European Food Safety Authority

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# REASONED OPINION OF EFSA

## Modification of the existing MRLs for difenoconazole in various leafy vegetables[1]

## Prepared by the Pesticides Unit (PRAPeR)

**(Question No EFSA-Q-2009-00638**

**Question No EFSA-Q-2009-00640)**

## Issued on 22 July 2009

**SUMMARY**

According to Article 6 of the Regulation (EC) No 396/2005, Belgium hereafter referred to as the Evaluating Member State (EMS), compiled two applications to modify the existing MRLs for difenoconazole in parsley, celery leaves, chervil and fennel. In order to accommodate for a new uses of difenoconazole in Belgium, it is proposed to raise the existing MRLs for fennel from 0.3 mg/kg to 5 mg/kg, for parsley, celery leaves from 3 mg/kg to 10 mg/kg and for chervil from 2 mg/kg to 10 mg/kg. Belgium drafted evaluation reports according to Article 8 of Regulation (EC) No 396/2005 which were submitted to the European Commission and forwarded to EFSA on 29 may 2009. EFSA considered both applications in one reasoned opinion.

EFSA derives the following conclusions regarding the applications, based on the above mentioned evaluation reports as well as the Draft Assessment Report prepared by Sweden.

The toxicological reference values for difenoconazole are reported in the DAR and currently the ADI is set at 0.01 mg/kg bw/d and the ARfD is set at 0.2 mg/kg bw.

According to the DAR metabolism of difenoconazole in primary crops is elucidated in four crop categories and residue definition for risk assessment and enforcement is proposed as parent difenoconazole. Nevertheless, apart from difenoconazole, in several parts of crops triazole derivative metabolites (TDMs), which are known as common metabolites of several substances belonging to the triazole chemical class, were identified as a major part of the TRR. Even though TDMs would not occur in amounts of concern following the proposed use, consideration should be given to the fact that TDMs can occur in plant commodities from other sources than difenoconazole therefore resulting in levels that might require consumer exposure assessment. For addressing this issue, a common EU approach on risk assessment of TDMs is under development. It would involve setting of toxicological reference values for TDMs and performing separate risk assessments for the parent compounds and TDMs. Since in leafy parts of the plants (foliage, leaves) parent difenoconazole was the major residue of

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concern according to metabolism studies, EFSA concludes that metabolic pathway in crops under consideration (leafy vegetables) is sufficiently addressed and no additional metabolism studies are currently required. This conclusion, however, might be reconsidered in a light of the outcome of the peer review and in accordance with the EU approach regarding risk assessment of TDMs. Adequate analytical methods are available to enforce the proposed MRLs.

Submitted supervised residue trials data on fennel, parsley, celery leaves and chervil indicate that higher MRLs than proposed by the EMS would be required in order to accommodate for the intended use of difenoconazole in Belgium. Processing studies have not been submitted with regard to the crops under consideration and are not necessary, since the contribution of them to the total dietary intake is very low.

All crops under consideration can be grown as rotational crops therefore occurrence of difenoconazole residues in rotational crops was also investigated. In the DAR it was concluded that the identified metabolites in rotational crops are in accordance with the metabolic pathway observed in primary crops. However, the situation in rotational crops regarding TDMs should be reconsidered taking into account all active substances which produce these common metabolites as soon as the methodology for this type of assessment is available. With regard to the current application, EFSA concludes that significant residue levels of difenoconazole are not expected in rotational crops provided that difenoconazole is applied according to the proposed GAP.

Residues in commodities of animal origin were not assessed in the framework of submitted applications since crops under consideration are not used as a livestock feed.

The consumer risk assessment was performed with revision 2 of the EFSA PRIMo. For the chronic intake assessment EFSA used the existing MRLs for difenoconazole as established in Annex III of Regulation (EC) No 396/2005 as well as the STMR values derived for the intended use of difenoconazole on crops under consideration. For various plant commodities STMR values were available to refine intake calculations. Acute intake assessment was performed only with regard to crops under consideration, using HR values as derived for the intended use of difenoconazole on these crops.

No consumer intake concerns were identified for any of the European diets. Total calculated intake values ranged from 16.6 - 98.7 % of the ADI. Contribution of celery leaves, parsley and chervil to the dietary intake is insignificant. The contribution of fennel to the total dietary intake amounts for a maximum of 1.62% of the ADI (IT Adult diet). No acute intake concerns were identified for the crops under consideration. Contribution to the ARfD amounts for a maximum of 33.7% for fennel, 16.3% for celery leaves, 3.7% for chervil and 2.2% for parsley.

Consequently, EFSA concludes that the intended use on fennel, parsley, celery leaves and chervil is sufficiently supported by data and no risk for consumers was identified.

It should be noted that the contribution of TDM residues in primary crops and rotational crops resulting from the use of difenoconazole has not been taken into account in the consumer risk assessment since at the moment the EU approach for the risk assessment of triazole metabolites is still under development. **As the DAR has not yet been peer reviewed by EFSA, the conclusions reached in this reasoned opinion have to be taken as provisional and might be reconsidered in the light of the conclusions reached in the peer review process for difenoconazole.**

## Overview of the proposed EC MRLs

| Commodity | Existing EC MRL (mg/kg) | Proposed EC MRL (mg/kg) | Justification for the proposal |
|---|---|---|---|
| Enforcement residue definition: difenoconazole | | | |
| Fennel | 0.3 | 6 | MRL proposals are sufficiently supported by data and no risk for consumer was identified for the intended uses. |
| Celery, parsley leaves | 3 | 12 | |
| Chervil | 2 | 12 | |

**Key words: Difenoconazole, parsley, celery leaves, chervil, fennel, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, triazole fungicide, triazole derivative metabolites**

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## BACKGROUND

Regulation (EC) No 396/2005 establishes the rules governing the setting of pesticide MRLs at Community level. Article 6 of that regulation lays down that where a Member State considers that the modification of an MRL is necessary, that Member State may compile and evaluate an application to modify the MRL in accordance with the provisions of Article 7 of that regulation.

Belgium, hereafter referred to as the Evaluating Member State (EMS), compiled two applications to modify the existing MRLs for difenoconazole in fennel, parsley, chervil and celery leaves. Both applications were notified to the European Commission and EFSA and subsequently evaluated in accordance with Article 8 of the Regulation.

After completion, evaluation reports of the EMS were submitted to the European Commission who forwarded the applications, the evaluation reports and the supporting dossiers to EFSA on 29 May 2009. The applications were included in the EFSA Register of Questions with the reference numbers EFSA-Q-2009-00638 and EFSA-Q-2009-00640 and the following subjects:

*Difenoconazole - Application to modify the existing MRLs for difenoconazole in parsley from 3 mg/kg to 10 mg/kg, in chervil from 2 mg/kg to 10 mg/kg and in celery leaves from 3 mg/kg to 10 mg/kg.*

*Difenoconazole - Application to modify the existing MRL for difenoconazole in fennel from 0.3 mg/kg to 5 mg/kg.*

On 3 July 2009 some data requirements were identified regarding MRL application registered as EFSA-Q-2009-00640, which prevented EFSA to conclude on the consumer risk assessment. An updated evaluation report, addressing those data requirements, was submitted by the EMS on 10 July 2009 and taken into consideration by EFSA for finalization of this reasoned opinion.

EFSA then proceeded with the assessment of the application as required by Article 10 of the Regulation.

## TERMS OF REFERENCE

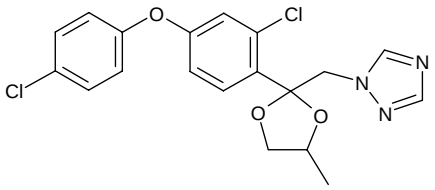
According to Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the Evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

According to Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within 3 months from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

In this particular case the calculated deadline for providing the reasoned opinion for MRL application registered as EFSA-Q-2009-00638 is 29 August 2009 and for EFSA-Q-2009-00640 it is 5 September 2009.

## THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Difenoconazole is the ISO common name for 1-[2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-4-methyl[1,3]dioxolan-2-ylmethyl]-1H-[1,2,4] triazole (IUPAC).




Difenoconazole is a systemic triazole fungicide that controls a broad-spectrum of foliar, seed and soil-borne diseases, caused by *Ascomycetes*, *Basidiomycetes* and *Deuteromycetes*, in cereals, soya, rice, grapes, pome fruit, stone fruit, potatoes, sugar beet and several vegetable and ornamental crops. It is applied by foliar spray or seed treatment. Difenoconazole acts by interference with the ergosterol biosynthesis in target fungi by inhibition of the C-14-demethylation of sterols, which leads to morphological and functional changes of the fungal cell membrane.

