FINAL REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: Protiokonazol 300 EC

Product name(s): HERA 300 EC

Chemical active substance:

prothioconazole, 300 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Pestila Spółka z ograniczoną odpowiedzialnością

Submission date: October 2023

MS Finalisation date: April 2024; July 2024

Version history

When	What
April 2024	ZRMs evaluated dRR submitted by Applicant.
July 2024	The final Registration Report

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

Storage stability

In the framework of the peer review, storage stability of prothioconazole and its metabolite prothioconazole-desthio residues was demonstrated at -18 °C for 18 months in high water content matrices (wheat green matter), cereal grain and straw and for 24 months in high oil content.

Storage stability data for TDMs are presented in EFSA Journal 2018;16(7):5376.

Residues are stable in wheat and barley grain for 12 month - 1,2,4-Triazole, for 26 month – TA, for 26 month – TAA and for 48 month – TLA.

Residues are stable in cereal straw for 12 month - 1,2,4-Triazole, for 53 month – TA, for 40 month – TAA and there is no data for TLA. However, storage stability for TLA in cereal straw is covered by acceptable storage stabilities in 5 different group matrices - 48 months covered

Residues of 1,2,4-Triazole and TA are not stable in oilseed rape (seed). Residues of TAA are stable for 53 month and TLA are stable for 48 month in oilseed rape (seed).

Applicant has LoA from Indofil Industries (Netherlands) B.V. to following study:

Longhi, D., 2022. *Storage stability of Triazole Derivative Metabolites (TDM) in wheat forage, wheat grain, rapeseed seeds, wheat straw, apple, tomato, carrot. Final Report No. GLP-STUDY-21-124.*

The applicant does not have access to a copy of the study. Therefore, the study was not summarized. The study was accepted by zRMS (PL) in *Prothioconazole_fRR Part B7_INDOFIL Prothio 250 EC_Indofil Industries_PL_rev 02.2024.*

Part of the study for which the access is granted:

Storage stability of TDM (TRZ, TA, TLA, TAA) in matrices:

- high water (green forage wheat)
- high starch (wheat grain)
- dry (wheat straw)

The study demonstrated the stability of all tested metabolites in all tested matrices for 7 months.

The study was found to be acceptable.

Metabolism in plants and animals

Plant residue definition for monitoring (RD-Mo):

Prothioconazole: Prothioconazole-desthio (sum of isomers)

Plant residue definition for risk assessment (RD-RA):

a) Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers) (EFSA, 2014)

b)TDMs (EFSA, 2018, SANCO/3923 /07 – final 10 December 2007, 26 January 2021), with separate assessment of:

- Triazole alanine (TA) and triazole lactic acid (TLA)

- Triazole acetic acid (TAA)

- 1,2,4-triazole (1,2,4-T)

Magnitude of residues in plants

Winter and spring: wheat, triticale and barley; rye

Proposed GAPs cereals: 1-2 Applications (14 days interval), BBCH 29-65, 150-195 g as/ha, PHI: 35 days

EU GAPs:

Wheat, rye, triticale: 3 x 0.2 kg a.s./ha, BBCH 69, PHI 35 d, int. 14-21 days

Barley: 2 x 0.2 kg a.s./ha, BBCH 69, PHI 35 d, int. 14-21 days

Prothioconazole

No new data are submitted in the framework of this application. The residue data on cereals were evaluated during the EU review of prothioconazole. Sufficient EU trials on wheat, barley are available to support the proposed uses. The residue data are valid with regard to storage stability. The residues arising from the proposed uses will not exceed the MRLs for Prothioconazole established for cereals (0.1 (wheat, triticale, durum, spelt), 0.2 (barley) mg/kg, 0.05 (oat, rye); Reg. (EU) 2019/552). Residues were measured according to the current enforcement residue definition - prothioconazole-desthio (sum of isomers).

Residues:

Wheat grain – 10 x <0.01 mg/kg

Barley grain - 9 x <0.01 mg/kg

Extrapolations from wheat to rye and triticale are possible.

TDMs

Considering TDMs, the intended uses are covered by the peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data (EFSA, 2018). Additional studies are no required.

Additionally the applicant has LoA from Indofil Industries (Netherlands) B.V. to following study:

Sala, A.2021. *Determination of difenoconazole and prothioconazole residues in winter or spring wheat raw and processed commodities (white flour and white bread) following two applications of IN233C1560 Northern and Southern Europe – 16 trials. GLP-STUDY-21-24.*

The applicant does not have access to a copy of the study. Therefore, the study was not summarized.

