Modification of the existing maximum residue levels for difenoconazole in various crops

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member States (EMS), Greece and Austria, received applications from Syngenta and Adama, respectively, to modify the existing maximum residue levels (MRLs) for the active substance difenoconazole in various crops and barley, respectively. The data submitted in support of the requests were found to be sufficient to derive MRL proposals for all crops under consideration. Adequate analytical methods for enforcement are available to control the residues of difenoconazole on the commodities under consideration. Based on the risk assessment results, EFSA concludes that the proposed uses of difenoconazole on the commodities under consideration will not result in a consumer exposure exceeding the toxicological reference values for the active substance and therefore are unlikely to pose a consumer health risk, except for the indoor use on scaroles. An acute consumer risk cannot be excluded for this use and a lower MRL is proposed based on the outdoor uses only.

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Keywords: difenoconazole, triazole derivative metabolites, various crops, MRL application, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member States (EMS), Greece and Austria, received the applications from Syngenta and Adama, respectively, to modify the existing maximum residue levels (MRLs) for the active substance difenoconazole in various crops and barley, respectively. To accommodate for the intended uses of difenoconazole, Greece proposed to raise the existing MRLs from 0.5 to 0.7 mg/kg in apricots, from 0.4 to 0.6 mg/kg in strawberries, from 0.2 to 0.3 mg/kg in Brussels sprouts and head cabbages, from 3 to 4 mg/kg in lettuces, from the limit of quantification (LOQ) of 0.05 to 1 mg/kg in scaroles/broad-leaved endives, from LOQ of 0.05 to 4 mg/kg in other salad plants (including Brassicacea, excluding rocket and lamb’s lettuce), from 0.2 to 4 mg/kg in chards (beet leaves), from 2 to 4 mg/kg in fresh herbs (excluding chervil, parsley, celery leaves), from 4 to 6 mg/kg in cardoons, from 5 to 6 mg/kg in celeries, from 0.5 to 0.7 mg/kg in leeks, from 0.3 to 0.6 mg/kg in rhubarbs, from 0.1 to 0.15 mg/kg in pulses group, and from 0.3 to 3 mg/kg in spices (roots and rhizomes). Austria proposed to raise the existing MRL from 0.05 to 0.3 mg/kg in barley. Greece and Austria drafted the evaluation reports in accordance with Article 8 of Regulation (EC) No 396/2005, which were submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 6 October 2015 and 23 January 2017, respectively.

EFSA bases its assessment on the evaluation reports submitted by the EMSs, the draft assessment report (DAR) and its addenda prepared under Directive 91/414/EEC, the Commission review report on difenoconazole, the conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole, the Joint Meeting on Pesticide Residues (JMPR) Evaluation reports as well as the conclusions from previous EFSA opinions and scientific reports on difenoconazole.

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 accept an acceptable daily intake (ADI) of 0.01 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.16 mg/kg bw.

The metabolism of difenoconazole in primary crops was investigated in the fruit, root/tuber, cereal/grass and pulses/oilseeds crop groups following foliar application. From these studies, the peer review established the residue definition for enforcement as parent difenoconazole and for risk assessment as difenoconazole and, provisionally, triazole derivative metabolites (TDMs). For the uses on crops under consideration, EFSA concludes that the metabolism of difenoconazole in primary crops has been sufficiently addressed and that the residue definitions derived are applicable.

EFSA concludes that the data submitted were found to be sufficient to derive MRL proposals of 0.7 mg/kg for apricots, 0.5 mg/kg for strawberries and rhubarbs, 0.3 mg/kg for Brussels sprouts and head cabbages, 4 mg/kg for lettuces, scaroles, cresses, land cresses, red mustard, baby leaf crops (including Brassica species) and other lettuces and salad plants, chards/beet leaves, chives, sage, rosemary, thyme, laurel/bay leaves, tarragon and other herbs and edible flowers, 7 mg/kg in cardoons and celeries, 0.6 mg/kg in leeks, 0.06 mg/kg in pulses, except peas, 3 mg/kg in spices (roots and rhizomes) and 0.3 mg/kg in barley. Adequate analytical enforcement methods are available to monitor the residues of difenoconazole on the commodities under consideration at the validated LOQ of 0.01 mg/kg.

Studies investigating the nature of difenoconazole residues under standard hydrolysis conditions were assessed during peer review and showed the active substance to be hydrolytically stable under standard processing conditions. Therefore for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable.

The occurrence of difenoconazole residues in rotational crops was investigated in the framework of the peer review. Based on the available information on the nature and magnitude of residues, EFSA concludes that significant residue levels are unlikely to occur in rotational crops, provided that the compound is used according to the proposed good agricultural practices (GAP).

As several crops under consideration and their by-products are used as feed products, a potential carry-over of difenoconazole into food of animal origin should be assessed. Nevertheless, according to the metabolism and livestock feeding studies assessed during the 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. Considering that the proposed residue definition was not implemented in the MRL Regulation and that the current residue definition established in the MRL Regulation is difenoconazole only, the modification of the existing MRL in products of animal origin according to this residue definition is not required. Moreover, the calculated dietary burdens are only indicative, may be overestimated and not reflecting the existing authorised GAPs. Therefore, EFSA is of the opinion that a
A full assessment of the metabolism and the magnitude of the residues in livestock should be performed in the framework of the MRL review under Article 12 of the Regulation 396/2005, when further information on the authorised uses of difenoconazole will be available.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMO). To calculate the chronic exposure, EFSA used median residue values (STMR) derived from the residue trials conducted for the crops under consideration, the STMR values reported in previous EFSA reasoned opinions and derived by JMPR for the CXLs implemented in the EU legislation. For the remaining commodities of plant and animal origin, the existing MRLs as established in Regulation (EU) No 2017/626 were used as input values. The acute consumer exposure assessment was performed only with regard to the commodities under consideration.

A long-term consumer intake concern was not identified for any of the European diets incorporated in the EFSA PRIMO. The total calculated chronic intake accounted for up to 86.7% of the ADI (WHO Cluster diet B). The contribution of residues in crops under consideration accounted for a maximum of 2.79% of ADI for lettuces (ES adult), 1.86% of ADI for celeries (IE adult) and 1.06% of ADI for scaroles (NL child, scenario 1). The contribution of residues in the other crops under consideration was lower than 1% of the ADI.

An acute consumer risk was identified in relation to the intended indoor use on scaroles. Considering the highest residue (HR) observed in the submitted residue trials and applying the currently agreed methodology, an exceedance of the ARfD (137.2%) was identified for this commodity (scenario 1). When using the HR derived from the outdoor GAPs, the acute intake accounted for 29% of the ARfD (scenario 2). No acute concern was identified for all the other uses under consideration, the highest calculated acute intake being 97.55% of the ARfD for celeries, 42.21% of the ARfD for lettuces, 27.5% of the ARfD for chards, 14.7% of the ARfD for leeks and less than 10% for the remaining crops.

EFSA concludes that, except for the indoor use on scaroles, the intended uses of difenoconazole on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a concern for public health.

EFSA emphasises that the above assessment does not yet take into consideration TDMs. As these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommended that a separate risk assessment should be performed for TDMs as soon as 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 TDMs is available.

Additionally, EFSA underlines that the above assessment does not consider the possible impact of plant metabolism on the isomer ratio of difenoconazole and further investigation on this matter would in principle be required. Since guidance on the consideration of isomer ratios in the consumer risk assessment is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

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

| Code  | Commodity     | EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification  |
|-------|---------------|----------------|-------------------------|------------------------|
| 0140010 | Apricots      | 0.5            | 0.7                     | SEU use supported. No consumer health risk was identified |
| 0152000 | Strawberries  | 0.4            | 0.5                     | Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| 0242010 | Brussels sprouts | 0.2          | 0.3                     | NEU/SEU uses supported. No consumer health risk was identified |
| 0242020 | Head cabbages | 0.2            | 0.3                     | NEU/SEU uses supported. No consumer health risk was identified |
| 0251020 | Lettuces      | 3              | 4                       | Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| Code<sup>(a)</sup> | Commodity | EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification<sup>(b)</sup> |
|-----------------|-------------|----------------|-------------------------|----------------------------------|
| 0251030         | Scaroles (broad-leaf endives) | 0.05* | 0.8 | Extrapolated from lettuces. Proposed MRL is derived from outdoor NEU/SEU uses (no consumer health risk was identified for the outdoor NEU/SEU uses). An acute intake concern was identified for the indoor use. |
| 0251040         | Cresses | 0.05* | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0251050         | Land cresses | 0.05* | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0251070         | Red mustards | 0.05* | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0251080         | Leaves and sprouts of *Brassica* spp., including turnip greens | 0.05* | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0251990         | Other lettuces and salad plants | 0.05* | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0252030         | Beat leaves (chards) | 0.2 | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256020         | Chives | 2 | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256050         | Sage | 2 | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256060         | Rosemary | 2 | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256070         | Thyme | 2 | 4 | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256090         | Bay leaves (laurel) | 2 | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256100         | Tarragon | 2 | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0256990         | Other herbs and edible flowers | 2 | 4 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0270020         | Cardoons | 4 | 7 | Indoor and NEU/SEU uses supported by extrapolation from celery. No consumer health risk was identified. |
| 0270030         | Celeries | 5 | 7 | Indoor and SEU uses supported. NEU use not supported. No consumer health risk was identified. |
| 0270060         | Leeks | 0.5 | 0.6 | Indoor and NEU/SEU uses supported. No consumer health risk was identified. |
| 0270070         | Rhubarbs | 0.3 | 0.5 | Extrapolated from data on celery stems. NEU/SEU use supported. No consumer health risk was identified. |
| 0300010         | Beans | 0.05* | 0.06 | NEU and SEU use supported by extrapolation from combined data set of residues on peas. No consumer health risk was identified. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses. |
| 0300020         | Lentils | 0.05* | 0.06 | NEU and SEU use supported by extrapolation from combined data set of residues on peas. No consumer health risk was identified. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses. |
| 0300040         | Lupins | 0.05* | 0.06 | NEU and SEU use supported by extrapolation from combined data set of residues on peas. No consumer health risk was identified. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses. |
| 0300090         | Other pulses | 0.05* | 0.06 | NEU and SEU use supported by extrapolation from combined data set of residues on peas. No consumer health risk was identified. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses. |
| 0840000         | Roots or rhizome | 0.3 | 3 | NEU and SEU uses supported by extrapolation from carrots applying a dehydration factor of 8. No consumer health risk was identified. |
| 0500010         | Barley | 0.05 | 0.3 | NEU use supported. No consumer health risk was identified. |

*Indicates that the MRL is set at the limit of analytical quantification (LOQ).
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.
(b): The contribution of TDMs to the consumer intake has not been considered for all crops.
Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the MRL Regulation’) establishes the rules governing the setting of pesticide maximum residue levels (MRLs) at European Union (EU) level. Article 6 of the 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,\(^2\) repealed by Regulation (EC) No 1107/2009\(^3\), shall submit to a Member State, when appropriate, an application to modify a MRL in accordance with the provisions of Article 7 of the Regulation.