Difenoconazole is a stage three "green track" substance with Sweden being the designated Rapporteur Member State. The Draft Assessment Report (DAR) is available. Difenoconazole is included in Annex I to Directive 91/414/EEC by Commission Directive 2008/69/EC which entered into force on 1 January 2009. The representative uses supported for the peer review refer to foliar application on pome fruit, carrots and seed treatment of various cereals (wheat, barley, triticale, rye and oats). The peer review of difenoconazole by EFSA is currently ongoing and a final conclusion is not expected within next months.

The EC MRLs for difenoconazole are set in Annex III to Regulation (EC) No 396/2005 (Appendix B). In Annex III the temporary MRLs were established for crops that were not covered by previous Community MRL legislation. The current MRL for fennel is set at 0.3 mg/kg, for parsley and celery leaves at 3 mg/kg and for chervil at 2 mg/kg. Codex Alimentarius has set CXLs for a wide range of commodities, but no CXLs are set for the crops under consideration.

The GAPs for which the authorizations in Belgium are requested refer to indoor and outdoor uses of difenoconazole once to three times at an application rate of 0.125 kg a.s./ha. The minimum waiting period is 14 days. The summary of GAPs can be found in Appendix A.

In addition to the MRL application and evaluation report submitted by the EMS, EFSA also relied on the DAR prepared under Directive 91/414/EEC. **Since the DAR has not yet been peer reviewed, the conclusions reached in this reasoned opinion have to be taken as provisional and might be reconsidered in the light of the conclusions reached in the peer review process for difenoconazole.**

ASSESSMENT

## 1. Methods of analysis

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

In the Draft Assessment Report for the determination of difenoconazole residues in food of plant origin the extended version of the multi-method DFG 19 (LC-MS/MS detection) was reported as sufficiently validated at the LOQ of 0.02 mg/kg for lettuce and apple and at 0.05 mg/kg for wheat grain and oil seed rape (Sweden, 2006).

Consequently, EFSA concludes that adequate analytical method is available for enforcement of the proposed MRLs in crops under consideration.

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

Availability of analytical methods for enforcement of residues in the foodstuffs of animal origin was not investigated because crops under consideration are not used as livestock feed.

## 2. Mammalian toxicology

The toxicological properties of difenoconazole have been evaluated in the DAR prepared under the Directive 91/414/EEC (Sweden, 2006) and reference values have been proposed. Awaiting the peer review process to be finalized by EFSA, it is proposed to rely on the conclusions of the RMS. The toxicological reference values derived by Sweden are summarized in the table below.

Table 2-1. **Overview of the toxicological reference values**

| | Source | Year | Value | Study relied upon | Safety factor |
|---|---|---|---|---|---|
| Difenoconazole | | | | | |
| ADI | SE | 2006 | 0.01 mg/kg bw/d | 2 yr rats (combined chronic toxicity/oncogenicity) | 100 |
| ARfD | SE | 2006 | 0.2 mg/kg bw | 90 d rat | 100 |

## 3. Residues

### 3.1. Nature and magnitude of residues in plant

#### 3.1.1. Primary crops

3.1.1.1. Nature of residues

Studies on metabolism of difenoconazole in plants were carried out in five crops, representing four crop categories and are reported in the DAR (Sweden, 2006):

- cereals (wheat) – seed application 1 x 2.4 g a.s./100 kg seed; foliar application 4 x 0.247 kg a.s/ha;

- root vegetables (potatoes) - foliar application 6 x 0.123.5 kg a.s./ha

- pulses/oilseeds (oilseed rape) - foliar application 2 x 0.125 kg a.s./ha

- fruits and fruiting vegetables (grape and tomato) - foliar application: 3 - 6 x 0.123 – 0.247 kg a.s./ha(tomatoes); 5 x 0.247 kg a.s./ha (grapes)

Studies were performed by using [phenyl-$^{14}$C] or [triazole-$^{14}$C] labelled difenoconazole.

In tomato studies with [phenyl-$^{14}$C] difenoconazole (phenyl study) parent difenoconazole was the major compound of the TRR (up to 66.3%) in ripe tomatoes and in foliage (68%). In study with [triazole-$^{14}$C] labelled difenoconazole (triazole study) the major components of the TRR in ripe tomatoes were parent difenoconazole and triazole alanine (CGA-131013[2]) accounting for a maximum of 50.9% and 19.3% of the TRR respectively.

In triazole study with wheat (seed treatment and foliar application) in mature straw and grain the major components of the TRR were 1,2,4-triazole (CGA-71019)[3] or triazole acetic acid (CGA-142856)[4] and triazole alanine (CGA-131013). In the phenyl study after foliar application the majority of the TRR in straw was parent difenoconazole (45.4%) along with its metabolite CGA-205375[5](17.3%), while in grains the conjugates of metabolite CGA-189138[6] comprised for up to 35% of the TRR.

In mature potato tubers in the phenyl study the main component of the TRR was metabolite CGA-205375, while in mature foliage the major component of the TRR was parent difenoconazole. In triazole study parent difenoconazole was the major component in mature foliage, but also triazole alanine was identified at levels exceeding 10% of the TRR. In mature tubers triazole alanine alone amounted for up to 78.9% of the TRR.

Regarding grapes, parent difenoconazole formed the major part of the TRR in mature leaves (12.3%) and grapes (17.1%) in the phenyl study. In triazole study parent difenoconazole was the major compound of the TRR in mature leaves and grapes (25.9%) while in immature leaves along with parent compound also metabolite CGA-205374[7] was identified at levels 10.7% of the TRR.

In metabolism study with oilseed rape, the phenyl and triazole studies indicated that in mature straw parent difenoconazole and metabolite CGA-205375 amounts for up to 17% and 13-14% of the TRR respectively. In mature seeds (phenyl study) parent compound was the major fraction of the TRR. In triazole study parent and triazole alanine comprised 13.7% and 12% of the TRR respectively in mature pods. In oilseed rape meal and seeds from the same study the major compound of radioactivity was triazole alanine (56%).

Difenoconazole was extensively degraded in wheat, potato, tomato, grape and oilseed rape with very similar pathways of metabolism in all four crop categories. Studies with wheat, potatoes and oilseed rape seed indicate translocation of triazole related residues to tubers, grains, seeds. Metabolite CGA-205375 is known to be difenoconazole specific. Its toxicity is considered to be covered by the toxicity of parent compound. Metabolites CGA-205374, CGA-205375 and CGA-189138 were investigated regarding acute oral toxicity and the ability to induce mutations in bacteria. The results raised no concern. Extensive metabolism of difenoconazole in several parts of the crop (seeds, grain) results in the formation of high levels (>10% TRR) of triazole alanine, 1,2,4-triazole and triazole acetic acid. All these

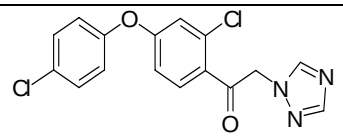
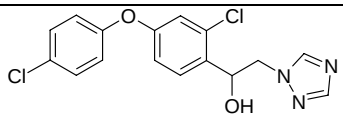
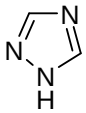
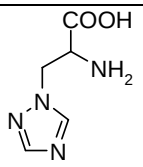
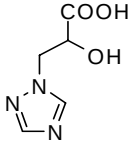
[2] CGA-131013:Triazole alanine:2 –amino-3-[1,2,4]triazol-1-yl-propionic acid
[3] CGA-71019: 1H-[1,2,4]triazole
[4] CGA-142856: Triazole acetic acid: [1,2,4]triazol-1-yl-acetic acid
[5] CGA-205375: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ehanol
[6] CGA-189138: 2-chloro-4-(4-chloro-phenoxy)-benzoic acid
[7] CGA-205374: 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazole-1-yl-ethanone

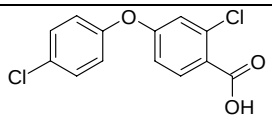
substances are known as triazole derivative metabolites (TDM) which are common metabolites of several other substances belonging to the triazole chemical class (tebuconazole, tetraconazole, penconazole). According to toxicity studies reported in the DAR, triazole acetic acid and triazole alanine are of no toxicological concern in plants. Additional studies are still required for 1,2,4-triazole. Even though TDMs would not occur in amounts of concern following the proposed use on crops, consideration should be given to the fact that TDMs can occur in plant commodities from other sources than difenoconazole therefore resulting in amounts that might require consumer exposure assessment. For addressing this issue, a common EU approach on risk assessment of TDMs is under development. It would involve setting of toxicological reference values for TDMs and performing separate risk assessments for the parent compounds and TDMs.