Part of the study for which the access is granted:

Determination of the residues level of the following analytes in wheat samples (whole plant, straw, grain) and processed commodities (white flour and white bread):

- prothioconazole-desthio
- tiazole derivative metabolites (TDMs)
- Prothioconazole-desthio-3-hydroxy
- Prothioconazole-desthio-4-hydroxy
- Prothioconazole-desthio-5-hydroxy
- Prothioconazole-desthio-6-hydroxy
- Prothioconazole-desthio-alpha-hydroxy

The study was accepted by zRMS (PL) in *Prothioconazole_fRR Part B7_INDOFIL Prothio 250*

EC_Indofil Industries_PL_rev 02.2024.

Oilseed Rape

Proposed GAPs:

1 Application (BBCH 13-19; Autumn, post emergence), 150 - 180 g as/ha, PHI: 56 days

2 Applications (interval 21 days, BBCH 61-72, Spring, post emergence), 150 - 180 g as/ha, PHI: 56 days

EU-GAP: 1-2 Applications (14 – 28 days interval), start BBCH 53, 0.175 kg as/ha, PHI: 56 days

Prothioconazole

No new data are submitted in the framework of this application. Applicant refers to the unprotected EU data.

Prothioconazole

Residues in Seed: 5 x <0.01, 0.01, 2 x 0.02 mg/kg.

Sufficient EU trials on oilseed Rape are available to support the proposed uses. The residue data are valid with regard to storage stability. The residues arising from the proposed uses will not exceed the MRLs for Prothioconazole established for oilseed Rape (0.15 mg/kg, Reg. (EU) 2019/552). Residues were measured according to the current enforcement residue definition - prothioconazole-desthio (sum of isomers).

TDMs

No data were provided (data gap).

Use is not accepted.

Livestock Feeding Studies

The calculated dietary burdens were found to be above the trigger value of 0.004 mg/kg bw (0.1 mg/kg dry matter (DM) for all types of livestock. Applicant refers to out of protection EU data. No exceedances of the existing EU MRLs for prothioconazole in animal commodities are anticipated as a result of the proposed uses.

TDMs

EFSA Journal 2018;16(7):5376:

The livestock exposure assessment cannot be finalised with regard to the outstanding data for acceptable residue trials in primary and rotational crops.

Data gap: *Poultry and ruminant feeding studies conducted with TLA or, alternatively, metabolism studies performed in accordance with the current recommendations as a surrogate to these feeding studies to determine the magnitude of TLA residues in products of animal origin* (data gap at EU level).

No further data is required.

Industrial Processing and/or Household Preparation

As quantifiable residues of prothioconazole exceeding 0.1 mg/kg are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing.

The TDMs remained stable under the standard hydrolysis conditions simulating processing of pasteurisation, baking, brewing and boiling and sterilisation (EFSA Journal 2018;16(7):5376).

No further data is required.

Residues in Representative Succeeding Crops

Prothioconazole

Considering available data dealing with nature of residues, no study dealing with magnitude of residues in succeeding crops is needed

TDMs

Data gap: Rotational crops field residue trials supported by acceptable storage stability data on TDMs.

(data gap at EU level).

No further data is required.

Other / special studies

Four new studies (2 NEU and 2 SEU trials) have been performed on phacelia crop to investigate the magnitude of prothioconazole residues in honey. These studies consider a "worst case" situation (the most critical scenario was used on a crop (phacelia) representing a worst case in terms of residues in honey). The intended GAP for oilseed rape is 2x 180 g as/ha, BBCH 61-72, outdoor. In four honey trials Protiokonazol 300 EC was applied at a rate 390 g as/ha at a flowering phase (BBCH 65). In these trials all residues of prothioconazole, prothioconazole-desthio and TDMs in honey were below LOD (<0.002 mg/kg).

All samples were analysed within 30 days from sampling (23 days), therefore there is no need to perform studies on the stability of residues during storage.

The residues will not exceed the MRL of 0.05 mg/kg established for honey (Regulation (EU) 2019/552).

No further data is required.