Greece and Austria, hereafter referred to as the evaluating Member States (EMS), received an application from the company Syngenta\(^4\) and ADAMA\(^5\), respectively, to modify the existing MRLs for the active substance difenoconazole in various crops and barley, respectively. These applications were notified to the European Commission and the European Food Safety Authority (EFSA) and were subsequently evaluated by the EMS in accordance with Article 8 of the Regulation.

After completion, the evaluation reports were submitted to the European Commission and to EFSA on 6 October 2015, updated in February 2016, and on 23 January 2017, respectively.

The applications were included in the EFSA Register of Questions with the reference numbers and the following subjects:

EFSA-Q-2015-00571 Difenoconazole – Modification of the existing MRLs in various crops
EFSA-Q-2017-00065 Difenoconazole – Modification of the existing MRL in barley

Greece proposed to raise the existing MRLs of difenoconazole in various crops as follows: from 0.5 to 0.7 mg/kg in apricots, from 0.4 to 0.6 mg/kg in strawberries, from 0.2 to 0.3 mg/kg in Brussels sprouts and head cabbage, from 3 to 4 mg/kg in lettuce, from the limit of quantification (LOQ) of 0.05 to 1 mg/kg in scaroles/broad-leaved endives, from the LOQ of 0.05 to 4 mg/kg in other salad plants (including Brassicaea, excluding rocket and lamb’s lettuce), from 0.2 to 4 mg/kg in chard (beet leaves), from 2 to 4 mg/kg in fresh herbs (excluding chervil, parsley, celery leaves), from 4 to 6 mg/kg in cardoon, from 5 to 6 mg/kg in celeries, from 0.5 to 0.7 mg/kg in leeks, from 0.3 to 0.6 mg/kg in rhubarbs, from 0.1 to 0.15 mg/kg in pulses group, and from 0.3 to 3 mg/kg in spices (roots and rhizomes). It is noted that in the meantime the MRL for basil (fresh herbs group) has been increased to 10 mg/kg based on an EFSA opinion (EFSA, 2014c). Hence, the request from the applicant for basil is superseded.

Austria proposed to raise the existing MRL of difenoconazole in barley from 0.05 to 0.3 mg/kg.

EFSA proceeded with the assessment of the applications and the evaluation reports as required by Article 10 of the Regulation.

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

The evaluation reports submitted by the EMS (Greece, 2016; Austria, 2017) 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.

In accordance with Article 11 of the Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within 3 months (which may be extended to 6 months if more detailed evaluations need to be carried out) from the date of receipt of the application. If EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided. On 9 November 2015, EFSA identified missing information in the evaluation report submitted by Greece. An updated evaluation report was therefore submitted on 10 March 2016.

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1 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.

2 Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.

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

4 SYNGENTA Hellas ABAE, Anthoussas Avenue, 15349 Athens, Greece.

5 ADAMA Deutschland GmbH, Edmund-Rumpler-Strasse 6, 51149 Cologne, Germany.
The active substance and its use pattern

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

Difenoconazole was evaluated in the framework of 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/EC6 which entered into force on 1 January 2009 for use as a fungicide only. In accordance with Commission Implementing Regulation (EU) No 540/20117 and Commission Implementing Regulation (EU) No 1100/20118 as regards the conditions of approval, difenoconazole is approved under Regulation (EC) No 1107/2009, repealing Directive 91/414/EEC.

The representative uses evaluated in the peer review were foliar applications on pome fruits and carrots and as a seed treatment on cereals. The draft assessment report (DAR) has been peer reviewed by EFSA (2011a).

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 MRLs for difenoconazole. The proposals from these reasoned opinions have been considered in the preparation of EU legislation. The MRL changes that were reported in the EU legislation since the entry into force of the Regulation are summarised in Table 1. The review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 has not yet been performed for difenoconazole.

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

| Procedure(a) | Considered by Regulation | Remarks |
|--------------|--------------------------|---------|
| Art. 10 (EFSA, 2009) | (EU) No 459/2010 | Various leafy vegetables |
| Art. 10 (EFSA, 2010) | (EU) No 765/2010 | Swedes, turnips |
| Art. 10 (EFSA, 2011b) | (EU) No 978/2011 | Beet leaves (chard), globe artichokes, broccoli, cardoons and strawberries |
| Art. 43 (EFSA, 2011c) | (EU) No 441/2012 | Implementation of CXLs (FAO, 2010) |
| Art. 10 (EFSA, 2012) | (EU) No 34/2013 | Raspberries, blackberries and cucurbits (edible peel) |
| Art. 10 (EFSA, 2013) | (EU) No 834/2013 | Various crops |
| Art. 10 (EFSA, 2014a) | (EU) No 2015/401 | Peppers, aubergines |
| Art. 43 (EFSA, 2014b) | (EU) No 2015/845 | Implementation of CXLs (FAO, 2011) |
| Art. 10 (EFSA, 2014c) | (EU) No 2015/1101 | Lettuces, other salad plants including Brassicaceae, basil |
| Art. 43 (EFSA, 2016) | (EU) No 2017/626 | Implementation of CXLs (FAO 2015) |

(a): Art. 10: Assessment of MRL application according to Article 6 to 10 of Regulation (EC) No 396/2005.
Art. 43: EFSA scientific opinion according to Article 43 of Regulation (EC) No 396/2005.

The details of the intended Good Agricultural Practices (GAPs) for difenoconazole are given in Appendix A.

**Assessment**

EFSA has based its assessment on the evaluation reports submitted by the EMS (Greece 2016; Austria 2017), the DAR and its addenda prepared under Directive 91/414/EEC (Sweden, 2006, 2010, 2014), 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).

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6 Commission Directive 2008/69/EC of 1 July 2008 amending Council Directive 91/414/EEC to include clonfentezine, dicamba, difenoconazole, diflubenzuron, imazaquin, lenacil, oxadiazon, picloram and pyriproxyfen as active substances, OJ L 172, 2.7.2008, p. 9–14.
7 Commission Implementing 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, 11.6.2011, p. 1–186.
8 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.
2011a), the JMPR Evaluation report (FAO, 2008, 2010, 2011, 2013, 2015), as well as the conclusions from previous EFSA opinions and scientific reports on difenoconazole (EFSA, 2009, 2010, 2011b,c, 2012, 2013, 2014a–c, 2016). 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 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a–g, 2000, 2010a,b, 2016; OECD, 2011, 2013).

1. Method of analysis

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

Analytical methods for the determination of difenoconazole residues in plant commodities were assessed during the peer review under Directive 91/414/EEC (Sweden 2006; EFSA, 2011a).

The multiresidues DFG S19 method using liquid chromatography with tandem mass spectrometry (LC-MS/MS) was sufficiently validated at the LOQ of 0.02 mg/kg in 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 multiresidue Quick, Easy, Cheap, Effective, Rugged, and Safe (method) (QuEChERS) LC-MS/MS method 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). No validation data are available for spices, which do not belong to any of the group above. Considering that spices are minor crops the deviation is acceptable, the analytical methods validated for the four major crop groups are expected to apply to spices as well.

EFSA concludes 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. Validation data on spices would be desirable.

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

The analytical methods for the determination of difenoconazole residues in commodities of animal origin were evaluated during the peer review under Directive 91/414/EEC (Sweden, 2006; EFSA, 2011a). Difenoconazole and CGA-205375 can be determined by LC-MS/MS with an LOQ of 0.01 mg/kg in tissues, fat and eggs, and with an LOQ of 0.005 mg/kg in milk.

The multiresidue QuEChERS method is also applicable (CEN, 2008). Difenoconazole and CGA-205375 can be determined by LC-MS/MS with an LOQ of 0.01 mg/kg in tissues, fat and eggs, and with an LOQ of 0.005 mg/kg in milk per each analyte.

EFSA concludes that sufficiently validated analytical methods for enforcing the MRLs for difenoconazole in food of animal origin are available.

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, European Commission, 2013). The data were sufficient to derive toxicological reference values compiled in Table 2.

| Source          | Year | Value               | Study            | Safety factor |
|-----------------|------|---------------------|------------------|---------------|
| Difenoconazole  |      |                     |                  |               |
| ADI             | 2013 | 0.01 mg/kg bw per day | 2-year rat       | 100           |
| ARfD            | 2013 | 0.16 mg/kg bw       | Rat, developmental | 100          |

ADI: acceptable daily intake; ARfD: acute reference dose; bw: body weight.

