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Modification of the existing maximum residue level (MRL) for prothioconazole in shallots

European Food Safety Authority (EFSA)

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS), United Kingdom, received an application from Bayer CropScience S.A.S. to modify the existing maximum residue level (MRL) for the active substance prothioconazole in shallots. In order to accommodate for the intended use of prothioconazole, United Kingdom proposed to set the MRL at the limit of quantification (LOQ) of 0.05 mg/kg. According to EFSA the data are sufficient to derive a MRL proposal of 0.05 mg/kg (LOQ) for the intended use on shallots in northern Europe. Adequate analytical enforcement methods are available to control the residues of prothioconazole-desthio in the commodity under consideration. Based on the risk assessment results, EFSA concludes that the proposed use of prothioconazole on shallots will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk. However, the consumer risk assessment should be regarded as provisional since the possible contribution of the triazole derivative metabolites (TDMs) in the consumer risk assessment was not taken into consideration.

Keywords: prothioconazole, shallots, MRL application, consumer risk assessment, triazole fungicide, prothioconazole-desthio

Requestor: European Commission

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, United Kingdom, hereafter referred to as the evaluating Member State (EMS), received an application from Bayer CropScience SAS to modify the maximum residue level (MRL) for the active substance prothioconazole in shallots. In order to accommodate for the intended use of prothioconazole, United Kingdom proposed to set the MRL at the limit of quantification (LOQ) of 0.05 mg/kg. United Kingdom drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005 which was submitted to the European Commission (EC) and forwarded to EFSA on 28 January 2015.

EFSA bases its assessment on the evaluation report submitted by the EMS, the draft assessment report (DAR) and its final addendum prepared under Council Directive 91/414/EEC, the Commission review report on prothioconazole, EFSA conclusions on the peer review of the pesticide risk assessment of the active substance prothioconazole and on the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005.

The toxicological profile of prothioconazole was assessed in the framework of the peer review under Council Directive 91/414/EEC. The data were sufficient to derive an acceptable daily intake (ADI) of 0.01 mg/kg bw per day and an acute reference dose (ARfD) of 0.01 mg/kg bw for prothioconazole-desthio, its main metabolite in plants. EFSA defined also toxicological reference values for the triazole derivative metabolites (TDMs).

The metabolism of prothioconazole in primary crops was investigated in root/tuber, pulse/oilseed and cereal crop groups following foliar application and in cereals following seed treatment. From these studies the peer review established the residue definition for enforcement as prothioconazole-desthio and for risk assessment as the sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2*H*-1,2,4-triazole moiety, expressed as prothioconazole-desthio. Pending the definition of a general approach to assess TDMs, the residue definitions should be regarded as provisional. For the use on shallots, EFSA concludes that the metabolism of prothioconazole in primary crops has been sufficiently addressed and the residue definitions are applicable.

EFSA concludes that sufficient information was provided to derive a MRL proposal of 0.05 mg/kg (LOQ) on shallots by extrapolation from the residue trials conducted on bulb onions. Adequate analytical enforcement methods are available to control the residues of prothioconazole as prothioconazole-desthio on the commodity under consideration at the validated LOQ of 0.05 mg/kg.

Specific studies investigating the magnitude of prothioconazole residues in processed commodities are not required as significant residues are not expected in the raw agricultural commodity (RAC).

Based on the available information on the nature and magnitude of residues in succeeding crops, EFSA concludes that significant residue levels of prothioconazole as prothioconazole-desthio are unlikely to occur in rotational crops provided that the compound is used on shallots in accordance with the proposed good agricultural practice (GAP). However, the possible occurrence of TDMs in rotational crops cannot be excluded and should be considered when a general approach on TDMs is defined.

Residues of prothioconazole in commodities of animal origin were not assessed in the framework of this application, since shallot is not fed to livestock.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). In the framework of the review of the existing MRLs for prothioconazole according to Article 12 of Regulation (EC) No 396/2005 a comprehensive long-term exposure assessment was performed taking into account all existing uses of prothioconazole at EU level and the acceptable Codex maximum residue limits (CXLs). EFSA updated this chronic risk assessment adding the median residue level derived for shallots from the supervised trials on onions. A default conversion factor (CF) of 2 established during the peer review was included in the calculation to consider all metabolites included in the residue definition for risk assessment. The acute risk assessment was performed only with regard to the crop under consideration.