The consumer risk assessment

The proposed uses of prothioconazole in the formulation Protiokonazol 300 EC does not represent unacceptable chronic and acute risks for the consumer.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation Protiokonazol 300 EC are presented in Table 7.1-1. A list of all intended uses within the zone is given in Part B, Section 0.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRL of 0.1 mg/kg (wheat incl. triticale), 0.2 mg/kg (barley) 0.05 mg/kg (rye) and 0.15 mg/kg (oilseed rape) for as laid down in Reg. (EU) 396/2005 (last amendment - Reg. (EU) 2019/552) is not expected.
The chronic and the short-term intakes of prothioconazole and triazole derivative metabolites (TDMs) residues are unlikely to present a public health concern.
As far as consumer health protection is concerned, zRMS agrees with the authorization of the intended use on winter and spring: wheat, triticale and barley; rye.

According to available data, no specific mitigation measures should apply.

Data gaps

Triazole derivative metabolites (TDMs): magnitude of residues in oilseed rape

Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)*	**Crop and/ or situa-tion ****	**Zone**	**Product code**	**F, Fn, Fpn G, Gn, Gpn or I*****	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment**			**PHI (days)**	**Conclusion**
						Type	**Conc. of as**	**method kind**	**growth stage & season**	**number min max**	**interval between applications (min)**	**g as/hL min max**	**water L/ha min max**	**g as/ha min max**		
1	Winter wheat	PL	Protiokonazol 300 EC	F	Controlled diseases - for details please refer to dRR Part B0 and B3	EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
2	Spring wheat	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
3	Winter triticale	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
4	Spring triticale	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
5	Spring barley	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
6	Winter barley	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
7	Rye	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 29-65 Spring, post emergence	1 2	14 days	37.5 - 195 g sa/hL	100-400	150 - 195 g sa/ha	35	A
8	Winter oilseed rape	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 13-19 Autumn, post emergence	1 1	n.a.	37.5 - 180 g sa/hL	100-400	150 - 180 g sa/ha	56	N Data gap: Triazole derivative metabolites (TDMs) - magnitude of residues in oilseed rape

9	Winter oilseed rape	PL	Protiokonazol 300 EC	F		EC	300 g/l	overall	BBCH 61-72 Spring, post emergence	1 2	21 days	37.5 - 180 g sa/hL	100-400	150 - 180 g sa/ha	56	N Data gap: Triazole derivative metabolites (TDMs) - magnitude of residues in oilseed rape

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** Use also code numbers according to Annex I of Regulation (EU) No 396/2005

*** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Explanation for Column 11 “Conclusion”

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

7.1.2 Summary of the evaluation

The preparation Protiokonazol 300 EC is composed of prothioconazole.

Table 7.1-2: Toxicological reference values for the dietary risk assessment of prothioconazole

Reference value	Source	Year	Value	Study relied upon	Safety factor
Prothioconazole					
ADI	EFSA Scientific Report (2007) 106, 1-98	2007	0.05 mg/kg bw/d	Rat, 2-year study dog, 1-year study	100
ARfD	EFSA Scientific Report (2007) 106, 1-98	2007	0.2 mg/kg bw	Rat, developmental study	100
Prothioconazole-desthio					
ADI	EFSA Scientific Report (2007) 106, 1-98	2007	0.01 mg/kg bw/d	Rat, carcinogenicity study	100
ARfD	EFSA Scientific Report (2007) 106, 1-98	2007	0.01 mg/kg bw	Rat, developmental study	100
1, 2, 4-triazole (1,2,4-T)					
ADI	EFSA Journal 2018; 16(7):5376	2018	0.023 mg/kg bw/day	Rat 12-month study	300
ARfD	EFSA Journal 2018; 16(7):5376	2018	0.1 mg/kg bw	Rabbit developmental study	300
Triazole alanine (TA)					
ADI	EFSA Journal 2018; 16(7):5376	2018	0.3 mg/kg bw/day	Rabbit developmental study	100
ARfD	EFSA Journal 2018; 16(7):5376	2018	0.3 mg/kg bw	Rabbit developmental study	100
Triazole acetic acid (TAA)					
ADI	EFSA Journal 2018; 16(7):5376	2018	1 mg/kg bw/day	Rat 2 generation and Rabbit developmental studies	100
ARfD	EFSA Journal 2018; 16(7):5376	2018	1 mg/kg bw	Rat 2 generation and Rabbit developmental studies	100
Triazole lactic acid (TLA)					
ADI	EFSA Journal 2018; 16(7):5376	2018	0.3 mg/kg bw/day	Bridging from TA	
ARfD	EFSA Journal 2018; 16(7):5376	2018	0.3 mg/kg bw	Bridging from TA	