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9 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.
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 framework of the peer review under Directive 91/414/EEC (Sweden, 2006, EFSA, 2011a). Metabolism studies were performed with foliar applications in fruit (tomatoes, grapes), root (potatoes) and pulses/oilseed (oilseed rape) crop groups, and with foliar and seed treatment in cereals (wheat) using [phenyl-14C]- and [triazole-14C]-labelled difenoconazole. An overview of the available metabolism studies is presented in Table 3.

Based on these studies, the peer review concluded on the residue definition for enforcement as parent difenoconazole. The residue definition in Regulation (EU) No 396/2005 is identical. For risk assessment, two residue definitions were proposed: (1) difenoconazole; (2) triazole derivative metabolites (TDMs, provisionally). Since difenoconazole consists of diastereo isomers, and since the available analytical methods are not stereoselective, the proposed residue definitions for enforcements and risk assessment are derived for the sum of the R- and S-isomers.

For the uses on the crops under consideration, 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. Nevertheless, the preferential metabolism/degradation of each enantiomer in plants needs to be investigated as requested by the peer review (EFSA, 2011a). EFSA emphasises that the above assessment does not yet take into consideration TDMs. As these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommended that a separate risk assessment should be performed for TDMs as soon as 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 TDMs is available. Furthermore, the above consumer risk assessment was performed disregarding the possible impact of plant and livestock metabolism on the enantiomers ratio of the active substance and further investigation on this matter would in principle be required. Since guidance is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

3.1.1.2. **Magnitude of residues**

In support of the MRL applications, a number of residue trials have been submitted for difenoconazole on the crops under consideration. Some trials were conducted with emulsifiable concentrate (EC) or water-dispersible granules (WG) formulations instead of suspension concentrate (SC) formulation. According to the current Guidance Document (European Commission, 2016), this deviation is considered as acceptable. No residue data on TDMs were reported.

- **Apricots** (GAP outdoor southern Europe (SEU) 2 × 112.5 g/ha, preharvest interval (PHI) 7 days)

Eight GAP-compliant (within 25% deviation of application rate) residue trials were submitted. Based on this data set, EFSA derived a MRL of 0.7 mg/kg for apricots.
b) Strawberries (GAP outdoor NEU/SEU 2 × 125 g/ha, PHI 3 days; Indoor 3 × 125 g/ha, PHI 3 days)

NEU. Eight outdoor GAP-compliant (within 25% deviation of application rate) residue trials on strawberries have been submitted.

SEU. Eight outdoor GAP-compliant (within 25% deviation of application rate) residue trials on strawberries have been submitted.

Data from NEU and SEU trials were pooled (U-test, 5%) to derive a more robust MRL proposal of 0.5 mg/kg.

Indoor. Twelve GAP-compliant (within 25% deviation of application rate) residue trials on strawberries under protected conditions have been submitted and support an MRL proposal of 0.5 mg/kg.

EFSA concludes on a MRL proposal of 0.510 mg/kg for strawberries, which covers both outdoor and indoor uses.

c) Brussels sprouts (GAP outdoor NEU 3 × 125 g/ha, SEU 2 × 125 g/ha PHI 21 days)

NEU. Eleven GAP-compliant (within 25% deviation of application rate) residue trials were submitted. Two trials from the UK were not considered as independent, thus only the highest value was selected for the MRL setting.

SEU. Four GAP-compliant (within 25% deviation of application rate) residue trials conducted over a single season were submitted.

Based on the most critical data set of the SEU use, EFSA derived a MRL proposal of 0.3 mg/kg for Brussels sprouts that cover both NEU and SEU uses.

d) Head cabbages (GAP outdoor NEU/SEU 3 × 125 g/ha, PHI 21 days)

NEU. Seventeen GAP-compliant (within 25% deviation of application rate) residue trials were submitted. Some trials cannot be considered as independent, thus the highest value from each pair of trials was selected for the MRL setting.

SEU. Four GAP-compliant (within 25% deviation of application rate) residue trials conducted in southern France were submitted.

Data from NEU and SEU trials were pooled (U-test, 5%) to derive a MRL proposal of 0.3 mg/kg that cover both NEU and SEU uses.

e) Lettuces, scaroles, cresses, land cresses, red mustard, baby leaf crops (including Brassica species) and other lettuces and salad plants, chives, sage, rosemary, thyme, laurel/bay leaves, tarragon and other herbs and edible flowers, chards/beet leaves (GAP outdoor NEU/SEU 2 × 125 g/ha, PHI 14 days, Indoor 2 × 100 g/ha, PHI 14 days)

NEU. Eight GAP-compliant (within 25% deviation of application rate) residue trials on open leaf varieties were submitted. In addition, the EMS proposed to include the results of 15 residue trials conducted according to the GAP on open leaf lettuces and already assessed by EFSA (2014c) to derive a more robust MRL.

SEU. Nine GAP-compliant (two trials were not independent and only the highest value from the pair was selected) residue trials conducted on open leaf (six) and on closed (two) varieties were submitted.

Data from NEU and SEU trials were pooled (U-test, 5%) to derive a more robust MRL proposal of 0.8 mg/kg.

Indoor. Eight GAP-compliant (within 25% deviation of application rate) residue trials conducted on open leaf varieties over a single season were submitted. Based on this data set, EFSA derived a MRL of 4 mg/kg.

EFSA concludes on a MRL proposal of 4 mg/kg for lettuces based on the most critical data set for the indoor use that cover also both NEU and SEU uses.

Since the indoor and outdoor GAPs are the same and the number of trials sufficient, the proposed extrapolation from lettuces (open leaf) to scaroles, cresses, land cresses, red mustard, baby leaf crops (including Brassica species) and other lettuces and salad plants, chives, sage, rosemary, thyme, laurel/bay leaves, tarragon and other herbs and edible flowers, chards/beet leaves is acceptable (European Commission, 2016). EFSA concludes on a MRL proposal of 4 mg/kg for the crops under consideration, which covers indoor and NEU/SEU uses.

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10 EMS Greece proposed a MRL of 0.6 mg/kg, based on the SEU data set only.
f) Celeries and cardoons (GAP outdoor NEU/SEU 3 × 125 g/ha, PHI 14 days, Indoor 2 × 125 g/ha, PHI 14 days)

Indoor. Eight GAP-compliant (within 25% deviation of application rate) residue trials conducted on celeries were submitted. Extrapolation is possible from celeries to cardoons (European Commission, 2016). Based on this data set, EFSA derived a MRL proposal of 7 mg/kg 11 in celeries and, by extrapolation, cardoons.

NEU/SEU. The residue trials on celeries already evaluated by EFSA (2011b) were considered by the EMS Greece for the extrapolation to cardoons. No new trials were submitted by the applicant. The number of trials (3) was not sufficient for deriving a MRL proposal for the NEU use. Nevertheless, the MRL proposal based on the indoor GAP is expected to cover the NEU use as well. Therefore, one additional trial compliant with the NEU GAP is only desirable.

EFSA derived a MRL proposal of 7 mg/kg for celeries and, by extrapolation, cardoons based on the most critical data set for the indoor use, which covers also the NEU and SEU use.

g) Rhubarbs (GAP outdoor NEU/SEU 3 × 125 g/ha, PHI 14 days)

The residue data from celeries (stems only) were used to support the NEU and SEU uses for rhubarbs.

Data from NEU and SEU trials were pooled (U-test, 5%) to derive a MRL proposal of 0.5 mg/kg.

h) Leeks (GAP outdoor NEU/SEU 3 × 125 g/ha, PHI 21 days)

Eight NEU and four SEU GAP-compliant (within 25% deviation of application rate) residue trials were conducted. Data from NEU and SEU trials were pooled (U-test, 5%) to derive a MRL proposal of 0.6 mg/kg.

i) Pulses (GAP outdoor NEU/SEU 2 × 100 g/ha, PHI 28 days)

Eight NEU and eight SEU GAP-compliant (within 25% tolerance deviation of application rate) residue trials were conducted in peas and extrapolated to the whole pulses. Data from NEU and SEU trials were pooled (U-test, 5%) to derive a MRL proposal of 0.06 mg/kg.

j) Roots and rhizome spices (GAP outdoor NEU/SEU 3 × 125 g/ha, PHI 14 days)

The applicant proposed to extrapolate the results from residue trials on carrots 12 to spices (roots and rhizomes). Since the trials on carrots previously assessed by EFSA (2013) were conducted at the same GAP and in a sufficient number, the extrapolation is acceptable (European Commission, 2016). Data from NEU and SEU trials were pooled (U-test, 5%).

A default dehydration factor of 8 based on a dry matter content of ca 12% in carrot and ca 90% in dried root was applied. It is noted that a slightly different dehydration factor of 6.77 has been applied by the EMS Greece.

EFSA derived a MRL proposal of 3 mg/kg for roots and rhizome spices, by extrapolation from a combined NEU/SEU data set on carrots.

k) Barley (GAP outdoor NEU 3 × 125 g/ha, BBCH 39-59, PHI n.a.)

Eight GAP-compliant supervised field trials conducted on barley in NEU in 2014 are available. Trials were analysed separately for cis- and trans-isomers. At harvest, the average ratio was 1.6 for grain and 1.5 for straw but information on cis/trans-isomer range was not given for the active substance difenoconazole. Residues in straw for the animal burden calculation were also provided. Based on this data set, EFSA derived a MRL proposal of 0.3 mg/kg for barley grains.

The results of the residue trials, the related risk assessment input values (highest residue, median residue) and the MRL proposals are summarised in Table 4. When more than one use has been assessed for a crop, EFSA proposes the MRL derived from the more critical residue situation and highlighted in bold in Table 4.

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). One new storage stability study was assessed by the EMS Austria (Austria, 2017). Residues of

11 EMS Greece proposed a MRL of 6 mg/kg, based on rounded EU MRL instead of OECD MRL.
12 The results from six new residue trials submitted by the applicant were disregarded because not GAP-compliant as conducted with two instead of three applications.
cis- and trans-difenoconazole, and difenoconazole alcohol were stable under deep frozen conditions (≤ 18°C) for a maximum of 12 months in high water (sugar beet), oil (rape seed seeds) and acid (grapes) and in dry (wheat grain) matrices.