According to the assessment of the RMS, it was proposed to set parent difenoconazole as risk assessment and enforcement residue definition for all plant commodities. Notice, however, was made by the RMS regarding foliar application on cereals and oilseed rape since any requested use on these crops would require re-evaluation of the residue definition.

Since in leafy parts of the plants (foliage, leaves) parent difenoconazole was major residue of concern according to metabolism studies, EFSA concludes that metabolic pathway in crops under consideration (leafy vegetables) is sufficiently addressed and no additional metabolism studies are currently required. This conclusion, however, might be reconsidered in a light of the outcome of the peer review and in accordance with the EU approach regarding risk assessment of TDMs.

**Overview of metabolites identified in metabolism study**

| | | |
|---|---|---|
| CGA-205374 |  | 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanone |
| CGA-205375 |  | 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanol |
| 1,2,4-triazole CGA-71019 |  | 1H-[1,2,4]triazole |
| Triazole alanine CGA-131013 |  | 2-amino-3-[1,2,4]triazol-1-yl-propionic acid |
| Triazole acetic acid CGA-142856 |  | 1,2,4]triazol-1-yl-acetic acid |

| | | |
|---|---|---|
| CGA-189138 |  | 2-chloro-4-(4-chloro-phenoxy)-benzoic acid |

3.1.1.2. Magnitude of residues

In support of the intended uses of difenoconazole on fennel, Belgium reported various trials on fennel and celery. Assessing the data EFSA took into consideration four indoor trials and four outdoor trials on celery which were performed in Belgium. Extrapolation of residue data from celery to fennel is possible.

In support of the intended uses of difenoconazole on parsley, chervil and celery leaves, Belgium reported four indoor trials on parsley. Regarding outdoor use, Belgium referred to residue trials on spinach available on CIRCA as reported by Germany in the framework of the setting of EC MRLs for herbs. These trials, however, EFSA did not take into account since on CIRCA specific residue trials on parsley leaves are available which were used for deriving MRL proposal and risk assessment values.

Residues trials data are summarized in Table 3-1.

The storage stability studies of difenoconazole residues in treated crops are reported in the DAR (Sweden, 2006). Studies demonstrate storage stability of difenoconazole under deep frozen conditions for at least 24 months in commodities with high water (tomatoes, potatoes), high oil content (cottonseed oil, meal and seeds) and in dry commodities (wheat grain, straw, forage). In lettuce head, soybeans, bananas the storage stability of difenoconazole is demonstrated for at least 12 months under deep freeze conditions. Supervised residue trial samples prior analysis where stored deep frozen from 1.5 to a maximum of 23 months, meaning that analytical data are acceptable with regard to storage stability.

According to the EMS, analytical methods used for analysing residue trial samples are considered sufficiently validated and fit for purpose.

Table 3-1. **Overview of the available residues trials data**

| Commodity | Region (a) | Outdoor /Indoor | Individual trial results (mg/kg) | | STMR (mg/kg) (b) | HR (mg/kg) (c) | MRL proposal (mg/kg) | Median CF (d) | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | | Enforcement | Risk assessment | | | | | |
| Enforcement residue definition: difenoconazole | | | | | | | | | |
| Fennel | NEU | Outdoor | 0.11; 0.789; 1.09; 3.31 | 0.11; 0.789; 1.09; 3.31 | 0.94 | 3.31 | 6.0 | 1.0 | Residue trials were performed on celery but residue data can be extrapolated to fennel. Data sets are comparable therefore they were combined to derive MRL proposal and risk assessment values.<br>$R_{ber(outdoor)}$=5.5 mg/kg<br>$R_{max(outdoor)}$=8.5 mg/kg<br>$R_{ber(indoor)}$=6.3 mg/kg<br>$R_{max(indoor)}$=10.1 mg/kg<br>Combined data set:<br>$R_{ber}$=5.99 mg/kg<br>$R_{max}$=6.3 mg/kg |
| | EU | Indoor | 0.09; 0.41; 2.91; 3.21 | 0.09; 0.41; 2.91; 3.21 | 1.66 | 3.21 | | | |
| Parsley, chervil, celery leaves | NEU | Outdoor | 0.17; 0.26; 0.415; 2 x 0.53; 0.86; 1.0 | 0.17; 0.26; 0.415; 2 x 0.53; 0.86; 1.0 | 0.53 | 1.0 | 2.0 | 1.0 | All trials were performed on parsley leaves, but residues data can be extrapolated to crops under consideration. Indoor use results in more critical residue situation therefore was used for deriving MRL proposal and risk assessment values (indicated in bold)<br>$R_{ber(outdoor)}$=1.72 mg/kg<br>$R_{max(outdoor)}$=1.56 mg/kg<br>$R_{ber(indoor)}$=11.34 mg/kg<br>$R_{max(indoor)}$=14.98 mg/kg |
| | EU | Indoor | 1.17; 3.67; 5.63; 5.68 | 1.17; 3.67; 5.63; 5.68 | **4.65** | **5.68** | **12** | **1.0** | |

(a): NEU, SEU, EU or Import (country code). In the case of indoor uses there is no necessity to differentiate between NEU and SEU.
(b): Median value of the individual trial results according to the enforcement residue definition.
(c): Highest value of the individual trial results according to the enforcement residue definition.
(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residues trial.

3.1.1.3. Effect of industrial processing and/or household preparation

The effects of processing on the nature of difenoconazole were investigated in hydrolysis study by stimulating pasteurization, baking, brewing boiling and sterilisation (Sweden, 2006). Studies demonstrate that the majority of applied radioactivity consisted of parent difenoconazole (95.6 - 98.6%). One minor degradation product was observed at very low levels (≤1% of radioactivity) at pH 5 and 6. Difenoconazole is considered stable under typical processing conditions.

Under the current application, no studies on the effects of processing on the magnitude of difenoconazole residues have been submitted. Such, however, are not considered necessary taking into account the low contribution of fennel, parsley, celery leaves and chervil to the total dietary intake.

### 3.1.2. Rotational crops

3.1.2.1. Preliminary considerations

All crops under consideration can be grown in rotation with other crops. The rate of degradation of difenoconazole in soil was investigated in several field and laboratory studies and results are reported in the DAR (Sweden, 2006). Difenoconazole is slowly degraded in soil under aerobic conditions and stable under anaerobic conditions. High treatment rate appears to result in slower degradation. The studies indicate that $DT_{90f}$ values for difenoconazole are in the range of 72 - 879 days. Two soil metabolites (CGA-205375 and CGA -71019) were identified close to or above 10% of the applied radioactivity. Both metabolites were addressed further but were not considered as an area of concern. Nevertheless, taking into account the persistence of difenoconazole in soil, special consideration should be given to difenoconazole residues in rotational crops.

3.1.2.2. Nature of residues

The metabolism of difenoconazole in rotational crops was investigated in studies with leafy vegetables (lettuce, spinach), root vegetables (carrot, sugar beet, turnip), in cereals (spring and winter wheat, maize) and in oilseeds (mustard) (Sweden, 2006). Confined and field studies are reported in the DAR.

In confined study 1 [phenyl-$^{14}$C] or [triazole-$^{14}$C] difenoconazole was applied on a bare soil once an application rate of 0.125 kg a.s/ha. In confined study 2 [phenyl-$^{14}$C] difenoconazole was applied on a bare soil at an application rate of 0.0324 kg a.s./ha. In study 1 lettuce, winter wheat, maize and sugar beet were sown or planted 98, 126, 342 and 369 DAT. In study 2, spring wheat, mustard and turnip were sown 30 and 33 DAT. Results from the confined studies indicate that with [phenyl-$^{14}$C] difenoconazole, TRR was at very low levels (≤0.01 mg/kg) and therefore not characterized. In studies with [triazole-$^{14}$C] difenoconazole TRR consisted of triazole alanine (10.4 - 66.2%), triazole lactic acid[8](9.7 - 54.3%) and triazole acetic acid (2.7 - 39.4%).

It was concluded in the DAR that generally the metabolic pathway is similar in primary and rotational crops and that a residue should be defined as parent difenoconazole. However, EFSA is of the opinion that the situation in rotational crops regarding TDMs should be

[8] CGA-205369: [1,2,4]triazol-1-yl-lactic acid

reconsidered taking into account all active substances which produce these common metabolites as soon as the methodology for this type of assessment is available.

3.1.2.3. Magnitude of residues

Two field studies on rotational crops are reported in the DAR (Sweden, 2006) and both were performed by applying difenoconazole and triazole alanine on a bare soil once at an application rate of 0.750 kg a.s./ha. In one study carrots were sown as rotational crops 30 DAT, but in other study spinach were sown as rotational crops 31 DAT. Samples were analysed for difenoconazole and triazole alanine. Residues of parent difenoconazole and triazole alanine in carrots and spinach were below the LOD of 0.02 mg/kg and 0.05 mg/kg, respectively.