7.1.2.1 Summary for prothioconazole

Table 7.1-3: Summary for prothioconazole

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1-4	Wheat, triticale, (spring and winter)	Yes	Yes **	Yes	Yes **	Yes	No	No
5-6	Barley (spring and winter)	Yes	Yes **	Yes	Yes **	Yes	No	No
7	Rye	Yes	Yes **	Yes	Yes **	Yes	No	No
8-9	Oilseed rape (winter)	Yes	~~Yes~~ ** No (no data for TDMs)	~~Yes~~ No (no data for TDMs)	~~Yes~~ ** No (no data for TDMs)	Yes	No	No

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1
** New data has been generated for TDMs. Please refer to the data to which the applicant has been granted access under the LoA.

As residues of prothioconazole do not exceed the trigger values defined in Reg (EU) No 283/2013, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. It is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, further investigation of residues as well as the modification of MRLs in commodities of animal origin is not necessary.

7.1.2.2 Summary for Protiokonazol 300 EC

Table 7.1-4: Information on Protiokonazol 300 EC (KCA 6.8)

Crop	PHI for Protiokonazol 300 EC proposed by applicant	PHI sufficiently supported for	PHI for Protiokonazol 300 EC proposed by zRMS	zRMS Comments (if different PHI proposed)
		prothioconazole		
Wheat, triticale, rye, barley (spring and winter)	35	yes		
~~Oilseed rape (winter)~~	~~56~~	~~yes~~		

Table 7.1-5: Waiting periods before planting succeeding crops

Waiting period before planting succeeding crops		Overall waiting period proposed by zRMS for Protiokonazol 300 EC
Crop group	**Led by prothioconazole**	
All crops	NR	

NR: not relevant

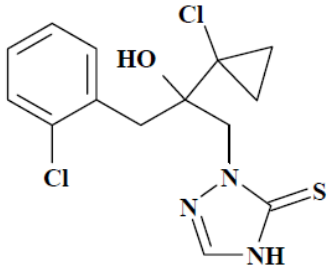
No significant residue levels are expected in rotational crops following application of prothioconazole according to GAP.

Assessment

7.2 Prothioconazole

General data on prothioconazole are summarized in the table below (last updated 2022/12/22)

Table 7.2-1: General information on prothioconazole

Active substance (ISO Common Name)	prothioconazole
IUPAC	(RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione
Chemical structure	
Molecular formula	$C_{14}H_{15}Cl_2N_3OS$
Molar mass	344.26 g/mol
Chemical group	Group of triazole compounds
Mode of action (if available)	Steroid demethylation in the ergosterol biosynthesis pathway
Systemic	Yes
Company (ies)	Bayer CropScience
Rapporteur Member State (RMS)	United Kingdom (inclusion), Poland (renewal)
Approval status	Approved Date of approval: 01/08/2008 Consolidated text: Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02011R0540-20221212 Commission Implementing Regulation (EU) 2020/869 of 24 June 2020 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances beflubutamid, benalaxyl, benthiavalicarb, bifenazate, boscalid, bromoxynil, captan, cyazofamid, dimethomorph, ethephon, etoxazole, famoxadone, fenamiphos, flumioxazine, fluoxastrobin, folpet, formetanate, metribuzin, milbemectin, Paecilomyces lilacinus strain 251, phenmedipham, phosmet, pirimiphos-methyl, propamocarb, prothioconazole and S-metolachlor https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1593089089989&uri=CELEX:32020R0869 Commission Implementing Regulation (EU) 2021/745 of 6 May 2021 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances aluminium ammonium sulphate, aluminium silicate, beflubutamid, benthiavalicarb, bifenazate, boscalid, calcium carbonate, captan, carbon