As the trial samples were stored for a maximum period of 18 months (8 months for barley) under conditions for which integrity of the samples was demonstrated, it is concluded that the residue data are valid with regard to storage stability.
### Table 4: Overview of the available residues trials data

| Crop (trial GAPs) | Region/indoor(a) | Residue levels observed in the supervised residue trials(b) (mg/kg) | Recommendations/comments(c) | MRL proposal (mg/kg) | HR(d) (mg/kg) | STMR(e) (mg/kg) |
|------------------|-------------------|---------------------------------------------------------------|-----------------------------|----------------------|--------------|--------------|
| Apricots (2 × 112.5 g/ha, PHI 7 days) | SEU | 0.10, 0.14, 0.16, 0.16, 0.17, 0.3, 0.35, 0.37 | MRL\_OECD: 0.65/0.7 Underlined: higher residues at a longer PHI of 10 days | 0.7 | 0.37 | 0.17 |
| Strawberries (2 × 125 g/ha, PHI 3 days) | NEU | 0.05, 0.06, 2 × 0.07, 0.08, 2 × 0.11, 0.25 | Combined NEU/SEU data set (U-test, 5%) MRL\_OECD: 0.46/0.50 MRL\_OECD: 0.36/0.40 (NEU) MRL\_OECD: 0.56/0.60 (SEU) | 0.5 | 0.37 | 0.08 |
| | SEU | 0.02, 0.04, 0.06, 0.08, 0.09, 0.11, 0.16, 0.37 | | | | |
| (3 × 125 g/ha, PHI 3 days) | Indoor | 0.04, 2 × 0.07, 0.11, 0.13, 2 × 0.14, 0.15, 2 × 0.20, 0.26, 0.28 | MRL\_OECD: 0.45/0.50 | 0.5 | 0.28 | 0.14 |
| Brussels sprouts (3 × 125 g/ha, PHI 21 days) | NEU | 0.02, 0.04, 3 × 0.05, 2 × 0.07, 0.08, 0.09, 0.14 | MRL\_OECD: 0.20/0.20 | 0.2 | 0.14 | 0.06 |
| | SEU | 0.04, 0.07, 0.10, 0.15 | MRL\_OECD: 0.27/0.30 | 0.3 | 0.15 | 0.09 |
| Head Cabbages (3 × 125 g/ha, PHI 21 days) | NEU | 3 × < 0.01, 4 × 0.02, 0.05, 0.06, 0.13, 0.19 | Combined NEU/SEU data set (U-test, 5%) MRL\_OECD: 0.25/0.30 MRL\_OECD: 0.28/0.30 (NEU) MRL\_OECD: 0.03/0.04 (SEU) | 0.3 | 0.19 | 0.02 |
| | SEU | 3 × < 0.01, 0.02 | | | | |
| Lettuces (2 × 125 g/ha, PHI 14 days) | NEU | 0.03, 0.12, 0.13, 0.16, 0.22, 0.23, 0.25, 0.26 < 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 | Combined NEU/SEU data set (U-test, 5%). All open leaf lettuces except underlined values. Part of NEU trials already assessed (EFSA, 2014b). MRL\_OECD: 0.75/0.80 MRL\_OECD: 0.63/0.70 (NEU) MRL\_OECD: 1.03/1.00 (SEU) Extrapolation to scaroles, cress, land cress, red mustard, leaves and sprouts of *Brassica* spp. and other lettuce and other salad plants Extrapolation to chives, sage, rosemary, thyme, laurel/bay leaves, tarragon and other herbs and edible flowers Extrapolation to chards | 0.8 | 0.53 | 0.18 |
| | SEU | 0.02, 0.06, 0.09, 0.11, 0.23, 0.32, 0.50, 0.53 | | | | |
| Crop (trial GAPs) | Region/indoor(a) | Residue levels observed in the supervised residue trials(b) (mg/kg) | Recommendations/comments(c) | MRL proposal (mg/kg) | HR(d) (mg/kg) | STMR(e) (mg/kg) |
|------------------|------------------|---------------------------------------------------------------|-----------------------------|---------------------|-------------|---------------|
| Lettuces (2 × 100 g/ha, PHI 14 days) | Indoor | 0.08, 0.15, 0.46, 0.49, 0.55, 0.68, 1.02, 2.51 | All open leaf lettuces. Extrapolation to scaroles, cresses, land cresses, red mustard, baby leaf crops (including Brassica species) and other lettuces and salad plants Extrapolation to chives, sage, rosemary, thyme, laurel/bay leaves, tarragon and other herbs and edible flowers Extrapolation to chards/beet leaves | | 4.0 | 2.51 | 0.52 |
| Celeries (3 × 125 g/ha, PHI 14 days) | NEU | 0.28, 0.49, 0.71 | Data evaluated by EFSA (2011b). NEU use is expected to be covered by the indoor GAP. One additional trial is only desirable | | – | – | – |
| | SEU | 0.32, 0.46, 1.2, 2.0 | Data evaluated by EFSA (2011b). | | 4 | 2.0 | 0.83 |
| (2 × 125 g/ha, PHI 14 days) | Indoor | 0.31, 0.52, 0.56, 0.83, 1.6, 1.7, 3.2, 3.4 | Extrapolation to cardoons | | 7 | 3.4 | 1.22 |
| Celery stems (3 × 125 g/ha, PHI 14 days) | NEU | 0.04, 0.06, 0.17, 0.26 | Combined NEU/SEU data set (U-test, 5%) Extrapolation to cardoons | | 0.5 | 0.26 | 0.06 |
| | SEU | 0.03, 0.04, 0.05, 0.14 | | | | | |
| Leeks (3 × 125 g/ha, PHI 21 days) | NEU | 0.02, 0.07, 0.09, 0.12, 0.13, 0.21, 0.32, 0.40 | Combined NEU/SEU data set (U-test, 5%) Extrapolation to rhubarbs | | 0.6 | 0.40 | 0.13 |
| | SEU | 0.03, 0.05, 0.14, 0.17 | | | | | |
| Peas (dry) (2 × 100 g/ha, PHI 28 days) | NEU | 7 × < 0.02, 0.05 | Combined NEU/SEU data set (U-test, 5%) Extrapolation to pulses. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses | | 0.06 | 0.05 | 0.02 |
| | SEU | 8 × < 0.02, 0.03 | | | | | |
| Crop (trial GAPs) | Region/ indoor\(^{(a)}\) | Residue levels observed in the supervised residue trials\(^{(b)}\) (mg/kg) | Recommendations/comments\(^{(c)}\) | MRL proposal (mg/kg) | HR\(^{(d)}\) (mg/kg) | STMR\(^{(e)}\) (mg/kg) |
|------------------|--------------------------|--------------------------------------------------|--------------------------------|----------------------|-------------------|-------------------|
| Carrots (3 × 125 g/ha, PHI 14 days) | NEU | 2 × 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.11, 0.12, 0.13, 0.22, 0.28 | Recalculated by a drying factor of 8 Combined NEU/SEU data set (U-test, 5%) MRL\(_{OECD}\): 2.87/3.0 (NEU/SEU) MRL\(_{OECD}\): 3.17/4.0 (NEU) MRL\(_{OECD}\): 2.27/3.0 (SEU) Extrapolation to roots and rhizome spices | – | 0.28 (carrots) | 0.08 (carrots) |
| | SEU | 0.02, 0.03, 0.07, 0.10, 0.11, 0.13, 0.15 | 3.0 (dried) | 2.24 (dried) | 0.64 (dried) |
| Barley grain (125 g/ha) PHI n.a. | NEU | 4 × < 0.02, 0.03, 0.04, 0.04, 0.15 | MRL\(_{OECD}\): 0.226/0.30 | 0.3 | 0.15 | 0.02 |
| Barley straw (125 g/ha) PHI n.a. | NEU | 0.07, 0.15, 0.22, 0.23, 0.39, 0.54, 0.61, 0.71 | MRL\(_{OECD}\): 1.3/1.5 | – | 0.71 | 0.31 |

MRL: maximum residue level; OECD: Organisation for Economic Co-operation and Development; PHI: preharvest interval; GAP: Good Agricultural Practice.

\(^{(a)}\): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.

\(^{(b)}\): Individual residue levels considered for MRL calculation are reported in ascending order and refer to difenoconazole only. Residues of TDMs are not reported.

\(^{(c)}\): Any information/comment supporting the decision and OECD MRL calculation (unrounded/rounded values).

\(^{(d)}\): HR: Highest residue level according to the residue definition for risk assessment.

\(^{(e)}\): STMR: Median residue level according to residue definition for risk assessment.
3.1.1.3. Effect of industrial processing and/or household preparation

The effect of processing on the nature of difenoconazole was investigated in studies performed at three test conditions representing pasteurisation, baking/brewing/boiling and sterilisation (20 min at 90°C, pH 4; 60 min at 100°C, pH 5; 20 min at 120°C, pH 6). The peer review concluded that the compound is hydrolytically stable under the representative processing conditions. Thus, for processed commodities the same residue definition as for raw agricultural commodities is applicable (EFSA, 2011a). No studies investigating the effect of processing on the magnitude of the residues in the commodities under assessment were submitted in the present application.

3.1.2. Rotational crops

Several crops under consideration can be grown in rotation with other crops and thus possible occurrence of difenoconazole residues in rotational/succeeding crops from the use on primary crops has to be assessed. Difenoconazole slowly degrades in the soil with a maximum DT90 value observed in field studies of 879 days (EFSA, 2011a) which is significantly above the trigger value of 100 days. According to European guidelines on rotational crops (European Commission, 1997c), further investigation of residues in rotational crops is required.