Confined studies (see section 3.1.2.2.) indicate that generally the uptake of radioactive residues in rotational crops following application of [triazole-$^{14}$C] difenoconazole at a rate of 0.125 kg a.s./ha to bare soil was higher than observed in the same study performed with [phenyl-$^{14}$C] difenoconazole. Due to low levels of residues in plant samples from phenyl studies, TRR were not characterized. In triazole study lettuce heads harvested 126 and 151 DAT contained 0.021 mg and 0.017 mg difenoconazole equiv./kg. Mature wheat and maize grains 0.34 mg and 0.211 mg difenoconazole equiv./kg, respectively. Further characterization was not performed. These residues occurred from selective transport of triazole derivatives from the soil to grain.

Considering the application rates proposed in the framework of this application (max. 0.375 kg a.s./ha) and taking into account that a part of the applied substance is intercepted by the treated crops, it is concluded that significant levels of difenoconazole are not expected in rotational crops provided that difenoconazole is applied according to the proposed GAP. Nevertheless, the studies on the nature and magnitude of difenoconazole residues in rotational crops indicate that triazole derivative metabolites are present in rotational crops and this situation has to be reconsidered as soon as a global approach on TDMs is defined.

## 3.2. Nature and magnitude of residues in livestock

Since crops under consideration and/or their by-products are not used as livestock feed, the nature and magnitude of residues in livestock was not considered under the current application.

# 4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA PRIMo (Pesticide Residues Intake Model). For the chronic intake assessment EFSA used the existing MRLs for difenoconazole as established in Annex III of Regulation (EC) No 396/2005 as well as the STMR values derived for the intended use of difenoconazole on fennel, chervil, parsley and celery leaves. For several plant commodities EFSA looked for available STMR values which were reported in the framework of setting the temporary MRLs for difenoconazole.

Acute intake assessment was performed only with regard to crops under consideration, using the HR values as derived for the intended use of difenoconazole on these crops.

Input values for risk assessment are summarized in Table 4-1.

Table 4-1. **Input values for the consumer risk assessment**

| Commodity | Chronic risk assessment | | Acute risk assessment | |
|---|---|---|---|---|
| | Input value (mg/kg) | Comment | Input value (mg/kg) | Comment |
| Risk assessment residue definition: difenoconazole | | | | |
| Fennel | 1.66 | STMR | 3.31 | HR |
| Herbs (parsley, celery leaves, chervil) | 4.65 | STMR | 5.68 | HR |
| Apples, pears, medlar, loquat | 0.12 | STMR (EC, 2008) | Acute risk assessment was performed only with regard to crops under consideration. | |
| Apricots | 0.14 | STMR (EC, 2008) | | |
| Peaches | 0.15 | STMR (EC, 2008) | | |
| Tomatoes | 0.72 | STMR (EC, 2008) | | |
| Beetroot | 0.05 | STMR (EC, 2008) | | |
| Olives | 0.47 | STMR (EC, 2008) | | |
| Other commodities | MRL | Appendix B | | |

Summary of intake calculations can be found in Appendix C.

No consumer intake concerns were identified for any of the European diets. Total calculated intake values ranged from 16.6 - 98.7 % of the ADI. The individual contribution of chervil, parsley leaves and celery leaves could not be estimated since no intake data are available. The MRL for herbs is set at 2 mg/kg, which is lower than the calculated STMR value for celery leaves, parsley and chervil. In a worst case estimation by applying the obtained STMR value for all herbs, the contribution of herbs to the total dietary intake is below 3.1% of the ADI. This means that individual contribution of celery leaves, parsley and chervil to the dietary intake is insignificant. The contribution of fennel to the total dietary intake amounts for a maximum of 1.62% of the ADI (IT Adult diet).

No acute intake concerns were identified for the crops under consideration. Contribution to the ARfD amounts for a maximum of 33.7% for fennel, 16.3% for celery leaves, 3.7% for chervil and 2.2% for parsley.

Consequently, EFSA concludes that the intended use on fennel, parsley, celery leaves and chervil is sufficiently supported by data and no risk for consumers was identified.

## CONCLUSIONS AND RECOMMENDATIONS

The toxicological reference values for difenoconazole are reported in the DAR and currently the ADI is set at 0.01 mg/kg bw/d and the ARfD is set at 0.2 mg/kg bw.

According to the DAR metabolism of difenoconazole in primary crops is elucidated in four crop categories and residue definition for risk assessment and enforcement is proposed as parent difenoconazole. Nevertheless, apart from difenoconazole, in several parts of crops triazole derivative metabolites (TDMs), which are known as common metabolites of several substances belonging to the triazole chemical class, were identified as a major part of the TRR. Even though TDMs would not occur in amounts of concern following the proposed use, consideration should be given to the fact that TDMs can occur in plant commodities from other sources than difenoconazole therefore resulting in levels that might require consumer exposure assessment. For addressing this issue, a common EU approach on risk assessment of TDMs is under development. It would involve setting of toxicological reference values for TDMs and performing separate risk assessments for the parent compounds and TDMs. Since in leafy parts of the plants (foliage, leaves) parent difenoconazole was the major residue of concern according to metabolism studies, EFSA concludes that metabolic pathway in crops under consideration (leafy vegetables) is sufficiently addressed and no additional metabolism studies are currently required. This conclusion, however, might be reconsidered in a light of the outcome of the peer review and in accordance with the EU approach regarding risk assessment of TDMs. Adequate analytical methods are available to enforce the proposed MRLs.

Submitted supervised residue trials data on fennel, parsley, celery leaves and chervil indicate that higher MRLs than proposed by the EMS would be required in order to accommodate for the intended use of difenoconazole in Belgium. Processing studies have not been submitted with regard to the crops under consideration and are not necessary, since the contribution of them to the total dietary intake is very low.

All crops under consideration can be grown as rotational crops therefore occurrence of difenoconazole residues in rotational crops was also investigated. In the DAR it was concluded that the identified metabolites in rotational crops are in accordance with the metabolic pathway observed in primary crops. However, the situation in rotational crops regarding TDMs should be reconsidered taking into account all active substances which produce these common metabolites as soon as the methodology for this type of assessment is available. With regard to the current application, EFSA concludes that significant residue levels of difenoconazole are not expected in rotational crops provided that difenoconazole is applied according to the proposed GAP.

Residues in commodities of animal origin were not assessed in the framework of submitted applications since crops under consideration are not used as a livestock feed.

The consumer risk assessment was performed with revision 2 of the EFSA PRIMo. For the chronic intake assessment EFSA used the existing MRLs for difenoconazole as established in Annex III of Regulation (EC) No 396/2005 as well as the STMR values derived for the intended use of difenoconazole on crops under consideration. For various plant commodities STMR values were available to refine intake calculations. Acute intake assessment was performed only with regard to crops under consideration, using HR values as derived for the intended use of difenoconazole on these crops.

No consumer intake concerns were identified for any of the European diets. Total calculated intake values ranged from 16.6 - 98.7 % of the ADI. Contribution of celery leaves, parsley and chervil to the dietary intake is insignificant. The contribution of fennel to the total dietary intake amounts for a maximum of 1.62% of the ADI (IT Adult diet). No acute intake concerns were identified for the crops under consideration. Contribution to the ARfD amounts for a maximum of 33.7% for fennel, 16.3% for celery leaves, 3.7% for chervil and 2.2% for parsley.

Consequently, EFSA concludes that the intended use on fennel, parsley, celery leaves and chervil is sufficiently supported by data and no risk for consumers was identified.

It should be noted that the contribution of TDM residues in primary crops and rotational crops resulting from the use of difenoconazole has not been taken into account in the consumer risk assessment since at the moment the EU approach for the risk assessment of triazole metabolites is still under development. **As the DAR has not yet been peer reviewed by EFSA, the conclusions reached in this reasoned opinion have to be taken as provisional and might be reconsidered in the light of the conclusions reached in the peer review process for difenoconazole.**

Table 5-1.**Overview of the proposed EC MRLs**

| Commodity | Existing EC MRL (mg/kg) | Proposed EC MRL (mg/kg) | Justification for the proposal |
|---|---|---|---|
| Enforcement residue definition: difenoconazole | | | |
| Fennel | 0.3 | 6 | MRL proposals are sufficiently supported by data and no risk for consumer was identified for the intended uses. |
| Celery, parsley leaves | 3 | 12 | |
| Chervil | 2 | 12 | |

## DOCUMENTATION PROVIDED TO EFSA

1. Evaluation report on the modification of the existing MRL for difenoconazole in parsley, chervil and celery leaves (herbs) prepared by Belgium under Regulation (EC) No 396/2005. March 2009.
2. Evaluation report on the modification of the existing MRL for difenoconazole in fennel prepared by Belgium under Regulation (EC) No 396/2005. March 2009. Updated on 10 July 2009.

