for less than 1 % of the ADI. Acute consumer risk is not expected regarding the MRL proposals for the crops under consideration in this application. The highest acute dietary intake was calculated to be 27 % of the ARfD for scarole (broad-leaf endive).

EFSA concludes that the proposed use of difenoconazole on the crops under consideration in this application will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

However, EFSA emphasises that the above assessment does not yet take into consideration the TDMs. Since these metabolites may be generated by several pesticides belonging to the triazole fungicides, EFSA recommends that a separate risk assessment should be performed for the TDMs when the confirmatory data requested for triazole compounds in the framework of Regulation (EC) No 1107/2009 have been evaluated and a general methodology on the risk assessment of triazole compounds and their triazole derivative metabolites is available. Furthermore, since difenoconazole consists of diastereo isomers, the preferential metabolism/degradation of each enantiomer in plants as well as the possible impact on the consumer risk assessment need to be further addressed. Therefore currently, the overall consumer risk assessment has to be considered as provisional.

Thus EFSA proposes to amend the existing MRLs as reported in the summary table.

RECOMMENDATIONS

Code number (a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
Enforcement residue definition: difenoconazole (sum of isomers)				
0251010	Lamb's lettuce	0.05*	7	The MRL proposals are sufficiently supported by data and no consumer health risk was identified for the intended NEU outdoor uses of
0251020	Lettuce	3	0.7	
0251030	Scarole	0.05*	0.7	

Code number (a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
0251060	Rocket, rucola	2	1.5	difenoconazole.
0256080	Basil (mint)	2	15 (10 optional)	The MRL proposal of 15 mg/kg was extrapolated from indoor trials on parsley conducted with 3 applications instead of 2, as proposed in the GAP reported for mint. This MRL covers the indoor and NEU outdoor uses of difenoconazole on mint. Since based on the same data set (indoor trials on parsley) EFSA would recommend to align the MRLs for basil, chervil, parsley and celery leaves to the value of 15 mg/kg, or optionally, to maintain the MRL of 10 mg/kg for chervil, parsley and celery leaves and to adopt a value of 10 mg/kg for basil, considering that the highest level was only 5.68 mg/kg.

(a): According to Annex I of Regulation (EC) No 396/2005.
(*): Indicates that the MRL is set at the limit of analytical quantification.

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APPENDICES

Appendix A. Good Agricultural Practice (GAPs)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
				type (d-f)	conc. a.s. (i)	method kind (f - h)	growth stage & season (j)	number min max (k)	interval min max	kg as/hL min max	Water L/ha min max	kg a.s./ha min max		
Lamb's lettuce	DE (NEU)	F	Fungal leaf spot diseases			Spraying	From BBCH 15	a) 2 (7-10 days) b) 2			400-600	a) 0.13 b) 0.25	14	
Lettuce,	DE (NEU)	F	Fungal leaf spot diseases			Spraying	From BBCH 43	a) 2 (7-10 days) b) 2			400-600	a) 0.13 b) 0.25	14	
Scarole (broad-leaf endive)	DE (NEU)	F	Fungal leaf spot diseases			Spraying	From BBCH 43	a)2(7-10 days) b) 2			400-600	a) 0.13 b) 0.25	14	
Rucola	DE (NEU)	F	Fungal leaf spot diseases			Spraying	From BBCH 33	a) 2 (7-10 days) b) 2			400-600	a) 0.13 b) 0.25	14	
Mint	BE (NEU)	F & G	Rust	EC	250 g/L	Spraying	-	1-2	14 days			0.125	14	

Remarks:
(a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Technical Monograph No 2, 4th Ed., 1999 or other codes, e.g. OECD/CIPAC, should be used
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (Growth stages of mono-and dicotyledonous plants. BBCH Monograph, 2nd Ed., 2001), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions (i.e. feeding, grazing)

Appendix B. Pesticide Residue Intake Model (PRIMo)

Difenoconazole				
Status of the active substance:		Code no.		
LOQ (mg/kg bw):		proposed LOQ:		
Toxicological end points				
ADI (mg/kg bw/day):	**0.01**	ARfD (mg/kg bw):	**0.16**	
Source of ADI:	**EFSA**	Source of ARfD:	**EFSA**	
Year of evaluation:	**2011**	Year of evaluation:	**2011**	

Prepare workbook for refined calculations

Undo refined calculations

Explain choice of toxicological reference values.

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).

The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment - refined calculations