3.1.2.1. Nature of residues

The studies on the nature of difenoconazole in rotational crops were described in detail during the peer review and in previously issued EFSA reasoned opinions (EFSA, 2011a, 2012, 2014a). The confined rotational crops studies were performed with leafy vegetables (lettuce and spinach), root vegetables (carrot, sugar beet and turnips), cereals (spring and winter wheat, and maize) and oilseeds (mustard). Difenoconazole was applied to bare soil at a rate of 750 g/ha one month prior to crop planting and samples were analysed for difenoconazole and triazole alanine. The residues of difenoconazole in the samples analysed were below the LOQ. The samples were not analysed for the other TDM and further information is still required (EFSA, 2011a).

Pending the outcome of the evaluation of confirmatory data [according to Regulation (EC) No 1100/2011] on the formation of TDMs in rotational crops, the same residue definitions as established in primary crops are currently applicable.

3.1.2.2. Magnitude of residues

Considering that the maximum seasonal application rate on the crops under consideration in the framework of these applications (max. 3 × 125 g/ha) is the same as in the rotational crop field studies (750 g/ha), it is unlikely that significant levels of parent difenoconazole will be found in rotational crops. 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.

3.2. Nature and magnitude of residues in livestock

Several crops under consideration (barley, cabbage, pulses) and their by-products may be fed to livestock, therefore the potential transfer of residues to products of animal origin was investigated.

The median and maximum dietary burden values for livestock were calculated in accordance with the OECD guidance document (OECD, 2013) and the animal dietary burden calculator developed by EFSA. To conduct the calculations, EFSA used the residue values reported in a previous reasoned opinion (EFSA, 2010), the STMR/HR of the feed items and/or its by-products for the CXLs implemented in the EU legislation and retrieved in the JMPR reports (FAO, 2013, 2015) and in the framework of these MRL applications. For the crops for which existing MRLs are above the LOQ (i.e. kale, potatoes, cassava, peas, linseeds) and input values were not available to refine the calculation, the existing MRL was used. Data on turnips/swedes leaves were not included as they were not available because not included in the list of feed items at time of the previous MRL assessment (EFSA, 2010). When specific processing factors (PFs) were not available, the default PFs were used to estimate the residue levels in the feed by-products. This calculation is conservative for difenoconazole as it includes MRL values and default PFs. A more comprehensive dietary burden calculation will be conducted under MRL review, when further information on the authorised uses of difenoconazole will be available to EFSA.
It should be noted that the dietary burden of TDMs present in animal feed has not been calculated because this would require a comprehensive approach, taking into account all active substances belonging to the triazole group.

The input values for the dietary burden calculation are summarised in Table 5.

**Table 5: Input values for the dietary burden calculation**

| Feed commodity                      | Median dietary burden | Maximum dietary burden |
|-------------------------------------|-----------------------|------------------------|
|                                     | Input (mg/kg)         | Comment                | Input (mg/kg) | Comment                |
| Barley straw                        | 0.31                  | STMR                   | 0.71          | HR                     |
| Barley grain                        | 0.02                  | STMR                   | 0.02          | STMR                   |
| Peas                                | 0.10                  | EU MRL                 | 0.10          | EU MRL                 |
| Beans, Lupin seed                   | 0.02                  | STMR                   | 0.02          | STMR                   |
| Sugar beet tops                     | 0.25                  | STMR (EFSA, 2010)      | 0.62          | HR (EFSA, 2010)        |
| Head cabbage leaves                 | 0.02                  | STMR                   | 0.19          | HR                     |
| Kale                                | 2.00                  | EU MRL                 | 2.00          | EU MRL                 |
| Wheat, rye straw                    | 0.48                  | STMR (EFSA, 2010)      | 1.30          | HR (EFSA, 2010)        |
| Carrot, culls                       | 0.10                  | STMR (EFSA, 2013)      | 0.28          | HR (EFSA, 2013)        |
| 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, 2010)      | 0.28          | HR (EFSA, 2010)        |
| Soybean seed                        | 0.01                  | STMR (FAO, 2015)       | –             |                        |
| Wheat, rye grain                    | 0.02                  | STMR (EFSA, 2010)      | 0.02          | STMR (EFSA, 2010)      |
| Apple pomace, wet                   | 0.69                  | STMR (FAO, 2013) × PF  | –             | (0.16 × 4.3)           |
| Citrus, dried pulp                  | 0.20                  | STMR (EFSA, 2010) × PF | –             | (0.02 × 10)            |
| Distiller’s grain, dried            | 0.07                  | STMR × PF (0.02 × 3.3) | –             |                        |
| Flaxseed/linseed, meal              | 0.40                  | EU MRL × PF (0.2 × 2)  | –             |                        |
| Lupin seed meal                     | 0.02                  | STMR × PF (0.02 × 1.1) | –             |                        |
| Potato process waste                | 2.00                  | EU MRL × PF (0.10 × 20) | –             |                        |
| Potato dried pulp                   | 3.80                  | EU MRL × PF (0.10 × 38) | –             |                        |
| Rape seed/canola meal               | 0.08                  | STMR (EFSA 2010) × PF  | –             | (0.04 × 2)             |
| Rice bran                           | 8.80                  | STMR (EFSA 2013) × PF  | –             | (0.88 × 10)            |
| Soybean hulls                       | 0.02                  | STMR × PF (FAO, 2015)  | –             | (0.01 × 2)             |
| Soybean meal                        | 0.004                 | STMR × PF (FAO, 2015)  | –             | (0.01 × 0.38)          |
| Wheat gluten, meal                  | 0.04                  | STMR (EFSA 2010) × PF  | –             | (0.02 × 1.8)           |
The estimated animal dietary intakes taking into account the feed commodities listed in Table 5 and including the crops under consideration are summarised in Table 6. The maximum animal intakes estimated in a previous EFSA opinion (EFSA 2010) according to the feedstuff tables reported in the EU guidance (European Commission, 1996) are reported in this table in the column ‘Previous assessment’.

The additional crops under consideration in these MRL applications did not significantly change the maximum animal intakes estimated in the previous EFSA opinion (EFSA, 2010) for poultry. For ruminants and pigs, the new dietary burden increased significantly. Therefore, the expected difenoconazole residues in these animal species should, in principle, be investigated.

Nevertheless, according to the metabolism and livestock feeding studies assessed during the 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 Regulation and that the current residue definition established in the MRL Regulation is difenoconazole only, the modification of the existing MRL in products of animal origin according to this residue definition is not required. Moreover, the calculated dietary burdens are only indicative, may be overestimated and not reflecting the existing authorised GAPs. Therefore, EFSA is of the opinion that a full assessment of the metabolism and the magnitude of the residues in livestock should be performed in the framework of the MRL review under Article 12 of the Regulation 396/2005, when further information on the authorised uses of difenoconazole will be available.

Table 6: Results of the dietary burden calculation

| Animal                  | Median burden (mg/kg bw) | Maximum burden (mg/kg bw) | Maximum burden (mg/kg DM) | > 0.1 mg/kg DM (Y/N) | Highest contributing commodity(a) | Previous assessment (max. burden)(b) |
|-------------------------|--------------------------|---------------------------|---------------------------|----------------------|-----------------------------------|--------------------------------------|
| Beef cattle             | 0.23                     | 0.25                      | 10.45                     | Yes                  | Potato, process waste             | 6.78                                 |
| Dairy cattle            | 0.30                     | 0.32                      | 8.25                      | Yes                  | Potato, process waste             | 6.18                                 |
| Ram/Ewe                 | 0.28                     | 0.29                      | 8.86                      | Yes                  | Potato, process waste             |                                       |
| Lamb                    | 0.21                     | 0.24                      | 5.53                      | Yes                  | Potato, process waste             |                                       |
| Swine (breeding)        | 0.12                     | 0.13                      | 5.81                      | Yes                  | Potato, process waste             | 3.88                                 |
| Swine (finishing)       | 0.04                     | 0.06                      | 2.01                      | Yes                  | Potato, dried pulp               |                                       |
| Poultry broiler         | 0.08                     | 0.09                      | 1.28                      | Yes                  | Rice, bran/pollard               | 1.37                                 |
| Poultry layer           | 0.06                     | 0.08                      | 1.10                      | Yes                  | Potato, dried pulp               |                                       |
| Turkey                  | 0.01                     | 0.03                      | 0.35                      | Yes                  | Swede, roots                      |                                       |

bw: body weight; DM: dry matter.
(a): Considering the maximum dietary animal burden.
(b): Previous assessment done according to the old calculator. The calculated dietary burdens only referred to ruminants (meat and milk) and poultry.

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

(a): In the absence of processing factors supported by data, default processing factors were included in the calculation to consider the potential concentration of residues in the processed commodities.
4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA PRIMo. This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population\(^{13}\) (EFSA, 2007).

To calculate the chronic exposure, EFSA used median residue values (STMR) derived from the residue trials conducted for the crop under consideration and reported in Table 4, the STMR values reported in previous EFSA reasoned opinions (EFSA, 2009, 2010, 2011b, 2011c, 2012, 2013, 2014a,b) and derived by JMPR (FAO, 2013, 2015) for the CXLs implemented in the EU legislation. For the remaining commodities of plant and animal origin, the existing MRLs as established in Regulation (EU) No 2017/626 were used as input values. The acute consumer exposure assessment was performed only with regard to the commodities under consideration. The input values used for the dietary exposure calculation are summarised in Table 7.