	dioxide, cymoxanil, dimethomorph, ethephon, extract from tea tree, famoxadone, fat distilation residues, fatty acids C7 to C20, flumioxazine, fluoxastrobin, flurochloridone, folpet, formetanate, gibberellic acid, gibberellins, heptamaloxyloglucan, hydrolysed proteins, iron sulphate, metazachlor, metribuzin, milbemectin, Paecilomyces lilacinus strain 251, phenmedipham, phosmet, pirimiphos-methyl, plant oils/rape seed oil, potassium hydrogen carbonate, propamocarb, prothioconazole, quartz sand, fish oil, repellents by smell of animal or plant origin/ sheep fat, S-metolachlor, Straight Chain Lepidopteran Pheromones, tebuconazole and urea https://eur-lex.europa.eu/eli/reg_impl/2021/745/oj Commission Implementing Regulation (EU) 2022/708 of 5 May 2022 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances 2,5-dichlorobenzoic acid methylester, acetic acid, aclonifen, aluminium ammonium sulphate, aluminium phosphide, aluminium silicate, beflubutamid, benthiavalicarb, boscalid, calcium carbide, captan, cymoxanil, dimethomorph, dodemorph, ethephon, ethylene, extract from tea tree, fat distilation residues, fatty acids C7 to C20, fluoxastrobin, flurochloridone, folpet, formetanate, gibberellic acid, gibberellins, hydrolysed proteins, iron sulphate, magnesium phosphide, metam, metamitron, metazachlor, metribuzin, milbemectin, phenmedipham, pirimiphos-methyl, plant oils/clove oil, plant oils/rape seed oil, plant oils/spear mint oil, propamocarb, proquinazid, prothioconazole, pyrethrins, quartz sand, fish oil, repellents by smell of animal or plant origin/sheep fat, S-metolachlor, Straight Chain Lepidopteran Pheromones, sulcotrione, tebuconazole and urea https://eur-lex.europa.eu/eli/reg_impl/2022/708/oj
Restriction	Restricted for use only as a fungicide.
Review Report	SANCO/3923/07 – final 10/12/2007, updated 26/01/2021
Current MRL regulation	Regulation (EU) No 2019/552
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal: Conclusion on the peer review	EFSA Scientific Report 2007; 106: 1-98
EFSA Journal: conclusion on article 12	EFSA Journal 2014; 12 (5): 3689 EFSA Journal 2020;18(2):5999 (Evaluation of confirmatory data)
Current MRL applications on intended uses	None

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application. For TDMs please refer to point 7.3.

Table 7.2-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Residue definition: Prothioconazole-desthio			
Wheat green matter	High water content	18 months	EFSA, 2007; United Kingdom, 2004, 2007
Wheat grain	High starch content	18 months	
Wheat straw	No specific category	18 months	
Spinach	High water content	24 months	EFSA, 2009, 2010a, 2010b, 2012; Netherlands, 2007; France, 2009
Sugar beet	High water content	24 months	
Tomato	High water content	24 months	
Oilseed rape	High oil content	24 months	
Dried peas	High protein content	24 months	
Oilseed rape straw	No specific category	24 months	
Animal products			
Residue definition: Prothioconazole desthio, M14 and M15			
Ruminant	Muscle	1 month	EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007
Ruminant	Fat	1 month	
Ruminant	Liver	1 month	
Ruminant	Kidney	1 month	

Conclusion on stability of residues during storage

In the framework of the peer review, storage stability of prothioconazole-desthio residues was demonstrated at -18 °C for 18 months in high water content matrices (wheat green matter), dry commodities (cereal grain) and straw (EFSA, 2007b; United Kingdom, 2004, 2007). Furthermore, storage stability of prothioconazole-desthio residues was subsequently demonstrated for a period of 24 months at -18 °C in commodities with high water content (spinach, sugar beet, tomatoes), high oil content (canola seeds), dry commodities (dried peas) and canola straw (EFSA, 2009, 2010a, 2010b, 2012; Netherlands, 2007). According to the RMS and the Member States which submitted additional data during the MS consultation, all residue trial samples reported in the PROFile were stored in compliance with the storage conditions reported above. Degradation of prothioconazole-desthio residues during storage of the trial samples is therefore not expected. However, storage stability was demonstrated for prothioconazole and prothioconazole-desthio only, while further metabolites are included in the residue definition for risk assessment. Therefore, further storage stability data for at least one hydroxylated metabolite included in the risk assessment residue definition are still required in the relevant commodity groups (EFSA, 2014).
Regarding animal matrices, the storage stability of prothioconazole-desthio, M14 and M15 was demonstrated in the framework of the feeding study with lactating cows, which was already submitted in the DAR (United Kingdom, 2004) and further reviewed in its addenda (United Kingdom, 2007). The storage stability was assured in all matrices for up to 1 month (EFSA, 2014).

zRMS:
Applicant has LoA from Indofil Industries (Netherlands) B.V. to following study:
Longhi, D., 2022. Storage stability of prothioconazole-desthio-3-hydroxy, prothioconazole-desthio-4-hydroxy, prothioconazole-desthio-5-hydroxy, prothioconazole-desthio-6-hydroxy prothioconazole-desthio-alpha-hydroxy in cereal straw. Report No.: GLP-STUDY-31-125

The applicant does not have access to a copy of the study.
Note: Study has been submitted for registration application of Indofil's plant protection product, Avtar (Product code: IN233C1560) which is currently undergoing zonal evaluation (by the z-RMS Poland)..