## REFERENCES

The Netherlands, 2006. Draft Assessment Report on difenoconazole prepared by the Netherlands under Directive 91/414/EEC. May 2006. Updated December 2006.

EC (European Commission), 2008. Expert meetings report (for establishing Annexes to Regulation (EC) No 396/2005). 28-31 January 2008.

## APPENDIX A – GOOD AGRICULTURAL PRACTICES (GAPS)

| Crop and/or situation (a) | Member State or Country | F G or I (b) | Pests or Group of pests controlled (c) | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) (l) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Type (d-f) | Conc. of as (i) | method kind (f-h) | growth stage & season (j) | No. min max (k) | interval between applic. (min) | kg as/hL min max | water L/ha min max | kg as/ha min max | |
| Parsley, chervil, celery leaves (dill, lovage, corriander) | Belgium | F & G | Leaf blight, powdery mildew | EC | 250 g/l | Spray | | 1-2 | 14 days | | | 0.125 | 14 |
| Fennel | Belgium | F & G | Leaf blight | EC | 250 g/l | Spray | | 1-3 | 14 days | | | 0.125 | 14 |

(a) In case of group of crops the Codex classification should be used
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
( c) e.g. biting and sucking insects, soil born insects, foliar fungi
(d) Suspension concentrate (= flowable concentrate) (SC)
(e) Use CIPAC/FAO Codes where appropriate
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants
(i) g/kg or g/l
(j) Growth stage at last treatment
(k) PHI = Pre-harvest interval
(l) Remarks may include: Extent of use/economic importance/restrictions (e.g. feeding, grazing)/minimal intervals between applications