**Table 7:** Input values for the consumer dietary exposure assessment

| Commodity | Chronic exposure assessment | Acute exposure assessment |
|-----------|----------------------------|--------------------------|
|           | Input (mg/kg) | Comment | Input (mg/kg) | Comment |
| **Risk assessment residue definition for plants:** difenoconazole | | | |
| Barley | \(0.02\) | STMR | \(0.02\) | STMR |
| Apricots | \(0.17\) | STMR | \(0.37\) | HR |
| Strawberries | \(0.14\) | STMR | \(0.37\) | HR |
| Brussels sprouts | \(0.09\) | STMR | \(0.15\) | HR |
| Head cabbages | \(0.02\) | STMR | \(0.19\) | HR |
| Lettuces and salad plants including Brassicacea, excluding Roman rocket/rucola and lamb’s lettuces | \(0.52\) | STMR | \(2.51\) | HR |
| Scaroles/broad-leaved endives\(^{(a)}\) | \(0.52\) | STMR (lettuce) (scenario 1) | \(2.51\) | HR (lettuce) (scenario 1) |
| | \(0.18\) | STMR (lettuce) (scenario 2) | \(0.53\) | HR (lettuce) (scenario 2) |
| Beet leaves (chard) | \(0.52\) | STMR (lettuce) | \(2.51\) | HR (lettuce) |
| Herbs and edible flowers (excluding chervil, parsley, celery leaves, basil) | \(0.52\) | STMR (lettuce) | \(2.51\) | HR (lettuce) |
| Celeries | \(1.22\) | STMR | \(3.40\) | HR |
| Cardoons | \(1.22\) | STMR (celery) | \(3.40\) | HR (celery) |
| Rhubarbs | \(0.12\) | STMR (celery stems) | \(0.26\) | HR (celery stems) |
| Leeks | \(0.13\) | STMR | \(0.40\) | HR |
| Pulses, except peas | \(0.02\) | STMR | \(0.02\) | STMR |
| Roots and rhizome (spices) | \(0.64\) | STMR (carrot) × PF (8) | \(2.24\) | HR (carrot) × PF (8) |
| Citrus, pome fruit | \(0.16\) | STMR (FAO, 2013) | | |
| Peaches | \(0.15\) | STMR (EFSA, 2010) | | Acute risk assessment was undertaken only with regard to the crops under consideration |
| Grapes (table and wine) | \(0.52\) | STMR (FAO, 2013) | | |
| Blackberries, raspberries | \(0.04\) | STMR (EFSA 2012) | | |
| Olives (table and oil) | \(0.47\) | STMR (EFSA, 2010) | | |
| Avocados | \(0.05\) | STMR (FAO, 2015) | | |
| Papaya | \(0.01\) | STMR-peel (EFSA, 2013) | | |

\(^{13}\) 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 1 regional and 4 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 Member States surveys are used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).
The estimated exposure was then compared with the toxicological reference values derived for difenoconazole (Table 2). The results of the intake calculation using the EFSA PRIMo is a key supporting document and is made publicly available as a background document to this reasoned opinion.

A long-term consumer intake concern was not identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated chronic intake accounted for up to 86.7% of the acceptable daily intake (ADI) (WHO Cluster diet B). The contribution of residues in crops under consideration accounted for a maximum of 2.79% of ADI for lettuces (ES adult), 1.86% of ADI for celeries (IE adult) and 1.06% of ADI for scaroles (NL child, scenario 1). The contribution of residues in the other crops under consideration was lower than 1% of the ADI.

An acute consumer risk was identified in relation to the intended indoor use on scaroles. Considering the HR observed in the submitted residue trials and applying the currently agreed methodology, an exceedance of the acute reference dose (ARfD) (137.2%) was identified (scenario 1). When considering the less critical outdoor GAPs the acute intake accounted for 29% of the ARfD (scenario 2). No acute concern was identified for all the other uses under consideration, the highest

| Commodity                        | Chronic exposure assessment | Acute exposure assessment |
|----------------------------------|----------------------------|---------------------------|
|                                  | Input (mg/kg) | Comment | Input (mg/kg) | Comment |
| Beetroots                        | 0.08          | STMR (EFSA, 2013) |              |         |
| Carrots                          | 0.08          | STMR (EFSA, 2013) |              |         |
| Horseradish                      | 0.08          | STMR (EFSA, 2013) |              |         |
| Jerusalem artichoke              | 0.08          | STMR (EFSA, 2013) |              |         |
| Parsnip                          | 0.08          | STMR (EFSA, 2013) |              |         |
| Parsley root                     | 0.08          | STMR (EFSA, 2013) |              |         |
| Radish                           | 0.08          | STMR (EFSA, 2013) |              |         |
| Salsify                          | 0.08          | STMR (EFSA, 2013) |              |         |
| Swedes, turnips                  | 0.08          | STMR (EFSA, 2010) |              |         |
| Garlic                           | 0.01          | STMR (EFSA, 2013) |              |         |
| Onion (bulb)                     | 0.01          | STMR (EFSA, 2013) |              |         |
| Shallots                         | 0.01          | STMR (EFSA, 2013) |              |         |
| Spring onions                    | 2.8           | STMR (FAO, 2013)  |              |         |
| Tomatoes                         | 0.72          | STMR (EFSA, 2010) |              |         |
| Peppers                          | 0.17          | STMR (EFSA, 2014a)|              |         |
| Aubergines                       | 0.18          | STMR (EFSA, 2014a)|              |         |
| Cucumbers, gherkins, courgettes  | 0.01          | STMR (EFSA, 2012) |              |         |
| Melons                           | 0.01          | STMR-peel (EFSA, 2013)|              |         |
| Pumpkin, watermelon              | 0.01          | STMR (EFSA, 2013) |              |         |
| Broccoli                         | 0.13          | STMR (EFSA, 2011b)|              |         |
| Lamb’s lettuces                  | 1.45          | STMR (EFSA, 2014b)|              |         |
| Rucola, rocket                   | 0.44          | STMR (EFSA, 2014b)|              |         |
| Witloof                          | 0.01          | STMR (EFSA, 2013) |              |         |
| Parsley, chervil, celery leaves  | 4.65          | STMR (EFSA, 2009) |              |         |
| Basil (mint)                     | 4.65          | STMR (EFSA, 2014b)|              |         |
| Fennel                           | 1.66          | STMR (EFSA, 2009) |              |         |
| Globe artichoke                  | 0.36          | STMR (EFSA, 2013) |              |         |
| Soya bean                        | 0.01          | STMR (FAO, 2015)  |              |         |
| Rice                             | 0.88          | STMR (EFSA, 2013) |              |         |
| Chicory roots                    | 0.20          | STMR (EFSA, 2013) |              |         |
| Wheat, rye                       | 0.02          | STMR (EFSA, 2010) |              |         |
| Other plant and animal commodities | MRL | MRLs in Regulation (EU) No 2017/626 |

STMR: supervised trials median residue; HR: highest residue; PF: processing factor; MRL: maximum residue level.
calculated acute intake being 97.55% of the ARfd for celeries, 42.21% of the ARfd for lettuces, 27.5% of the ARfd for chards, 14.7% of the ARfd for leeks and less than 10% for the remaining crops.

EFSA concludes that, except for the indoor use on scaroles, the intended uses of difenoconazole on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a concern for public health.

EFSA emphasises that the above assessment does not yet take into consideration TDMs. As these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommended that a separate risk assessment should be performed for TDMs as soon as 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 TDMs is available.

Furthermore, the above consumer risk assessment was performed disregarding the possible impact of plant and livestock metabolism on the enantiomers ratio of the active substance and further investigation on this matter would in principle be required. Since guidance is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

**Conclusions and recommendations**

The information submitted was sufficient to propose the MRLs summarised in the table below:

| Code   | Commodity                  | EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification(b) |
|--------|----------------------------|----------------|-------------------------|--------------------------|
| 0140010| Apricots                   | 0.5            | 0.7                     | SEU use supported. No consumer health risk was identified |
| 0152000| Strawberries               | 0.4            | 0.5                     | Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| 0242010| Brussels sprouts           | 0.2            | 0.3                     | NEU/SEU uses supported. No consumer health risk was identified |
| 0242020| Head cabbages              | 0.2            | 0.3                     | NEU/SEU uses supported. No consumer health risk was identified |
| 0251020| Lettuces                   | 3              | 4                       | Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| 0251030| Scaroles (broad-leaf endives) | 0.05*       | 0.8                     | Extrapolated from lettuces. Proposed MRL is derived from outdoor NEU/SEU uses (no consumer health risk was identified for the outdoor NEU/SEU uses). An acute intake concern was identified for the indoor use |
| 0251040| Cresses                    | 0.05*          | 4                       | Extrapolated from lettuce (indoor uses). |
| 0251050| Land cresses               | 0.05*          | 4                       | Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| 0251070| Red mustards               | 0.05*          | 4                       | |
| 0251080| Leaves and sprouts of *Brassica* spp., including turnip greens | 0.05* | 4 | |
| 0251990| Other lettuces and salad plants | 0.05* | 4 | |
| 0252030| Beat leaves (chards)       | 0.2            | 4                       | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| Code(a) | Commodity                  | EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification(b)                                                                 |
|---------|----------------------------|----------------|------------------------|------------------------------------------------------------------------------------------|
| 0256020 | Chives                     | 2              | 4                      | Extrapolated from lettuce (indoor uses). Indoor and NEU/SEU uses supported. No consumer health risk was identified |
| 0256050 | Sage                       | 2              | 4                      |                                                                                                                                                    |
| 0256060 | Rosemary                   | 2              | 4                      |                                                                                                                                                    |
| 0256070 | Thyme                      | 2              | 4                      |                                                                                                                                                    |
| 0256090 | Bay leaves                  | 2              | 4                      |                                                                                                                                                    |
| 0256100 | Tarragon                   | 2              | 4                      |                                                                                                                                                    |
| 0256990 | Other herbs and edible flowers | 2              | 4                      |                                                                                                                                                    |
| 0270020 | Cardoons                   | 4              | 7                      | Indoor and NEU/SEU uses supported by extrapolation from celery. No consumer health risk was identified                                                |
| 0270030 | Celeris                    | 5              | 7                      | Indoor and SEU uses supported. NEU use not supported. No consumer health risk was identified                                                        |
| 0270060 | Leeks                      | 0.5            | 0.6                    | NEU/SEU uses supported. No consumer health risk was identified                                                                               |
| 0270070 | Rhubarbs                   | 0.3            | 0.5                    | Extrapolated from data on celery stems. NEU/SEU use supported. No consumer health risk was identified                                            |
| 0300010 | Beans                      | 0.05*          | 0.06                   | NEU and SEU use supported by extrapolation from combined data set of residues on peas. No consumer health risk was identified. No modification of the MRL is required for dry peas since the existing MRL for this commodity is already covering the new GAP for pulses |
| 0300020 | Lentils                    | 0.05*          | 0.06                   |                                                                                                                                                    |
| 0300040 | Lupins                     | 0.05*          | 0.06                   |                                                                                                                                                    |
| 0300990 | Other pulses               | 0.05*          | 0.06                   |                                                                                                                                                    |
| 0840000 | Roots or rhizome           | 0.3            | 3                      | NEU and SEU uses supported by extrapolation from carrots applying a dehydration factor of 8. No consumer health risk was identified               |
| 0500010 | Barley                     | 0.05           | 0.3                    | NEU use supported. No consumer health risk was identified                                                                                        |

*Indicates that the MRL is set at the limit of analytical quantification (LOQ).
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.
(b): The contribution of TDMs to the consumer intake has not been considered for all crops.