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Not relevant.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-3: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No (interval in days)	Sampling (DAT)	Remarks	
EU data								
Root and tuber vege-tables	Sugar beet	[U-^{14}C-phenyl] prothioconazole	foliar treatment, F (b)	0.29	4 (14 days)	Roots & Tops/leaves: 7		EFSA, 2009; FAO, 2008a, 2008b; Nether-lands, 2007
		[3, 5-^{14}C-tiazole] prothio-conazole	foliar treatment, F (c)	0.29	4 (14 days)	Roots & Tops/leaves: 7		FAO, 2008a, 2008b
Pulses and oilseeds	Peanut	[U-^{14}C-phenyl] prothioconazole	foliar treatment, G	0.30 (d)	3 (21 days) (BBCH 66-75)	Hay & nuts without shells: 14		EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007
		[3, 5-^{14}C-tiazole] prothio-conazole	foliar treatment, G	0.30 (d)	3 (21 days) (BBCH 66-75)	Hay & nuts without shells: 14		FAO, 2008a, 2008b
Cereals	Wheat	[U-^{14}C-phenyl] prothioconazole	foliar treatment, G (e)	0.22	2 (BBCH 32-65)	Forage: 6 Hay: 26 Grain & straw: 48		EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007
		[U-^{14}C-phenyl] prothioconazole-desthio	foliar treatment, G (e)	0.25	2 (27 days) (BBCH 31-59)	Forage: 0, 14 Grain & Straw: 48		EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007
		[3, 5-^{14}C-tiazole] prothio-conazole	foliar treatment, F (f)	0.18 and 0.29	2 (BBCH 32-65)	Forage, hay, grain, Straw		FAO, 2008a, 2008b
		[U-^{14}C-phenyl] prothioconazole	Seed, G (spring wheat)	0.02 or 0.10 kg/100 kg sedes (*ca.* 220 kg seeds/ha)	1	Forage: 57 Hay: 110 Grain & straw: 153		EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007

Summary of plant metabolism studies reported in the EU

Prothioconazole was investigated for foliar application on pulses and oilseeds (peanut) and cereals (wheat) using [U-^{14}C-phenyl]-labelled prothioconazole during the inclusion of the active substance. The metabolism of prothioconazole-desthio was also investigated for foliar application on cereals (wheat) using [3,5-^{14}C-triazole]-labelled prothioconazole-desthio (United Kingdom, 2004, 2007). Additional studies investigating the metabolism of prothioconazole in root and tuber vegetables (sugar beet), pulses and oilseeds (peanut) and cereals (wheat) using [U-^{14}C-phenyl]-labelled prothioconazole are reported in the literature (EFSA, 2007b, 2009; Netherlands, 2007). Finally, three additional metabolism studies were conducted on root and tuber vegetables (sugar beet), pulses and oilseeds (peanut) and cereals (wheat) by foliar application using [3,5-^{14}C-triazole]-labelled prothioconazole (FAO, 2008a, 2008b).

Summary of new plant metabolism studies

No new studies are submitted by the applicant.