## APPENDIX B – EXISTING EC MRLS

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 100000 | 1. FRUIT FRESH OR FROZEN; NUTS | |
| 110000 | (i) Citrus fruit | 0,1 |
| 110010 | Grapefruit (Shaddocks, pomelos, sweeties, tangelo, ugli and other hybrids) | 0,1 |
| 110020 | Oranges (Bergamot, bitter orange, chinotto and other hybrids) | 0,1 |
| 110030 | Lemons (Citron, lemon ) | 0,1 |
| 110040 | Limes | 0,1 |
| 110050 | Mandarins (Clementine, tangerine and other hybrids) | 0,1 |
| 110990 | Others | 0,1 |
| 120000 | (ii) Tree nuts (shelled or unshelled) | 0,05* |
| 120010 | Almonds | 0,05* |
| 120020 | Brazil nuts | 0,05* |
| 120030 | Cashew nuts | 0,05* |
| 120040 | Chestnuts | 0,05* |
| 120050 | Coconuts | 0,05* |
| 120060 | Hazelnuts (Filbert) | 0,05* |
| 120070 | Macadamia | 0,05* |
| 120080 | Pecans | 0,05* |
| 120090 | Pine nuts | 0,05* |
| 120100 | Pistachios | 0,05* |
| 120110 | Walnuts | 0,05* |
| 120990 | Others | 0,05* |
| 130000 | (iii) Pome fruit | |
| 130010 | Apples (Crab apple) | 0,5 |
| 130020 | Pears (Oriental pear) | 0,5 |
| 130030 | Quinces | 0,2 |
| 130040 | Medlar | 0,5 |
| 130050 | Loquat | 0,5 |
| 130990 | Others | 0,2 |
| 140000 | (iv) Stone fruit | |
| 140010 | Apricots | 0,5 |
| 140020 | Cherries (sweet cherries, sour cherries) | 0,3 |
| 140030 | Peaches (Nectarines and similar hybrids) | 0,5 |
| 140040 | Plums (Damson, greengage, mirabelle) | 0,5 |
| 140990 | Others | 0,1 |
| 150000 | (v) Berries & small fruit | |
| 151000 | (a) Table and wine grapes | 0,5 |
| 151010 | Table grapes | 0,5 |
| 151020 | Wine grapes | 0,5 |
| 152000 | (b) Strawberries | 0,1 |
| 153000 | (c) Cane fruit | |
| 153010 | Blackberries | 0,3 |
| 153020 | Dewberries (Loganberries, Boysenberries, and cloudberries) | 0,1 |
| 153030 | Raspberries (Wineberries ) | 0,3 |
| 153990 | Others | 0,1 |
| 154000 | (d) Other small fruit & berries | |
| 154010 | Blueberries (Bilberries cowberries (red bilberries)) | 0,1 |
| 154020 | Cranberries | 0,1 |
| 154030 | Currants (red, black and white) | 0,2 |
| 154040 | Gooseberries (Including hybrids with other ribes species) | 0,1 |
| 154050 | Rose hips | 0,1 |
| 154060 | Mulberries (arbutus berry) | 0,1 |
| 154070 | Azarole (mediteranean medlar) | 0,1 |
| 154080 | Elderberries (Black chokeberry (appleberry), mountain ash, azarole, buckthorn (sea sallowthorn), hawthorn, service berries, and other treeberries) | 0,1 |
| 154990 | Others | 0,1 |
| 160000 | (vi) Miscellaneous fruit | 0,1 |
| 161000 | (a) Edible peel | 0,1 |
| 161010 | Dates | 0,1 |
| 161020 | Figs | 0,1 |
| 161030 | Table olives | 2 |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 161040 | Kumquats (Marumi kumquats, nagami kumquats) | 0,1 |
| 161050 | Carambola (Bilimbi) | 0,1 |
| 161060 | Persimmon | 0,1 |
| 161070 | Jambolan (java plum) (Java apple (water apple), pomerac, rose apple, Brazilean cherry (grumichama), Surinam cherry) | 0,1 |
| 161990 | Others | 0,1 |
| 162000 | (b) Inedible peel, small | 0,1 |
| 162010 | Kiwi | 0,1 |
| 162020 | Lychee (Litchi) (Pulasan, rambutan (hairy litchi)) | 0,1 |
| 162030 | Passion fruit | 0,1 |
| 162040 | Prickly pear (cactus fruit) | 0,1 |
| 162050 | Star apple | 0,1 |
| 162060 | American persimmon (Virginia kaki) (Black sapote, white sapote, green sapote, canistel (yellow sapote), and mammey sapote) | 0,1 |
| 162990 | Others | 0,1 |
| 163000 | (c) Inedible peel, large | 0,1 |
| 163010 | Avocados | 0,1 |
| 163020 | Bananas (Dwarf banana, plantain, apple banana) | 0,1 |
| 163030 | Mangoes | 0,1 |
| 163040 | Papaya | 0,1 |
| 163050 | Pomegranate | 0,1 |
| 163060 | Cherimoya (Custard apple, sugar apple (sweetsop) , llama and other medium sized Annonaceae) | 0,1 |
| 163070 | Guava | 0,1 |
| 163080 | Pineapples | 0,1 |
| 163090 | Bread fruit (Jackfruit) | 0,1 |
| 163100 | Durian | 0,1 |
| 163110 | Soursop (guanabana) | 0,1 |
| 163990 | Others | 0,1 |
| 200000 | 2. VEGETABLES FRESH OR FROZEN | |
| 210000 | (i) Root and tuber vegetables | |
| 211000 | (a) Potatoes | 0,1 |
| 212000 | (b) Tropical root and tuber vegetables | 0,1 |
| 212010 | Cassava (Dasheen, eddoe (Japanese taro), tannia) | 0,1 |
| 212020 | Sweet potatoes | 0,1 |
| 212030 | Yams (Potato bean (yam bean), Mexican yam bean) | 0,1 |
| 212040 | Arrowroot | 0,1 |
| 212990 | Others | 0,1 |
| 213000 | (c) Other root and tuber vegetables except sugar beet | |
| 213010 | Beetroot | 0,2 |
| 213020 | Carrots | 0,3 |
| 213030 | Celeriac | 2 |
| 213040 | Horseradish | 0,2 |
| 213050 | Jerusalem artichokes | 0,1 |
| 213060 | Parsnips | 0,3 |
| 213070 | Parsley root | 0,2 |
| 213080 | Radishes (Black radish, Japanese radish, small radish and similar varieties) | 0,05* |
| 213090 | Salsify (Scorzonera, Spanish salsify (Spanish oysterplant)) | 0,2 |
| 213100 | Swedes | 0,1 |
| 213110 | Turnips | 0,1 |
| 213990 | Others | 0,05* |
| 220000 | (ii) Bulb vegetables | |
| 220010 | Garlic | 0,05* |
| 220020 | Onions (Silverskin onions) | 0,05* |
| 220030 | Shallots | 0,05* |
| 220040 | Spring onions (Welsh onion and similar varieties) | 0,1 |
| 220990 | Others | 0,05* |
| 230000 | (iii) Fruiting vegetables | |
| 231000 | (a) Solanacea | |
| 231010 | Tomatoes (Cherry tomatoes, ) | 2 |
| 231020 | Peppers (Chilli peppers) | 0,05* |
| 231030 | Aubergines (egg plants) (Pepino) | 0,05* |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 231040 | Okra, lady's fingers | 0,05* |
| 231990 | Others | 0,05* |
| 232000 | (b) Cucurbits - edible peel | 0,1 |
| 232010 | Cucumbers | 0,1 |
| 232020 | Gherkins | 0,1 |
| 232030 | Courgettes (Summer squash, marrow (patisson)) | 0,1 |
| 232990 | Others | 0,1 |
| 233000 | (c) Cucurbits-inedible peel | 0,05* |
| 233010 | Melons (Kiwano ) | 0,05* |
| 233020 | Pumpkins (Winter squash) | 0,05* |
| 233030 | Watermelons | 0,05* |
| 233990 | Others | 0,05* |
| 234000 | (d) Sweet corn | 0,05* |
| 239000 | (e) Other fruiting vegetables | 0,05* |
| 240000 | (iv) Brassica vegetables | |
| 241000 | (a) Flowering brassica | |
| 241010 | Broccoli (Calabrese, Chinese broccoli, Broccoli raab) | 0,2 |
| 241020 | Cauliflower | 0,2 |
| 241990 | Others | 0,05* |
| 242000 | (b) Head brassica | 0,2 |
| 242010 | Brussels sprouts | 0,2 |
| 242020 | Head cabbage (Pointed head cabbage, red cabbage, savoy cabbage, white cabbage) | 0,2 |
| 242990 | Others | 0,2 |
| 243000 | (c) Leafy brassica | 2 |
| 243010 | Chinese cabbage (Indian (Chinese) mustard, pak choi, Chinese flat cabbage (tai goo choi), peking cabbage (pe-tsai), cow cabbage) | 2 |
| 243020 | Kale (Borecole (curly kale), collards) | 2 |
| 243990 | Others | 2 |
| 244000 | (d) Kohlrabi | 0,05* |
| 250000 | (v) Leaf vegetables & fresh herbs | |
| 251000 | (a) Lettuce and other salad plants including Brassicacea | |
| 251010 | Lamb´s lettuce (Italian cornsalad) | 0,05* |
| 251020 | Lettuce (Head lettuce, lollo rosso (cutting lettuce), iceberg lettuce, romaine (cos) lettuce) | 3 |
| 251030 | Scarole (broad-leaf endive) (Wild chicory, red-leaved chicory, radicchio, curld leave endive, sugar loaf) | 0,05* |
| 251040 | Cress | 0,05* |
| 251050 | Land cress | 0,05* |
| 251060 | Rocket, Rucola (Wild rocket) | 2 |
| 251070 | Red mustard | 0,05* |
| 251080 | Leaves and sprouts of Brassica spp (Mizuna) | 0,05* |
| 251990 | Others | 0,05* |
| 252000 | (b) Spinach & similar (leaves) | |
| 252010 | Spinach (New Zealand spinach, turnip greens (turnip tops)) | 2 |
| 252020 | Purslane (Winter purslane (miner's lettuce), garden purslane, common purslane, sorrel, glassworth) | 2 |
| 252030 | Beet leaves (chard) (Leaves of beetroot) | 0,05* |
| 252990 | Others | 0,05* |
| 253000 | (c) Vine leaves (grape leaves) | 0,05* |
| 254000 | (d) Water cress | 0,5 |
| 255000 | (e) Witloof | 0,05* |
| 256000 | (f) Herbs | |
| 256010 | Chervil | 2 |
| 256020 | Chives | 2 |
| 256030 | Celery leaves (fennel leaves , Coriander leaves, dill leaves, Caraway leaves, lovage, angelica, sweet cisely and other Apiacea) | 3 |