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**Abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| a.s.         | active substance |
| ADI          | acceptable daily intake |
| ARfD         | acute reference dose |
| BBCH         | growth stages of mono- and dicotyledonous plants |
| bw           | body weight |
| CCPR         | Codex Committee on Pesticide Residues |
| CEN          | European Committee for Standardisation (Comité Européen de Normalisation) |
| cGAP         | critical GAP |
| CXL          | Codex maximum residue limit |
| DALA         | days after last application |
| DAR          | draft assessment report |
| DM           | dry matter |
| DT$_{90}$    | period required for 90% dissipation (define method of estimation) |
| EC           | emulsifiable concentrate |
| EMS          | evaluating Member State |
| FAO          | Food and Agriculture Organization of the United Nations |
| GAP          | Good Agricultural Practice |
| HR           | highest residue |
| ISO          | International Organisation for Standardisation |
| IUPAC        | International Union of Pure and Applied Chemistry |
| JMPR         | Joint FAO/WHO Meeting on Pesticide Residues |
| LC           | liquid chromatography |
| LOQ          | limit of quantification |
| MRL          | maximum residue level |
| MS           | Member States |
| MS/MS        | tandem mass spectrometry detector |
| NEU          | northern Europe |
| OECD         | Organisation for Economic Co-operation and Development |
| PF           | processing factor |
| PHI          | preharvest interval |
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| QuEChERS     | Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| RAC          | raw agricultural commodity |
| RMS          | rapporteur Member State |
| SANCO        | Directorate-General for Health and Consumers |
| SEU          | southern Europe |
| SC           | suspension concentrate |
| STMR         | supervised trials median residue |
| TDM          | triazole derivative metabolites |
| WG           | water-dispersible granules |
| WHO          | World Health Organization |
## Appendix A – Good Agricultural Practice (GAPs)

| 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) | Remarks |
|-----------------------|-------------------------|---------------|-----------------------------------|-------------|----------------|------------------------------|-----------|---------|
|                        |                         |               |                                    | Type (b)    | Method kind | Conc. a.s. (g/L) | Range of growth stages & season(c) | Number min-max | Interval between application (min) | Water L/ha min-max | g a.s./ha min-max |               |           |
| Apricots              | SEU                     | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | BBCH 88 | 2                     | 7 days | 1,500 | 112.5 | 7 | 1 Fruit set 2 14-day preharvest 3 7-day preharvest |
| Strawberries          | EU                      | G             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | BBCH 85-89 | 3                     | 7 days | 500-2,000 | 125 | 3 |               |           |
| Strawberries          | NEU, SEU                | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | BBCH 85-89 | 2                     | 7 days | 500-2,000 | 125 | 3 |               |           |
| Brussels sprouts      | NEU                     | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40-49 | 3                     | 14 days | 250-400 | 125 | 21 |               |           |
| Brussels sprouts      | SEU                     | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40-49 | 2                     | 14 days | 300-1,000 | 125 | 21 |               |           |
| Cabbage               | NEU, SEU                | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40-49 | 3                     | 14 days | 400-1,000 | 125 | 21 |               |           |
| Lettuce               | EU                      | G             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40 | 2                     | 7 days | 300-1,000 | 100 | 14 |               |           |
| Lettuce               | NEU                     | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40 | 2                     | 7 days | 300-1,200 | 125 | 14 |               |           |
| Lettuce               | SEU                     | F             | Fungal diseases                    | SC          | Foliar spray | 125 g/L         | From BBCH 40 | 2                     | 7 days | 500-1,000 | 125 | 14 |               |           |
| Other salad plants (excluding rocket, lamb’s lettuce) | EU | G | Fungal diseases | SC | Foliar spray | 125 g/L | From BBCH 40 | 2 | 7 days | 300-1,000 | 100 | 14 |               |           |
| Crop and/or situation | NEU, SEU, MS or country | F, G, or T(1) | Pests or Group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|-------------------------|--------------|-----------------------------------|-------------|-----------------|-----------------------------|-----------|---------|
| Other salad plants (excluding rocket, lamb’s lettuce) | NEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 300–1,200 | 125 | 14 |
| Other salad plants (excluding rocket, lamb’s lettuce) | SEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 500–1,000 | 125 | 14 |
| Chard | EU | G | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 300–1,000 | 100 | 14 |
| Chard | NEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 300–1,200 | 125 | 14 |
| Chard | SEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 500–1,000 | 125 | 14 |
| Herbs and edible flowers (excluding chervil, parsley and celery leaf) | NEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 300–1,200 | 125 | 14 |
| Herbs and edible flowers (excluding chervil, parsley and celery leaf) | SEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40 | 2 | 7 days | 500–1,000 | 125 | 14 |
| Cardoon | EU | G | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40–48 | 2 | 14 days | 300–800 | 125 | 14 |
| Cardoon | NEU, SEU | F | Fungal diseases | SC 125 g/L | Foliar spray From BBCH 40–48 | 3 | 14 days | 300–800 | 125 | 14 |
| Crop and/or situation | NEU, SEU, MS or country | F, G, or I(a) | Pests or Group of pests controlled | Preparation Type (b) | Conc. a.s. | Application Method kind | Application Range of growth stages & season(c) | Number min–max | Interval between application (min) | Application rate per treatment g a.s./hL min–max | Water L/ha min–max | g a.s./ha min–max | PHI (days) (d) | Remarks |
|-----------------------|-------------------------|--------------|------------------------------------|--------------------|----------|------------------------|---------------------------------|--------------|----------------------------------|----------------------------------|-----------------|-----------------|-----------|---------|
| Celery                | EU                      | G            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 40–48                 | 2            | 14 days                          | 300–800                  | 125             | 14              |          |         |
| Celery                | NEU, SEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 40–48                 | 3            | 14 days                          | 300–800                  | 125             | 14              |          |         |
| Leek                  | NEU, SEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 41–49                 | 3            | 12 days                          | 400–1,000               | 125             | 21              |          |         |
| Rhubarbs              | NEU, SEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 41–49                 | 3            | 14 days                          | 300–800                  | 125             | 14              |          |         |
| Pulses                | NEU, SEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 69–79                 | 2            | 21 days                          | 400–500                  | 100             | 28              |          |         |
| Spices (roots and rhizome) | NEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 40–49                 | 3            | 14 days                          | 200–800                  | 125             | 14              |          |         |
| Spices (roots and rhizome) | SEU                | F            | Fungal diseases                    | SC                 | 125 g/L | Foliar spray           | From BBCH 40–49                 | 3            | 14 days                          | 200–1,000               | 125             | 14              |          |         |
| Barley                | NEU                      | F            | Various fungi                      | EC                 | 250 g/L | Foliar spray           | BBCH 39–59                      | 1            | 31.25–83.3                       | 150–400                  | 125             | n.a.            |          |         |

NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; EC: emulsifiable concentrate; SC: suspension concentrate.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.
(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 preharvest interval.
### Appendix B – Used compound codes

| Code/Trivial name | Chemical name | Structural formula |
|-------------------|---------------|--------------------|
| Difenconazole     | 3-Chloro-4-\{(2RS,4RS;2RS,4SR)-4-methyl-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl\}phenyl 4-chlorophenyl ether | ![Structural formula of Difenconazole](image1) |
| Difenconazole     | (1RS)-1-[2-Chloro-4-(4-chlorophenoxy)phenyl]-2-(1H-1,2,4-triazol-1-yl)ethanol | ![Structural formula of Difenconazole alcohol](image2) |
| Difenconazole     | 1,2,4-Triazole | ![Structural formula of 1,2,4-Triazole](image3) |
| Difenconazole     | Triazole alanine | ![Structural formula of Triazole alanine](image4) |
| Difenconazole     | Triazole acetic acid | ![Structural formula of Triazole acetic acid](image5) |
| Difenconazole     | Triazole lactic acid or Triazole hydroxy propionic acid | ![Structural formula of Triazole lactic acid or Triazole hydroxy propionic acid](image6) |

### Triazole derivative metabolites (TDMs)

| 1,2,4-Triazole     | 1H-1,2,4-Triazole c1ncnn1 | ![Structural formula of 1,2,4-Triazole](image3) |
| Triazole alanine   | 3-(1H-1,2,4-Triazol-1-yl)-D,L-alanine NC(Cn1cncn1)C(-)=O | ![Structural formula of Triazole alanine](image4) |
| Triazole acetic acid | 1H-1,2,4-Triazol-1-ylacetic acid O=C(O)Cn1cncn1 | ![Structural formula of Triazole acetic acid](image5) |
| Triazole lactic acid or Triazole hydroxy propionic acid | (2RS)-2-Hydroxy-3-(1H-1,2,4-triazol-1-yl)propanoic acid OC(Cn1cncn1)C(-)=O | ![Structural formula of Triazole lactic acid or Triazole hydroxy propionic acid](image6) |
Appendix C – Pesticide Residue Intake Model (PRIMo)