Conclusion on metabolism in primary crops

Based on the available metabolism studies, prothioconazole is extensively metabolised and the metabolic pathway is similar in all crops investigated. The main metabolic pathway consisted in the formation of prothioconazole-desthio: the sulphur group of the triazolinethione ring of parent prothioconazole is firstly oxidized to the corresponding sulfonic acid with subsequent elimination of the sulfonic acid moiety. This metabolite subsequently undergoes different pathways either by hydroxylation on the chlorophenyl ring, forming various hydroxyl-desthio isomers (M14, M15, M17), dihydroxy-olefins (M27) and hydroxy-dienyl-cysteine (M24) isomers followed by a glucosidation step or by cleavage of the triazole moiety of prothioconazole-desthio resulting in the formation of 'triazole derivative metabolites' (TDMs), mainly triazole alanine, triazole lactic acid and triazole acetic acid.
These compounds are common metabolites to all triazole fungicides. Finally, a dimerisation of the parent molecule was observed resulting from the combined oxidation of the sulphur atom followed by hydroxylation of the chlorophenyl ring.
Apart from the triazole derivative metabolites (TDMs), all the identified metabolites are structurally closely related to prothioconazole-desthio, being formed by hydroxylation on the phenyl ring. During the peer review, it was assumed as a worst case that the toxicological end points allocated to prothioconazole-desthio should also be applied to these metabolites (EFSA, 2014).
EFSA concludes that a general residue definition which includes prothioconazole-desthio (sum of isomers) only can be proposed for enforcement purposes. For risk assessment, EFSA proposes to take into account the numerous metabolites which are structurally related to prothioconazole-desthio. As they occur together at a significant proportion, they may have a significant contribution to the toxicological burden the consumer is exposed to. Assuming that all these metabolites have a toxicological profile similar to prothioconazole-desthio, the residue for risk assessment is defined as the sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers). The proposed residue definitions apply for all plant commodities, for both foliar and seed treatments. Since all compounds included in the residue definitions are a mixture of enantiomers and since there are no enantiospecific analytical methods, the residue definitions are expressed as "sum of isomers". Validated analytical methods for enforcement of the proposed residue definition are available (EFSA, 2014).

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-4: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Swiss chard	[U-^{14}C-phenyl] prothioconazole	Bare soil application	0.58	28, 146, 269	80, 188, 348	-	United Kingdom, 2004, 2007
Root and tuber vegetables	Turnip	[U-^{14}C-phenyl] prothioconazole	Bare soil application	0.58	28, 146, 269	Root tops: 94, 201, 349	-	
Cereals	Spring wheat	[U-^{14}C-phenyl] prothioconazole	Bare soil application	0.58	28, 146, 269	Green material: 73, 178, 327 Hay: 111, 231, 377 Grain straw: 145, 269, 412		

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported in the EU

The metabolism of prothioconazole in rotational crops – Swiss chard, turnips, spring wheat - has been evaluated (EFSA, 2007b, 2009, 2010a, 2010b, 2012; FAO, 2008a, 2008b; United Kingdom, 2004, 2007). The metabolism of prothioconazole in primary and rotational crops was found to be similar and a specific residue definition for rotational crops is not deemed necessary (EFSA, 2014).

Summary of new plant metabolism studies

Not relevant.

Conclusion on metabolism in rotational crops

The metabolism of prothioconazole in primary and rotational crops was found to be similar and a specific residue definition for rotational crops is not deemed necessary. Considering the application rates of prothioconazole reported in the authorized European GAPs, it can be concluded that prothioconazole residue levels in food and feed rotational commodities are expected to be covered by the residue levels in primary crops and no risk mitigation measures need to be proposed (EFSA, 2014).

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-5: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Pasteurisation (20 minutes, 90°C, pH 4)	Prothioconazole (89.1%), JAU6476-desthio (2.8%)	FAO, 2008a, 2008b

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Prothioconazole (86.2%), JAU6476-desthio (7.4%)	FAO, 2008a, 2008b
Sterilisation (20 minutes, 120°C, pH 6)	Prothioconazole (79.0%), JAU6476-desthio (10.6%)	FAO, 2008a, 2008b

Conclusion on nature of residues in processed commodities

As residues were not expected to exceed the trigger value of 0.1 mg/kg, studies investigating the nature of the residue in processed commodities were not required for the DAR submission (United Kingdom, 2004, 2007). However, standard hydrolysis studies have been assessed by the JMPR (FAO, 2008a, 2008b). It was concluded that prothioconazole is stable under processing conditions representative of pasteurisation and boiling but slightly degraded (≤ 11%) to prothioconazole-desthio under sterilisation (EFSA, 2014).

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2-6: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Root and tuber vegetables (Sugar beet) Cereals (Wheat) Pulses and oilseeds (Peanut)
Rotational crops covered	Leafy vegetables (Swiss chard) Cereals (Spring wheat) Root and tuber vegetables (Turnip)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not applicable
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Prothioconazole-desthio (sum of isomers) (Regulation (EU) 2019/552, EFSA, 2014)
Plant residue definition for risk assessment	Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety) expressed as prothioconazole-desthio (EFSA, 2007, EFSA, 2014). 1) Triazole parent compound and any other relevant metabolite exclusively linked to the parent compound; 2) Sum of TA (triazole alanine) and TLA (triazole lactic acid), since these compounds share the same toxicity; 3) TAA (triazole acetic acid); 4) 1,2,4-T (1,2,4-triazole) (EFSA, 2018)
Conversion factor from enforcement to RA	2 (cereal grain, pulses and oilseeds, leafy vegetables and root and tuber vegetables) 3 (cereal straw)