Under the assumption that the MRLs will be amended as proposed in the Article 12 review, no long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA

PRIMo. The total calculated chronic intake accounted for 6 % of the ADI (WHO Cluster B) with residues on shallots contributing to a maximum of 0.02 % to the total consumer exposure. No acute consumer risk was identified, the highest calculated acute exposure for shallots being 0.1 % of the ARfD (German child).

EFSA concludes that the proposed use of prothioconazole on shallots will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a health risk to consumers.

EFSA emphasises that the above assessment should be regarded as provisional as it does not take into consideration the impact of the possible presence of TDMs residues or the possible change of the isomer ratio of the active substance. Regarding TDMs, a separate risk assessment should be performed when a general methodology on the risk assessment of triazole compounds and their TDMs is available.

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

Summary Table

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)		Comment/Justification
			Art 12.[(b)]	Art. 10	
Enforcement residue definition: Prothioconazole (Prothioconazole-desthio)					
0220030	Shallots	0.02*	0.01*	0.05*	Extrapolation from bulb onions.

(*): indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): commodity code number according to Annex I of Regulation (EC) 396/2005.
(b): lowering of the MRL to the LOQ of 0.01 mg/kg as recommended in the framework of the Article 12 MRL review (EFSA, 2014).

Table of contents

Background

Regulation (EC) No 396/2005[1] establishes the rules governing the setting of pesticide MRLs at European Union (EU) level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC,[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 that Regulation.

United Kingdom, hereafter referred to as the evaluating Member State (EMS), received an application from the company Bayer CropScience S.A.S.[4] to modify the existing MRL for the active substance prothioconazole in shallots. This application was notified to the European Commission and the European Food Safety Authority (EFSA) and was subsequently evaluated by the EMS in accordance with Article 8 of the Regulation.

After completion, the evaluation report was submitted to the European Commission and to EFSA on 28 January 2015.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2015-00075 and the following subject:

Prothioconazole - Setting new MRLs in shallot.

United Kingdom proposed to raise the existing MRL of prothioconazole in shallots from the LOQ of 0.02 mg/kg to the LOQ of 0.05 mg/kg.

EFSA proceeded with the assessment of the application and the evaluation report 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 application.

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

The active substance and its use pattern

Prothioconazole is the ISO common name for (*RS*)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione (IUPAC). The active substance used in the pesticide formulations is a racemic mixture of the two stereoisomers (*R* –and *S* – enantiomer). The chemical structures of the active substance and its main metabolite are reported in Appendix C. Prothioconazole is a triazole fungicide.

Prothioconazole was evaluated in the framework of Council Directive 91/414/EEC with United Kingdom designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Commission Directive 2008/44/EC[5] which entered into force on 01 August 2008 for use as a fungicide. In accordance with Commission Implementing Regulation (EU) No 540/2011[6] prothioconazole is

[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, 16.03.2005, 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, 19.08.1991, 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] Bayer CropScience S.A.S., 16 Rue Jean Marie Leclair, Cedex 09, 69009 Lyon, France.
[5] Commission Directive 2008/44/EC of 4 April 2008 amending Council Directive 91/414/EEC to include benthiavalicarb, boscalid, carvone, fluoxastrobin, *Paecilomyces lilacinus* and prothioconazole as active substances. OJ L 94, 05.04.2008, p. 13–20.
[6] 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, 11.06.2011, p. 1–186.

approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC. The representative uses supported for the peer review process were outdoor foliar applications on cereals and rape seeds, with 2 to 3 applications at rates ranging between 175 and 200 g a.s./ha and with a PHI of 35 days (cereals) or 56 days (rape seeds). The draft assessment report (DAR) of prothioconazole has been peer reviewed by EFSA (EFSA, 2007b).

The EU MRLs for prothioconazole are established as prothioconazole-desthio in Annex IIIA of Regulation (EC) No 396/2005. Since the entry into force of the abovementioned regulation, EFSA has issued several reasoned opinions on the modification of MRLs for prothioconazole, these proposals have been considered in the EU legislation. An overview of the MRL changes that occurred is provided in the Table below.