| 256040 | Parsley | 3 |
| 256050 | Sage (Winter savory, summer savory, ) | 2 |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 256060 | Rosemary | 2 |
| 256070 | Thyme ( marjoram, oregano) | 2 |
| 256080 | Basil (Balm leaves, mint, peppermint) | 2 |
| 256090 | Bay leaves (laurel) | 2 |
| 256100 | Tarragon (Hyssop) | 2 |
| 256990 | Others | 2 |
| 260000 | (vi) Legume vegetables (fresh) | |
| 260010 | Beans (with pods) (Green bean (french beans, snap beans), scarlet runner bean, slicing bean, yardlong beans) | 1 |
| 260020 | Beans (without pods) (Broad beans, Flageolets, jack bean, lima bean, cowpea) | 1 |
| 260030 | Peas (with pods) (Mangetout (sugar peas)) | 1 |
| 260040 | Peas (without pods) (Garden pea, green pea, chickpea) | 1 |
| 260050 | Lentils | 0,05* |
| 260990 | Others | 0,05* |
| 270000 | (vii) Stem vegetables (fresh) | |
| 270010 | Asparagus | 0,05* |
| 270020 | Cardoons | 0,3 |
| 270030 | Celery | 5 |
| 270040 | Fennel | 0,3 |
| 270050 | Globe artichokes | 0,05* |
| 270060 | Leek | 0,5 |
| 270070 | Rhubarb | 0,3 |
| 270080 | Bamboo shoots | 0,05* |
| 270090 | Palm hearts | 0,05* |
| 270990 | Others | 0,05* |
| 280000 | (viii) Fungi | 0,05* |
| 280010 | Cultivated (Common mushroom, Oyster mushroom, Shi-take) | 0,05* |
| 280020 | Wild (Chanterelle, Truffle, Morel ,) | 0,05* |
| 280990 | Others | 0,05* |
| 290000 | (ix) Sea weeds | 0,05* |
| 300000 | 3. PULSES, DRY | |
| 300010 | Beans (Broad beans, navy beans, flageolets, jack beans, lima beans, field beans, cowpeas) | 0,05* |
| 300020 | Lentils | 0,05* |
| 300030 | Peas (Chickpeas, field peas, chickling vetch) | 0,1 |
| 300040 | Lupins | 0,05* |
| 300990 | Others | 0,05* |
| 400000 | 4. OILSEEDS AND OILFRUITS | |
| 401000 | (i) Oilseeds | |
| 401010 | Linseed | 0,2 |
| 401020 | Peanuts | 0,05* |
| 401030 | Poppy seed | 0,05* |
| 401040 | Sesame seed | 0,05* |
| 401050 | Sunflower seed | 0,05* |
| 401060 | Rape seed (Bird rapeseed, turnip rape) | 0,5 |
| 401070 | Soya bean | 0,05* |
| 401080 | Mustard seed | 0,2 |
| 401090 | Cotton seed | 0,05* |
| 401100 | Pumpkin seeds | 0,05* |
| 401110 | Safflower | 0,05* |
| 401120 | Borage | 0,05* |
| 401130 | Gold of pleasure | 0,05* |
| 401140 | Hempseed | 0,05* |
| 401150 | Castor bean | 0,05* |
| 401990 | Others | 0,05* |
| 402000 | (ii) Oilfruits | |
| 402010 | Olives for oil production | 2 |
| 402020 | Palm nuts (palmoil kernels) | 0,05* |
| 402030 | Palmfruit | 0,05* |
| 402040 | Kapok | 0,05* |
| 402990 | Others | 0,05* |
| 500000 | 5. CEREALS | |
| 500010 | Barley | 0,05* |
| 500020 | Buckwheat | 0,05* |
| 500030 | Maize | 0,05* |
| 500040 | Millet (Foxtail millet, teff) | 0,05* |
| 500050 | Oats | 0,05* |
| 500060 | Rice | 0,05* |
| 500070 | Rye | 0,1 |
| 500080 | Sorghum | 0,05* |
| 500090 | Wheat (Spelt Triticale) | 0,1 |
| 500990 | Others | 0,05* |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 600000 | 6. TEA, COFFEE, HERBAL INFUSIONS AND COCOA | |
| 610000 | (i) Tea (dried leaves and stalks, fermented or otherwise of Camellia sinensis) | 0,05* |
| 620000 | (ii) Coffee beans | 0,05* |
| 630000 | (iii) Herbal infusions (dried) | 20 |
| 631000 | (a) Flowers | 20 |
| 631010 | Camomille flowers | 20 |
| 631020 | Hybiscus flowers | 20 |
| 631030 | Rose petals | 20 |
| 631040 | Jasmine flowers | 20 |
| 631050 | Lime (linden) | 20 |
| 631990 | Others | 20 |
| 632000 | (b) Leaves | 20 |
| 632010 | Strawberry leaves | 20 |
| 632020 | Rooibos leaves | 20 |
| 632030 | Maté | 20 |
| 632990 | Others | 20 |
| 633000 | (c) Roots | 20 |
| 633010 | Valerian root | 20 |
| 633020 | Ginseng root | 20 |
| 633990 | Others | 20 |
| 639000 | (d) Other herbal infusions | 20 |
| 640000 | (iv) Cocoa (fermented beans) | 0,05* |
| 650000 | (v) Carob (st johns bread) | 0,05* |
| 700000 | 7. HOPS (dried) , including hop pellets and unconcentrated powder | 0,05* |
| 800000 | 8. SPICES | 0,3 |
| 810000 | (i) Seeds | 0,3 |
| 810010 | Anise | 0,3 |
| 810020 | Black caraway | 0,3 |
| 810030 | Celery seed (Lovage seed) | 0,3 |
| 810040 | Coriander seed | 0,3 |
| 810050 | Cumin seed | 0,3 |
| 810060 | Dill seed | 0,3 |
| 810070 | Fennel seed | 0,3 |
| 810080 | Fenugreek | 0,3 |
| 810090 | Nutmeg | 0,3 |
| 810990 | Others | 0,3 |
| 820000 | (ii) Fruits and berries | 0,3 |
| 820010 | Allspice | 0,3 |
| 820020 | Anise pepper (Japan pepper) | 0,3 |
| 820030 | Caraway | 0,3 |
| 820040 | Cardamom | 0,3 |
| 820050 | Juniper berries | 0,3 |
| 820060 | Pepper, black and white (Long pepper, pink pepper) | 0,3 |
| 820070 | Vanilla pods | 0,3 |
| 820080 | Tamarind | 0,3 |
| 820990 | Others | 0,3 |
| 830000 | (iii) Bark | 0,3 |
| 830010 | Cinnamon (Cassia ) | 0,3 |
| 830990 | Others | 0,3 |
| 840000 | (iv) Roots or rhizome | 0,3 |
| 840010 | Liquorice | 0,3 |
| 840020 | Ginger | 0,3 |
| 840030 | Turmeric (Curcuma) | 0,3 |
| 840040 | Horseradish | 0,3 |
| 840990 | Others | 0,3 |
| 850000 | (v) Buds | 0,3 |
| 850010 | Cloves | 0,3 |
| 850020 | Capers | 0,3 |
| 850990 | Others | 0,3 |
| 860000 | (vi) Flower stigma | 0,3 |
| 860010 | Saffron | 0,3 |
| 860990 | Others | 0,3 |
| 870000 | (vii) Aril | 0,3 |
| 870010 | Mace | 0,3 |
| 870990 | Others | 0,3 |
| 900000 | 9. SUGAR PLANTS | |
| 900010 | Sugar beet (root) | 0,2 |
| 900020 | Sugar cane | 0,05* |
| 900030 | Chicory roots | 0,1 |
| 900990 | Others | 0,05* |
| 1000000 | 10. PRODUCTS OF ANIMAL ORIGIN- TERRESTRIAL ANIMALS | |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 1010000 | (i) Meat, preparations of meat, offals, blood, animal fats fresh chilled or frozen, salted, in brine, dried or smoked or processed as flours or meals other processed products such as sausages and food preparations based on these | |
| 1011000 | (a) Swine | |
| 1011010 | Meat | 0,02* |
| 1011020 | Fat free of lean meat | 0,05 |
| 1011030 | Liver | 0,2 |
| 1011040 | Kidney | 0,05 |
| 1011050 | Edible offal | 0,1 |
| 1011990 | Others | 0,1 |
| 1012000 | (b) Bovine | |
| 1012010 | Meat | 0,02* |
| 1012020 | Fat | 0,05 |
| 1012030 | Liver | 0,2 |
| 1012040 | Kidney | 0,05 |
| 1012050 | Edible offal | 0,1 |
| 1012990 | Others | 0,1 |
| 1013000 | (c) Sheep | |
| 1013010 | Meat | 0,02* |
| 1013020 | Fat | 0,05 |
| 1013030 | Liver | 0,2 |
| 1013040 | Kidney | 0,05 |
| 1013050 | Edible offal | 0,1 |
| 1013990 | Others | 0,1 |
| 1014000 | (d) Goat | |
| 1014010 | Meat | 0,02* |
| 1014020 | Fat | 0,05 |
| 1014030 | Liver | 0,2 |
| 1014040 | Kidney | 0,05 |
| 1014050 | Edible offal | 0,1 |
| 1014990 | Others | 0,1 |
| 1015000 | (e) Horses, asses, mules or hinnies | |
| 1015010 | Meat | 0,02* |
| 1015020 | Fat | 0,05 |
| 1015030 | Liver | 0,2 |
| 1015040 | Kidney | 0,05 |
| 1015050 | Edible offal | 0,1 |
| 1015990 | Others | 0,1 |
| 1016000 | (f) Poultry -chicken, geese, duck, turkey and Guinea fowl-, ostrich, pigeon | 0,1 |
| 1016010 | Meat | 0,1 |
| 1016020 | Fat | 0,1 |
| 1016030 | Liver | 0,1 |
| 1016040 | Kidney | 0,1 |
| 1016050 | Edible offal | 0,1 |
| 1016990 | Others | 0,1 |
| 1017000 | (g) Other farm animals (Rabbit, Kangaroo) | 0,1 |
| 1017010 | Meat | 0,1 |
| 1017020 | Fat | 0,1 |
| 1017030 | Liver | 0,1 |
| 1017040 | Kidney | 0,1 |
| 1017050 | Edible offal | 0,1 |
| 1017990 | Others | 0,1 |
| 1020000 | (ii) Milk and cream, not concentrated, nor containing added sugar or sweetening matter, butter and other fats derived from milk, cheese and curd | 0,01* |
| 1020010 | Cattle | 0,01* |
| 1020020 | Sheep | 0,01* |
| 1020030 | Goat | 0,01* |
| 1020040 | Horse | 0,01* |
| 1020990 | Others | 0,01* |
| 1030000 | (iii) Birds' eggs, fresh preserved or cooked Shelled eggs and egg yolks fresh, dried, cooked by steaming or boiling in water, moulded, frozen or otherwise preserved whether or not containing added sugar or sweetening matter | 0,05* |
| 1030010 | Chicken | 0,05* |
| 1030020 | Duck | 0,05* |
| 1030030 | Goose | 0,05* |
| 1030040 | Quail | 0,05* |
| 1030990 | Others | 0,05* |
| 1040000 | (iv) Honey (Royal jelly, pollen) | 0,05* |