**Scenario 1**

- **Status of the active substance:** Code no.
- **LOQ (mg/kg bw):** Proposed LOQ.

| Difenoconazole | Source of ADI | Source of ARfD | Year of evaluation |
|----------------|---------------|----------------|--------------------|
| ADI (mg/kg bw/day) | EFSA | EFSA | 2011 |
| ARfD (mg/kg bw) | 0.16 | | |

- **Year of evaluation:** 2011

| Source ADI | Source ARfD | Year of evaluation |
|------------|-------------|--------------------|
| EFSA | EFSA | 2011 |

**Chronic risk assessment – refined calculations**

| Commodity/group of commodities | 1st contributor to MS diet | 2nd contributor to MS diet | 3rd contributor to MS diet |
|--------------------------------|---------------------------|---------------------------|---------------------------|
| | (in % of ADI) | (in % of ADI) | (in % of ADI) |
| Tomatoes | 9.1 | 9.9 | Citrus for oil production |
| Citrus fruit | 8.7 | 6.5 | Citrus fruit |
| WHO Cluster diet E | 6.3 | 4.0 | Other leafy brassica |
| DE child | 6.2 | 4.0 | Other leafy brassica |
| NL child | 5.3 | 4.0 | Other leafy brassica |
| FR toddler | 5.3 | 4.0 | Other leafy brassica |
| IE adult | 5.0 | 4.0 | Other leafy brassica |
| FR general population | 5.0 | 4.0 | Other leafy brassica |
| WHO Cluster diet D | 5.0 | 4.0 | Other leafy brassica |
| WHO regional European diet | 5.0 | 4.0 | Other leafy brassica |
| ES child | 5.0 | 4.0 | Other leafy brassica |
| FR all population | 5.0 | 4.0 | Other leafy brassica |
| SE general population 50th percentile | 5.0 | 4.0 | Other leafy brassica |
| UK Toddler | 5.0 | 4.0 | Other leafy brassica |
| NL general | 5.0 | 4.0 | Other leafy brassica |
| UK infant | 5.0 | 4.0 | Other leafy brassica |
| WHO Cluster diet F | 5.0 | 4.0 | Other leafy brassica |
| UK adult | 5.0 | 4.0 | Other leafy brassica |
| PL general population | 5.0 | 4.0 | Other leafy brassica |
| DK adult | 5.0 | 4.0 | Other leafy brassica |
| LT adult | 5.0 | 4.0 | Other leafy brassica |
| FI adult | 5.0 | 4.0 | Other leafy brassica |

**Commodity/group of commodities:**

- Tomatoes
- Citrus fruit
- WHO Cluster diet E
- DE child
- NL child
- FR toddler
- IE adult
- FR general population
- WHO Cluster diet D
- WHO regional European diet
- ES child
- FR all population
- SE general population 50th percentile
- UK Toddler
- NL general
- UK infant
- WHO Cluster diet F
- UK adult
- PL general population
- DK adult
- LT adult
- FI adult

**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.
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 calculation, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100 % of the ARfD.

ACUTE RISK ASSESSMENT /CHILDREN – REFINED CALCULATIONS

Conclusion:

For Difenoconazole, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

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 variability factor of 3.
**Scenario 2**

**Difenoconazole**

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

| No of diets exceeding ADI:   | 13 - 67 |

| Commodity/group of commodities | pTMRLs at LOQ (in % of ADI) |
|--------------------------------|-----------------------------|
| Tomatoes                       | 86.7 WHO Cluster diet B     |
| Pome fruit                     | 77.1 DE child               |
| Wine grapes                    | 69.8 NL child               |
| Spinach                        | 65.3 FR toddler             |
| Citrus fruit                   | 62.0 IE adult               |
| Tomatoes                       | 46.4 WHO cluster diet E     |
| Tomatoes                       | 43.1 FR infant              |
| Tomatoes                       | 40.7 WHO cluster diet D     |
| Tomatoes                       | 39.1 ES child               |
| Pome fruit                     | 38.3 FR all population      |
| Tomatoes                       | 35.7 SE general population  |
| Tomatoes                       | 34.6 UK Toddlers            |
| Tomatoes                       | 33.4 NL general             |
| Tomatoes                       | 31.7 UK Infant              |
| Tomatoes                       | 31.3 WHO Cluster diet F     |
| Tomatoes                       | 30.7 ES adult               |
| Tomatoes                       | 29.9 IT kids and toddler    |
| Tomatoes                       | 28.2 IT adult               |
| Tomatoes                       | 24.7 UK vegetarian          |
| Tomatoes                       | 21.8 DK child               |
| Tomatoes                       | 21.6 UK Adult               |
| Tomatoes                       | 20.4 NL general population  |
| Tomatoes                       | 19.6 DK adult               |
| Tomatoes                       | 16.7 LT adult               |
| Tomatoes                       | 12.9 FI adult               |

**Chronic risk assessment – refined calculations**

| Commodity/group of commodities | TMDI (range) in % of ADI | 3rd contributor to MS diet |
|--------------------------------|--------------------------|---------------------------|
| Tomatoes                       | 9.3 Wine grapes          |
| Pome fruit                     | 9.9 Olive for oil production |
| Citrus fruit                   | 8.7 Herbal infusions (dried) |
| Spinach                        | 7.4 Spinach              |
| Beans (with pods)              | 7.4 Citrus fruit         |
| Tomatoes                       | 6.9 Vine grapes          |
| Citrus fruit                   | 6.4 Tomatoes             |
| Bears (with pods)              | 6.4 Tomatoes             |
| Tomatoes                       | 5.9 Tomatoes             |
| Rice                           | 5.8 Tomatoes             |
| Rice                           | 5.7 Tomatoes             |
| Rice                           | 5.6 Tomatoes             |
| Rice                           | 5.5 Tomatoes             |
| Rice                           | 5.4 Tomatoes             |
| Rice                           | 5.3 Tomatoes             |
| Rice                           | 5.2 Tomatoes             |
| Rice                           | 5.1 Tomatoes             |
| Rice                           | 5.0 Tomatoes             |
| Rice                           | 4.9 Tomatoes             |
| Rice                           | 4.8 Tomatoes             |
| Rice                           | 4.7 Tomatoes             |
| Rice                           | 4.6 Tomatoes             |
| Rice                           | 4.5 Tomatoes             |
| Rice                           | 4.4 Tomatoes             |
| Rice                           | 4.3 Tomatoes             |
| Rice                           | 4.2 Tomatoes             |
| Rice                           | 4.1 Tomatoes             |
| Rice                           | 4.0 Tomatoes             |
| Rice                           | 3.9 Tomatoes             |
| Rice                           | 3.8 Tomatoes             |
| Rice                           | 3.7 Tomatoes             |
| Rice                           | 3.6 Tomatoes             |
| Rice                           | 3.5 Tomatoes             |
| Rice                           | 3.4 Tomatoes             |
| Rice                           | 3.3 Tomatoes             |
| Rice                           | 3.2 Tomatoes             |
| Rice                           | 3.1 Tomatoes             |
| Rice                           | 3.0 Tomatoes             |
| Rice                           | 2.9 Tomatoes             |
| Rice                           | 2.8 Tomatoes             |
| Rice                           | 2.7 Tomatoes             |
| Rice                           | 2.6 Tomatoes             |
| Rice                           | 2.5 Tomatoes             |
| Rice                           | 2.4 Tomatoes             |
| Rice                           | 2.3 Tomatoes             |
| Rice                           | 2.2 Tomatoes             |
| Rice                           | 2.1 Tomatoes             |
| Rice                           | 2.0 Tomatoes             |
| Rice                           | 1.9 Tomatoes             |
| Rice                           | 1.8 Tomatoes             |
| Rice                           | 1.7 Tomatoes             |
| Rice                           | 1.6 Tomatoes             |

**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

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 calculation, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100 % of the ARfD.

#### Table: Commodity comparisons

| Commodity               | pTMRL | threshold MRL | ARfD/ADI (%) | IESTI 1 | IESTI 2 |
|-------------------------|-------|---------------|--------------|---------|---------|
| Celery                  | 3.4   | -             | 97.6         | 97.6    | 97.6    |
| Lettuce                 | 2.51  | -             | 49.0         | 49.0    | 49.0    |
| Scarcle (broad-leaf)    | 0.53  | -             | 42.21        | 29.0    | 29.0    |
| Beet leaves (chard)     | 2.51  | -             | 14.7         | 10.5    | 10.5    |
| Lentuce                 | 2.51  | -             | 6.3          | 4.3     | 4.3     |
| Rhubarb                 | 0.26  | -             | 0.53         | 0.26    | 0.26    |
| Cherry                  | 2.51  | -             | 20.0         | 1.8     | 1.8     |
| Brussels sprouts        | 0.15  | -             | 20.0         | 0.26    | 0.26    |
| Thyme                   | 0.26  | -             | 0.15         | 0.26    | 0.26    |
| Rosemary                | 0.25  | -             | 5.0          | 0.25    | 0.25    |
| Cress                   | 0.25  | -             | 5.0          | 0.25    | 0.25    |
| Cress                   | 0.25  | -             | 0.0          | 0.0     | 0.0     |
| Ginger                  | 2.24  | -             | 0.1          | 0.2     | 0.2     |
| Bay leaves              | 2.51  | -             | 0.1          | 2.51    | 2.51    |

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

### Acute risk assessment/adults/general population – refined calculations

**Conclusion:**

For Difenoconazole, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

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 calculation, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100 % of the ARfD.

**No exceedance of the ARfD/ADI was identified for any unprocessed commodity.**