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)	(EC) No 1050/2009	Head cabbage, Brussels sprouts.
Implementation of CXLs	(EU) No 459/2010	CAC 2009
Art. 10 (EFSA, 2010a)	(EU) No 893/2010	Broccoli, cauliflower.
Art. 10 (EFSA, 2010b)	(EU) No 508/2011	Various root vegetables.
Implem. of CXLs (EFSA, 2010c)	(EU) No 520/2011	CAC 2010
Art. 10 (EFSA, 2012)	(EU) No 834/2013	Rape seed, linseed, poppy seed, mustard seed.
Art. 12 (EFSA, 2014)	Pending	Full review of all existing MRLs

(a): Article 10: Assessment of MRL application according to Article 6 to 10 of Regulation (EC) No 396/2005.
Article 12: Review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005.

EFSA has recently issued a reasoned opinion for prothioconazole which reviewed all existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014). Modifications of the existing MRLs were proposed for several crops, including the lowering to the LOQ of 0.01 mg/kg for shallots, which are currently under discussion at the Plants, Animals, Food and Feed Committee (PAFF) (draft Regulation SANCO/11481/2014). Codex Alimentarius has established CXLs for a number of commodities, but no CXL has been set for shallots.

The details of the intended GAP for prothioconazole in northern Europe (NEU) is given in Appendix A.

Assessment

EFSA bases its assessment on the evaluation report submitted by the EMS (United Kingdom, 2014), the DAR and its final addendum prepared under Council Directive 91/414/EEC (United Kingdom, 2004, 2007), the Commission review report on prothioconazole (European Commission, 2007), EFSA conclusions on the peer review of the pesticide risk assessment of the active substance prothioconazole and on the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2007b, 2014). The latter took into consideration previous EFSA opinions issues between 2009 and 2012 (see Table 1) and the JMPR reports. 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[7] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a-g, 2000, 2010a, b, 2011; OECD, 2011).

[7] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.06.2011, p. 127–175.

1. Method of analysis

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

Analytical methods for the determination of prothioconazole-desthio (the relevant residue for enforcement) in plant commodities were assessed in the framework of the peer review and the Article 12 review. EFSA concluded that adequate analytical methods are available to monitor residues in high water content commodities, to which group shallot belongs, with a LOQ of 0.05 mg/kg (EFSA, 2007b, 2014). The methods are not enantiomer-selective.

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

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

2. Mammalian toxicology

The toxicological profile of the active substance prothioconazole was assessed in the framework of the peer review under Council Directive 91/414/EEC (EFSA, 2007b). The prothioconazole-desthio metabolite, identified as the major metabolite in treated plants, was concluded to be the relevant component to be considered for the consumer risk assessment, as more toxic than the parent prothioconazole (EFSA, 2007b; European Commission, 2007). Therefore, ADI and ARfD were established for the metabolite and are compiled in Table 2. These reference values were set for the racemic mixture of isomers. In addition, since prothioconazole belongs to the class of triazole fungicides, which are metabolised in plants and animals to common metabolites known as TDMs, EFSA defined toxicological reference values also for the major TDMs (EFSA, 2011), which are compiled in Table 2.

Table 2: Overview of the toxicological reference values

	Source	Year	Value	Study	Safety factor
Prothioconazole-desthio					
ADI	European Commission	2007	0.01 mg/kg bw per day	Rat, carcinogenicity study	100
ARfD	European Commission	2007	0.01 mg/kg bw	Rat, developmental study	100
1,2,4-triazole, triazole acetic acid and triazole lactic acid[(a)]					
ADI	EFSA	2011	0.02 mg/kg bw per day	Rat, multigeneration study	1000
ARfD	EFSA	2011	0.06 mg/kg bw	Rat, developmental study	500
Triazole alanine					
ADI	EFSA	2011	0.1 mg/kg bw per day	Rat, developmental study	1000
ARfD	EFSA	2011	0.1 mg/kg bw	Rat, developmental study	1000

(a): In absence of reproductive toxicity data, EFSA concluded to apply to triazole acetic acid and triazole lactic acid the same toxicological reference values as for 1,2,4 triazole (EFSA, 2011).

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 prothioconazole in primary crops was evaluated in the framework of the peer review under Council Directive 91/414/EEC and in the framework of the Article 12 MRL review (EFSA, 2007b, 2014). The details of the metabolism studies are reported in a previous EFSA reasoned opinion (EFSA, 2014). The overview of the metabolism study designs is presented in Table 3.