| Code number | Groups and examples of individual products to which the MRLs apply (a) | Difenoconazole |
|---|---|---|
| 1050000 | (v) Amphibians and reptiles (Frog legs, crocodiles) | 0,05* |
| 1060000 | (vi) Snails | 0,05* |
| 1070000 | (vii) Other terrestrial animal products | 0,05* |
| *-indicates limit of analytical quantification | | |

# APPENDIX C – PESTICIDE RESIDUES INTAKE MODEL (PRIMO)

## Difenoconazole

| | | | |
|---|---|---|---|
| Status of the active substance: | **Included** | Code no. | **50** |
| LOQ (mg/kg bw): | | proposed LOQ: | |
| **Toxicological end points** | | | |
| ADI (mg/kg bw/day): | **0.01** | ARfD (mg/kg bw): | **0.2** |
| Source of ADI: | **DAR- SE** | Source of ARfD: | **DAR-SE** |
| Year of evaluation: | **2006** | Year of evaluation: | **2006** |

## Chronic risk assessment - refined calculations

| | TMDI (range) in % of ADI minimum - maximum |
|---|---|
| | 17 99 |
| **No of diets exceeding ADI:** | --- |

| Highest calculated TMDI values in % of ADI | MS Diet | Highest contributor to MS diet (in % of ADI) | Commodity / group of commodities | 2nd contributor to MS diet (in % of ADI) | Commodity / group of commodities | 3rd contributor to MS diet (in % of ADI) | Commodity / group of commodities | pTMRLs at LOQ (in % of ADI) |
|---|---|---|---|---|---|---|---|---|
| 98.7 | WHO Cluster diet B | 22.2 | Tomatoes | 10.8 | Lettuce | 9.0 | Olives for oil production | |
| 79.8 | UK Toddler | 45.7 | Sugar beet (root) | 4.2 | Tomatoes | 3.9 | Wheat | |
| 76.9 | DE child | 14.5 | Apples | 8.7 | Herbal infusions (dried) | 7.0 | Tomatoes | |
| 75.3 | FR toddler | 14.2 | Spinach | 11.0 | Beans (with pods) | 7.3 | Carrots | |
| 73.4 | NL child | 7.6 | Apples | 7.4 | Spinach | 5.9 | Potatoes | |
| 72.7 | IE adult | 6.4 | Celery | 6.3 | Wine grapes | 4.0 | Other leafy brassica | |
| 55.6 | UK Infant | 20.2 | Sugar beet (root) | 5.7 | Peas (without pods) | 5.0 | Milk and cream, | |
| 54.3 | WHO cluster diet E | 8.0 | Wine grapes | 3.9 | Wheat | 3.8 | Potatoes | |
| 52.4 | WHO regional European diet | 11.3 | Lettuce | 7.9 | Tomatoes | 4.0 | Potatoes | |
| 51.3 | FR infant | 8.9 | Spinach | 8.4 | Beans (with pods) | 7.9 | Carrots | |
| 48.3 | ES child | 12.5 | Lettuce | 7.1 | Tomatoes | 4.4 | Wheat | |
| 44.1 | WHO cluster diet D | 7.3 | Tomatoes | 6.5 | Wheat | 4.1 | Potatoes | |
| 44.0 | PT General population | 12.4 | Wine grapes | 6.4 | Tomatoes | 5.3 | Potatoes | |
| 43.0 | ES adult | 16.1 | Lettuce | 5.6 | Tomatoes | 2.3 | Wheat | |
| 41.9 | FR all population | 20.0 | Wine grapes | 3.3 | Wheat | 3.1 | Tomatoes | |
| 41.2 | WHO Cluster diet F | 9.0 | Lettuce | 4.9 | Tomatoes | 3.6 | Wheat | |
| 41.1 | IT kids/toddler | 10.3 | Tomatoes | 8.7 | Lettuce | 6.6 | Wheat | |
| 40.7 | SE general population 90th percentile | 5.5 | Tomatoes | 4.2 | Potatoes | 4.0 | Chinese cabbage | |
| 39.5 | IT adult | 11.3 | Lettuce | 8.4 | Tomatoes | 4.1 | Wheat | |
| 38.6 | DK child | 5.5 | Wheat | 4.4 | Rye | 4.2 | Lettuce | |
| 37.5 | NL general | 3.6 | Lettuce | 3.1 | Wine grapes | 3.1 | Tomatoes | |
| 35.1 | UK vegetarian | 7.6 | Sugar beet (root) | 4.5 | Tomatoes | 4.2 | Lettuce | |
| 31.3 | UK Adult | 8.0 | Sugar beet (root) | 5.4 | Wine grapes | 3.5 | Lettuce | |
| 22.9 | DK adult | 7.0 | Wine grapes | 3.0 | Tomatoes | 2.0 | Wheat | |
| 21.4 | PL general population | 6.4 | Tomatoes | 3.4 | Potatoes | 2.5 | Apples | |
| 18.7 | LT adult | 4.5 | Tomatoes | 3.2 | Potatoes | 2.2 | Apples | |
| 16.6 | FI adult | 3.1 | Tomatoes | 2.3 | Lettuce | 1.5 | Wine grapes | |

**Conclusion:**

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Difenoconazole is unlikely to present a public health concern.

| Acute risk assessment /children - refined calculations | Acute risk assessment / adults / general population - refined calculations |
|---|---|

The acute risk assessment is based on the ARfD.

For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.

In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.

In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.

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

**Unprocessed commodities**

| **No of commodities for which ARfD/ADI is exceeded (IESTI 1):** --- | | | **No of commodities for which ARfD/ADI is exceeded (IESTI 2):** --- | | | **No of commodities for which ARfD/ADI is exceeded (IESTI 1):** --- | | | **No of commodities for which ARfD/ADI is exceeded (IESTI 2):** --- | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **IESTI 1** | ***)** | ****)** | **IESTI 2** | ***)** | ****)** | **IESTI 1** | ***)** | ****)** | **IESTI 2** | ***)** | **) |
| Highest % of ARfD/ADI | Commodities | pTMRL/ threshold MRL (mg/kg) | Highest % of ARfD/ADI | Commodities | pTMRL/ threshold MRL (mg/kg) | Highest % of ARfD/ADI | Commodities | pTMRL/ threshold MRL (mg/kg) | Highest % of ARfD/ADI | Commodities | pTMRL/ threshold MRL (mg/kg) |
| 33.7 | Fennel | 3.31 / - | 33.7 | Fennel | 3.31 / - | 43.3 | Fennel | 3.31 / - | 31.6 | Fennel | 3.31 / - |
| 16.3 | Celery leaves | 5.68 / - | 16.3 | Celery leaves | 5.68 / - | 3.4 | Parsley | 5.68 / - | 3.4 | Parsley | 5.68 / - |
| 3.7 | Chervil | 5.68 / - | 3.7 | Chervil | 5.68 / - | 0.4 | Celery leaves | 5.68 / - | 0.4 | Celery leaves | 5.68 / - |
| 2.2 | Parsley | 5.68 / - | 2.2 | Parsley | 5.68 / - | | | | | | |
| **No of critical MRLs (IESTI 1)** | | | --- | | | **No of critical MRLs (IESTI 2)** | | | --- | | |

**Processed commodities**

| **No of commodities for which ARfD/ADI is exceeded:** --- | | | | | | **No of commodities for which ARfD/ADI is exceeded:** --- | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *****)** | | | | | | *****)** | | | |
| Highest % of ARfD/ADI | Processed commodities | pTMRL/ threshold MRL (mg/kg) | | | | Highest % of ARfD/ADI | Processed commodities | pTMRL/ threshold MRL (mg/kg) | | | |
| 17.4 | Tomato juice | 2 / - | | | | 1.9 | Tomato (preserved- | 2 / - | | | |
| 13.2 | Celeriac juice | 2 / - | | | | 1.6 | Apple juice | 0.5 / - | | | |
| 12.7 | Apple juice | 0.5 / - | | | | 1.0 | Wine | 0.5 / - | | | |
| 8.2 | Grape juice | 0.5 / - | | | | 0.5 | Orange juice | 0.1 / - | | | |
| 6.4 | Carrot, juice | 0.3 / - | | | | 0.5 | Peach preserved with | 0.5 / - | | | |

*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

**) pTMRL: provisional temporary MRL

***) pTMRL: provisional temporary MRL for unprocessed commodity

**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.

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

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

## GLOSSARY / ABBREVIATIONS

| | |
|---|---|
| a.s. | active substance |
| ADI | acceptable daily intake |
| ARfD | acute reference dose |
| BBCH | Federal Biological Research Centre for Agriculture and Forestry (Germany) |
| bw | body weight |
| CAC | Codex Alimentarius Commission |
| CAS | Chemical Abstract Service |
| CF | conversion factor for enforcement residue definition to risk assessment residue definition |
| CIPAC | Collaborative International Pesticide Analytical Council Limited |
| CXL | codex maximum residue limit |
| d | day |
| DAR | Draft Assessment Report (prepared under Directive 91/414/eec) |
| DAT | days after treatment |
| $DT_{90f}$ | period required for 90 percent dissipation (field method) |
| dw | dry weight |
| EC | emulsifiable concentrate |
| EFSA | European Food Safety Authority |
| EMS | Evaluating Member State |
| EU | European Union |
| FAO | Food and Agriculture Organisation of the United Nations |
| GAP | good agricultural practice |
| GC | gas chromatography |
| ha | hectare |
| hL | hectolitre |
| HPLC | high performance liquid chromatography |
| HR | highest residue |
| ILV | independent laboratory validation |
| ISO | International Organization for Standardization |
| IUPAC | International Union of Pure and Applied Chemistry |
| JMPR | Joint FAO/WHO Meeting on Pesticide Residues |
| L | litre |

| | |
|---|---|
| LC | liquid chromatography |
| LC-MS | liquid chromatography-mass spectrometry |
| LC-MS-MS | liquid chromatography with tandem mass spectrometry |
| LOD | limit of detection |
| LOQ | limit of quantification |
| MRL | maximum residue limit |
| MS | Member States |
| NEU | Northern European Union |
| NOAEL | no observed adverse effect level |
| PF | processing factor |
| PHI | pre harvest interval |
| ppm | parts per million ($10^{-6}$) |
| PRIMo | Pesticide Residues Intake Model |
| RMS | Rapporteur Member State |
| STMR | supervised trials median residue |
| TDM | triazole derivative metabolites |
| TMDI | theoretical maximum daily intake |
| TRR | total radioactive residue |