	TMDI (range) in % of ADI minimum - maximum
	14 - 86
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	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	pTMRLs at LOQ (in % of ADI)
85.6	WHO Cluster diet B	22.2	Tomatoes	9.0	Olives for oil production	9.0	Wine grapes	
69.2	DE child	13.3	Apples	8.7	Herbal infusions (dried)	7.0	Tomatoes	
67.9	FR toddler	14.2	Spinach	11.0	Beans (with pods)	5.6	Tomatoes	
67.6	NL child	7.4	Spinach	7.0	Apples	5.9	Potatoes	
55.9	IE adult	6.3	Wine grapes	4.0	Other leafy brassica	3.5	Sweet potatoes	
48.0	PT General population	12.4	Wine grapes	6.9	Rice	6.4	Tomatoes	
46.5	WHO cluster diet E	8.0	Wine grapes	3.9	Wheat	3.8	Potatoes	
42.2	FR infant	8.9	Spinach	8.4	Beans (with pods)	4.1	Potatoes	
41.8	WHO cluster diet D	7.3	Tomatoes	6.5	Wheat	4.9	Rice	
38.8	SE general population 90th percentile	5.5	Tomatoes	4.2	Potatoes	4.0	Chinese cabbage	
38.3	UK Toddler	5.1	Rice	4.6	Sugar beet (root)	4.2	Tomatoes	
37.4	FR all population	20.0	Wine grapes	3.3	Wheat	3.1	Tomatoes	
37.1	UK Infant	5.7	Peas (without pods)	5.6	Rice	3.9	Milk and cream,	
37.0	WHO regional European diet	7.9	Tomatoes	4.0	Potatoes	3.0	Wheat	
36.8	ES child	7.1	Tomatoes	4.4	Wheat	4.3	Rice	
32.9	NL general	3.1	Wine grapes	3.1	Tomatoes	2.8	Spinach	
31.6	WHO Cluster diet F	4.9	Tomatoes	3.6	Wheat	3.4	Potatoes	
31.0	IT kids/toddler	10.3	Tomatoes	6.6	Wheat	1.7	Rice	
28.8	DK child	5.5	Wheat	4.4	Rye	3.8	Tomatoes	
27.8	ES adult	5.6	Tomatoes	2.3	Wheat	2.3	Beans (with pods)	
27.3	IT adult	8.4	Tomatoes	4.1	Wheat	1.9	Spinach	
25.1	UK vegetarian	4.5	Tomatoes	4.1	Wine grapes	3.4	Rice	
22.1	UK Adult	5.4	Wine grapes	3.2	Rice	3.1	Tomatoes	
21.1	DK adult	7.0	Wine grapes	3.0	Tomatoes	2.0	Wheat	
18.9	PL general population	6.4	Tomatoes	3.4	Potatoes	2.2	Apples	
17.1	LT adult	4.5	Tomatoes	3.2	Potatoes	2.1	Apples	
13.9	FI adult	3.1	Tomatoes	1.5	Wine grapes	1.2	Potatoes	

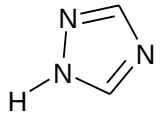
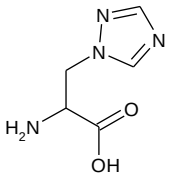
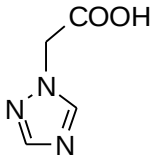
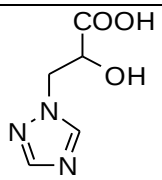
Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.

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

	Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations					
	The acute risk assessment is based on the ARfD.											
	For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
	In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
	Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	26.8	Scarole (broad-leaf	0.49 / -	26.8	Scarole (broad-leaf	0.49 / -	4.0	Lamb's lettuce	3.4 / -	4.0	Lamb's lettuce	3.4 / -
	8.2	Lettuce	0.49 / -	6.0	Lamb's lettuce	3.4 / -	3.4	Lettuce	0.49 / -	2.7	Scarole (broad-leaf endive)	0.49 / -
	6.0	Lamb's lettuce	3.4 / -	4.9	Lettuce	0.49 / -	2.7	Scarole (broad-leaf	0.49 / -	2.0	Lettuce	0.49 / -
	2.4	Basil	5.68 / -	2.4	Basil	5.68 / -	0.1	Basil	5.68 / -	0.1	Basil	5.68 / -
	1.4	Rocket, Rucola	0.7 / -	1.4	Rocket, Rucola	0.7 / -						

Appendix C. List of metabolites and related structural formula

Code/Trivial name	Chemical name[(a)]	Structural formula[(a)]
Triazole derivative metabolites (TDMs)		
1,2,4-triazole (free triazole)	1*H*-1,2,4-triazole	
Triazole alanine	2–amino-3-[1,2,4]triazol-1-yl-propionic acid	
Triazole acetic acid	[1,2,4]triazol-1-yl-acetic acid	
Triazole lactic acid	[1,2,4]triazol-1-yl-lactic acid	

(a): ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

ABBREVIATIONS

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CEN	European Committee for Standardisation (Comité Européen de Normalisation)
CF	conversion factor for enforcement to risk assessment residue definition
cGAP	critical GAP
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DALA	days after last application
DAR	Draft Assessment Report
DT_{90}	period required for 90 % dissipation (define method of estimation)
EC	European Community
EC	Emulsifiable concentrate
EFSA	European Food Safety Authority
EMS	evaluating Member State
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GAP	good agricultural practice
ha	hectare
hL	hectolitre
HR	highest residue
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
kg	kilogram
L	litre
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
NEU	northern European Union
OECD	Organisation for Economic Co-operation and Development
PF	processing factor

PHI	pre-harvest interval
PRAPeR	Pesticide Risk Assessment Peer Review
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (method)
R_{ber}	statistical calculation of the MRL by using a non-parametric method
R_{max}	statistical calculation of the MRL by using a parametric method
RAC	raw agricultural commodity
RD	residue definition
RMS	rapporteur Member State
SCFCAH	Standing Committee on the Food Chain and Animal Health
SEU	Southern European Union
STMR	supervised trials median residue
TDMs	Triazole Derivative Metabolites
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization
HPLC	high performance liquid chromatography
MS/MS	tandem mass spectrometry