Table 3: Summary of available metabolism studies in plants

Crop group	Crops	Application[(a)]	Sampling[(b)]	Comments
Root/tuber	Sugar beet	Foliar, 4 ×290 g/ha, interval 14 days (Ph, Tyr)	7 DALA	Outdoor
Pulse/Oilseed	Peanuts	Foliar, 3 ×300 g/ha, interval 21 days (Ph, Tyr)	14 DALA	Indoor
Cereal	Wheat	Foliar, 2 ×220 g/ha, BBCH 32-65 (Ph)	6 (forage), 26 (hay), 48 (grain, straw) DALA	Indoor
		Foliar, 2 ×250 g/ha, BBCH 31-59 (Tyr)	0, 14 (forage), 48 (grain, straw) DALA	Indoor
		Foliar, 2 ×180 & 290 g/ha, BBCH 32-65 (Tyr)	not reported	Outdoor
		Seed, 20 or 100 g/100 kg seed (Ph)	57 (forage), 110 (hay), 153 (grain, straw) DAT	Indoor

(a): BBCH: growth scale for monopcotyledonous and docotyledonous plants; (Ph) ^{14}C-phenyl labelled prothioconazole; (Tyr) ^{14}C-triazole labelled prothioconazole.
(b): DALA: days after last application; DAT: days after treatment.

The review of the existing MRLs for prothioconazole performed under Article 12 of Regulation (EC) No 396/2005 confirmed the conclusion of the peer review that the relevant component for enforcement of the residues is prothioconazole-desthio. However, EFSA proposed to report that this residue definition refers to the "sum of isomers", since no enantiospecific analytical methods are available (EFSA, 2014). The current residue definition set in Regulation (EC) No 396/2005 is similar and refers to prothioconazole-desthio.

The residue for risk assessment was defined as the sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2*H*-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers), assuming that all these metabolites have a toxicological profile similar to prothioconazole-desthio (EFSA, 2007b).

EFSA already highlighted that the possible isomer ratio change of prothioconazole was not investigated in plant metabolism and should be considered when a specific guidance is available. Furthermore, the above residue definitions do not take into consideration the TDMs. Pending the general approach to assess TDMs, the residue definitions should be regarded as provisional (EFSA, 2014).

For the uses on shallots, EFSA concludes that the metabolism of prothioconazole is sufficiently addressed and the derived residue definitions for enforcement and risk assessment are applicable.

3.1.1.2. Magnitude of residues

No specific residue trials on shallots have been submitted. It is proposed to extrapolate to shallots the MRL of 0.05 mg/kg (LOQ) derived on bulb onions from the NEU residue trials conducted according to the proposed GAP and already assessed in the framework of the Article 12 MRL review (EFSA, 2014).

The results of the residue trials, the related risk assessment input values (HR, STMR) and the MRL proposal are summarised in Table 4. Since the samples from the residue trials were not analysed for

the metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2*H*-1,2,4-triazole moiety, EFSA used the default CF of 2 derived for root/tuber crops from the metabolism study on sugar beet (EFSA, 2014).

Residues of prothioconazole-desthio were found to be stable at ≤ -18 °C for up to 24 months in matrices with high water content (EFSA, 2007b, 2014). The supervised residue trial samples were already assessed by EFSA and considered as valid with regards to storage stability and the analytical determination of residues (EFSA, 2014).

It is noted that under the Article 12 MRL review, it was highlighted that a validated method of analysis and storage stability data for at least one hydroxylated metabolite included in the risk assessment residue definition are required, to confirm the MRL proposals derived from the residue trials where samples were analysed according the residue definition for risk assessment (EFSA, 2014).

EFSA concludes that the data are sufficient to extrapolate to shallots the MRL of 0.05 mg/kg (LOQ) derived from the residue trials conducted on bulb onions according to the intended use in the NEU.

Table 4: Overview of the available residues trials data

Crop (Trial GAPs)	Region/ Indoor[a]	Individual residue levels (mg/kg)[b]	Recommendations/comments[c]	MRL proposals (mg/kg)	HR (mg/kg)[d]	STMR (mg/kg)[e]
Onions (4 × 125 g/ha, PHI 14 d)	NEU	Mo: 7 × <0.01; 0.01; 0.02 RA: No data. A default CF of 2 derived from the metabolism study on sugar beet was considered for the calculation of the STMR and HR values	Trials on onions previously assessed (EFSA, 2014). **Extrapolation to shallots.** MRL proposal of 0.05*mg/kg based on the LOQ achieved by the enforcement method. MRL_{OECD}: 0.02/0.03	0.05*	(0.01) 0.02	(0.02) 0.04

(*): Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(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.
Mo: residue level according to the monitoring residue definition
RA: residue level according to the residue definition for risk assessment
(c): Any information/comment supporting the decision and OECD MRL calculation (e.g. MRL_{OECD}: unrounded/rounded values)
(d): STMR: Median value of the individual trial results according to residue definition for risk assessment was tentatively obtained using the CF of 2 for root/tuber crops.
$STMR_{Mo}$: Median value of the individual trial results according to residue definition for monitoring is in brackets.
(e): HR: Highest value of the individual trial results according to the residue definition for risk assessment was tentatively obtained using the CF of 2 for root/tuber crops.
HR_{Mo}: Highest value of the individual trial results according to residue definition for monitoring is in brackets.

3.1.1.3. Effect of industrial processing and/or household preparation

Based on the available information on the nature of prothioconazole-desthio residues, EFSA concluded that the compound is hydrolytically stable under the representative processing conditions. Assuming that the metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2*H*-1,2,4-triazole moiety have a similar hydrolysis behaviour as prothioconazole-desthio, for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable (EFSA, 2014).

Specific studies to assess the magnitude of residues of prothioconazole and its metabolites during the processing of shallots are not necessary as the residue levels in RAC did not exceed the trigger value of 0.1 mg/kg (European Commission, 1997d).

3.1.2. Rotational crops

Since shallots can be grown in rotation with other plants and prothioconazole-desthio degradation in soil is above the trigger value of 100 days (EFSA, 2014), the possible occurrence of residues in succeeding crops resulting from the use of prothioconazole on primary crops has to be assessed (EC, 1997c).

The nature and magnitude of prothioconazole residues in rotational crops was investigated in the course of the peer review (EFSA, 2007b). EFSA concluded that the residue definitions set for primary crops are also applicable to rotational crops and that significant residues are not expected in rotational crops when the active substance is applied on primary crops up to a maximum dose rate of 580 g/ha (EFSA, 2007b).

Since the intended use of prothioconazole on shallots is limited to a maximum application rate of 500 g/ha (4 × 125 g/ha), EFSA concludes that significant residues are unlikely to occur in rotational crops provided that the active substance is applied according to the proposed GAP. However, the possible occurrence of TDMs in rotational crops cannot be excluded and will be considered when a general approach on TDMs is defined.

3.2. Nature and magnitude of residues in livestock

As shallots are not normally fed to livestock, the nature and magnitude of prothioconazole residues in livestock is not assessed in the framework of this application (European Commission, 1996).

4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population[8] (EFSA, 2007a).

In the framework of the review of the existing MRLs for prothioconazole according to Article 12 of Regulation (EC) No 396/2005 a comprehensive long-term exposure assessment was performed taking into account only the existing uses of prothioconazole at EU level supported by data and the existing acceptable CXLs. Those food commodities for which no uses were reported in the framework of Article 12 review were excluded from the exposure calculation assuming that there is no use on these crops (EFSA, 2014).

EFSA updated the chronic risk assessment performed under the Article 12 review with the median residue value for shallots derived from the residue trials (see Table 4). The acute exposure assessment was performed only with regard to the commodity under consideration assuming the consumption of a large portion of the food item as reported in the national food surveys and that these items contained residues at the highest residue level as observed in supervised field trials (EFSA, 2007a). A default CF of 2 established during the peer review on the basis of the metabolism data on sugar beet (EFSA, 2007b, 2014) was included in the calculation in order to take into

[8] 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 MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007a).

consideration the exposure to the total residues (prothioconazole-desthio and the metabolites according to the residue definition for risk assessment).

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

Table 5: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2*H*-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers).				
Shallots	0.02	$STMR_{Mo}$ × CF (2) (onion, NEU)	0.04	HR_{Mo} × CF (2) (onion, NEU)
Other plant and animal origin commodities	STMR	See Table 4-2 of the Reasoned opinion on the review of the existing maximum residue levels (MRLs) for prothioconazole according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014).	Acute risk assessment was undertaken only with regard to the crop under consideration.	

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

Under the assumption that the MRLs will be amended as proposed in the Article 12 review, no long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for 6 % of the ADI (WHO Cluster B), the contribution to the total exposure of the residues in shallots accounting for a maximum of 0.02 %.

No acute consumer risk was identified in relation to the MRL proposal for shallots, the highest calculated acute exposure being 0.1 % of the ARfD (German child).

EFSA concludes that the proposed use of prothioconazole on shallots will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a health risk to consumers.

EFSA emphasises that the above assessment should be regarded as provisional as it does not take into consideration the impact of the possible presence of TDMs residues or the possible change of the isomer ratio of the active substance. Regarding TDMs, a separate risk assessment should be performed when a general methodology on the risk assessment of triazole compounds and their TDMs is available.

Conclusions and recommendations

The submitted information was sufficient to derive the MRL proposal summarised in the table below.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)		Comment/Justification
			Art 12.[(b)]	Art. 10	
Enforcement residue definition: Prothioconazole (Prothioconazole-desthio) (R)					
0220030	Shallots	0.02*	0.01*	0.05*	Extrapolation from bulb onions.

(*): indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): commodity code number according to Annex I of Regulation (EC) 396/2005.
(b): lowering of the MRL to the LOQ of 0.01 mg/kg as recommended in the framework of the MRL review (EFSA, 2014).

References

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European Commission, 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3.

European Commission, 1997b. Appendix B. General recommendations for the design, preparation and realisation of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6.

European Commission, 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement to risk assessment residue definition
CXL	Codex maximum residue limit (Codex MRL)
d	day
DALA	days after last application
DAR	draft assessment report
DAT	days after treatment
EC	emulsifiable concentrate
EMS	evaluating Member State
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly International Group of National Associations of Manufacturers of Agrochemical Products (GIFAP))
HR	highest residue
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LOQ	limit of quantification
MRL	maximum residue level
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
RAC	raw agricultural commodity
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SCPAFF	Standing Committee on Plants, Animals, Food and Feed (formerly: Standing Committee on the Food Chain and Animal Health; SCFCAH)
SEU	southern Europe
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
WHO	World Health Organization

Appendix A – Good Agricultural Practice (GAPs)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
				Type (d-f)	Conc. a.s. (i)	Method kind (f-h)	Growth stage & season (j)	Number min-max (k)	Interval min-max	g a.s./hL min-max	Water L/ha min-max	g a.s./ha min-max		
Shallots	NEU	F	fungi	EC	100 g/L	Foliar spraying	Up to BBCH 47	4	5-10	-	-	125	14	

Remarks:

(a): For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the usage situation should be described (e.g. fumigation of a structure)
(b): Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c): e.g. biting and sucking insects, soil-born insects, foliar fungi, weeds
(d): e.g. wettable powder (WP), water soluble granule (WG)
(e): GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f): all abbreviations must be explained
(g): Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h): Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants. type of equipment used must be indicated
(i): g/kg or µg/L
(j): Growth stage at last treatment (Meier U, 2001. Growth Stages of mono- and dicotyledonous plants. BBCH Monograph, 2nd Ed., Federal Biological Research Centre of Agriculture and Forestry, Braunschweig, Germany, 2001), including where relevant, information on season at time of application
(k): The minimum and maximum number of application possible under practical conditions of use must be provided
(l): PHI - minimum pre-harvest interval
(m): Remarks may include: Extent of use/economic importance/restrictions

Appendix B – Pesticide Residue Intake Model (PRIMo)

Prothioconazole-desthio			
Status of the active substance:	approved	Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	0.01	ARfD (mg/kg bw):	0.01
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	2007	Year of evaluation:	2007

Chronic risk assessment - refined calculations

	TMDI (range) in % of ADI minimum - maximum
	1 6
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)
6.1	WHO Cluster diet B	3.4	Wheat	0.4	Beetroot	0.3	Potatoes	
5.9	FR toddler	2.0	Milk and cream,	1.5	Carrots	1.0	Wheat	
5.5	NL child	1.9	Wheat	1.5	Milk and cream,	0.6	Potatoes	
5.2	DK child	2.2	Wheat	0.9	Rye	0.8	Carrots	
4.9	UK Infant	1.9	Milk and cream,	1.0	Wheat	0.8	Carrots	
4.7	IE adult	1.0	Barley	0.9	Wheat	0.4	Parsnips	
4.4	WHO cluster diet D	2.6	Wheat	0.4	Potatoes	0.3	Milk and cream,	
4.3	WHO cluster diet E	1.6	Wheat	0.6	Barley	0.4	Potatoes	
4.1	FR infant	1.6	Carrots	1.3	Milk and cream,	0.4	Potatoes	
4.0	WHO Cluster diet F	1.4	Wheat	0.5	Barley	0.3	Potatoes	
3.9	DE child	1.6	Wheat	0.7	Milk and cream,	0.6	Carrots	
3.7	ES child	1.8	Wheat	0.6	Milk and cream,	0.2	Lentils	
3.7	UK Toddler	1.6	Wheat	1.0	Milk and cream,	0.3	Potatoes	
3.5	SE general population 90th percentile	1.3	Wheat	0.6	Milk and cream,	0.5	Carrots	
3.3	WHO regional European diet	1.2	Wheat	0.4	Potatoes	0.3	Barley	
3.0	IT kids/toddler	2.7	Wheat	0.1	Carrots	0.1	Potatoes	
2.7	PT General population	1.6	Wheat	0.5	Potatoes	0.4	Carrots	
2.5	NL general	0.8	Wheat	0.3	Milk and cream,	0.3	Barley	
2.3	ES adult	0.9	Wheat	0.4	Barley	0.2	Milk and cream,	
2.1	FR all population	1.3	Wheat	0.2	Carrots	0.1	Milk and cream,	
1.9	IT adult	1.7	Wheat	0.1	Carrots	0.1	Potatoes	
1.9	DK adult	0.8	Wheat	0.3	Milk and cream,	0.3	Carrots	
1.7	LT adult	0.4	Wheat	0.3	Potatoes	0.2	Rye	
1.6	UK vegetarian	0.8	Wheat	0.2	Milk and cream,	0.1	Potatoes	
1.3	UK Adult	0.7	Wheat	0.1	Milk and cream,	0.1	Potatoes	
1.2	FI adult	0.4	Wheat	0.3	Milk and cream,	0.1	Rye	
0.9	PL general population	0.3	Potatoes	0.2	Carrots	0.1	Beetroot	

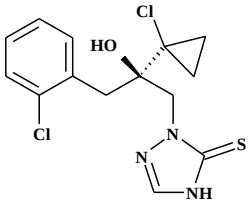
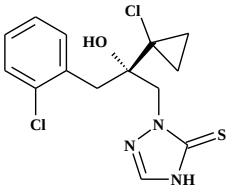
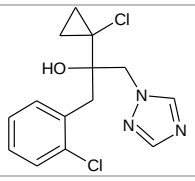
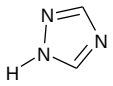
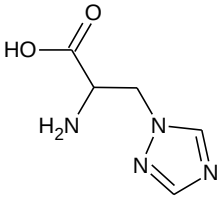
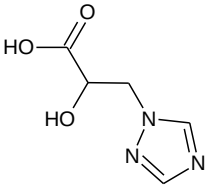
Conclusion:

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

A long-term intake of residues of Prothioconazole-desthio 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):**			**---**		
	IESTI 1	***)**	****)**			**IESTI 2**	***)**	****)**			
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)			Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)			
	0.1	Shallots	0.04 / -			0.1	Shallots	0.04 / -			
	No of critical MRLs (IESTI 1)			---		**No of critical MRLs (IESTI 2)**			---		
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**			**---**							
			*****)**								
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)								
	42.9	Carrot, juice	0.1 / -								
	11.8	Wheat flour	0.1 / -								
	1.4	Potato puree (flakes)	0.01 / -								
	0.4	Maize flour	0.01 / -								
	0.1	Fried potatoes	0.01 / -								
	No of commodities for which ARfD/ADI is exceeded:			**---**							
			*****)**								
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)								
	4.4	Bread/pizza	0.1 / -								
	0.1	Potato uree (flakes)	0.01 / -								
	0.1	Fried potatoes	0.01 / -								
	0.0	Maize flour	0.01 / -								
*) 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 Prothioconazole-desthio 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.											

Appendix C – Used compound codes

Code/Trivial name	Chemical name	Structural formula
Prothioconazole	(RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione (IUPAC)	
	R - enantiomer	
	S - enantiomer	
Prothioconazole-desthio (M04)	(2RS)-2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1H-1,2,4-triazol-1-yl) propan-2-ol	
Triazole derivative metabolites		
1,2,4-triazole (free triazole)	1H-1,2,4-triazole	
Triazole alanine	3-(1H-1,2,4-triazol-1-yl)-D,L-alanine	
Triazole acetic acid	1H-1,2,4-triazol-1-ylacetic acid	
Triazole lactic acid	(2RS)-2-hydroxy-3-(1H-1,2,4-triazol-1-yl) propanoic acid