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

Table 7.2-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	[U-^{14}C-phenyl] prothioconazole	1	10 (250 mg a.s./kg feed)	3	Milk	twice daily	United Kingdom, 2004, 2007; FAO, 2008a, 2008b
						Urine and faeces	daily and at sacrifice	
						Tissues	at sacrifice	
		[U-^{14}C-phenyl] prothioconazole-desthio	1	10 (195 mg a.s./kg feed)	3	Milk	twice daily	
						Urine and faeces	daily and at sacrifice	
						Tissues	at sacrifice	
		[3, 5-^{14}C-triazole] prothioconazole	1	10	3	Milk	twice daily	FAO, 2008a, 2008b
						Urine and faeces	daily and at sacrifice	
						Tissues	at sacrifice	
Laying poultry	Hens	[U-^{14}C-phenyl] prothioconazole	6	10	3	Eggs	Once dayly	United Kingdom, 2004, 2007; FAO, 2008a, 2008b
						Excreta	At regular intervals	
						Tissues	At sacrifice (5h after last administration)	
		[3, 5-^{14}C-triazole] prothioconazole	6	10	3	Eggs	Once dayly	FAO, 2008a, 2008b
						Excreta	At regular intervals	
						Tissues	At sacrifice (5h after last administration)	

Summary of animal metabolism studies reported in the EU

The nature of prothioconazole residues in commodities of animal origin was investigated in the framework of Directive 91/414/EEC (United Kingdom, 2004, 2007). Reported metabolism studies include two studies in lactating goats using respectively [U-^{14}C-phenyl]-labelled prothioconazole and prothioconazole-desthio and one study in laying hens using [U-^{14}C-phenyl]-labelled prothioconazole. Besides, two additional studies were assessed by the JMPR (FAO, 2008a, 2008b) on lactating goats and laying hens, using both [3,5-^{14}C-triazole]-labelled prothioconazole (EFSA, 2014).

Lactating goats (EFSA, 2014)
In each study, lactating goats were dosed with 10 mg/kg bw per d of prothioconazole or prothioconazole-desthio. The metabolism study conducted with prothioconazole was reported for information purposes only since the animals are mainly exposed to the prothioconazole-desthio residues. For prothioconazole-desthio, the application rate was overdosed, corresponding to approximately 48 times the exposure of meat ruminants.
In the studies performed with both phenyl and triazole labellings of prothioconazole, the highest residue levels were found in kidney (6.8 - 4.5 mg eq/kg) and liver (6.1 - 6.2 mg eq/kg), respectively.
The total radioactive residues accounted respectively for 0.037 - 0.15 mg eq/kg in milk, 0.088 - 0.117 mg eq/kg in muscle and 0.169 - 0.174 mg eq/kg in fat. The extractabilities of the radioactive residues in all matrices ranged from 77 % (fat) to 98 % of the TRR (kidney). Identified radioactivity accounted for 57 % to 78 % of the TRR. Prothioconazole was rapidly adsorbed and extensively metabolised in all matrices but remained a significant compound of the residues in liver (13 – 17 % TRR), muscle, kidney and fat (7 - 20 % TRR) and to a minor extent in milk (0.9 % - 3 % TRR). Prothioconazole-desthio was detected at low levels in all matrices (< 5 % TRR), except in fat (19 % TRR, 0.032 mg eq/kg). The only identified triazole related metabolite was the thiocyanate metabolite: 41 % TRR (0.061 mg eq/kg) in milk, 30 % TRR (0.035 mg eq/kg) in muscle, 12 % TRR (0.022 mg eq/kg) in fat, 9 % TRR (0.41 mg eq/kg) in kidney and 2 % TRR (0.13 mg eq/kg) in liver. At the maximum dietary burden of meat ruminants, this metabolite is expected to occur at a trace level in all matrices (up to 0.004 mg eq/kg in kidney). There is therefore no need to further address its toxicological properties.
In the study performed with [U-14C-phenyl]-labelled prothioconazole-desthio, the highest residue levels were found in kidney and liver (up to 19 mg eq/kg). Total radioactive residues in milk, muscle and fat accounted for 0.286 mg eq/kg, 0.266 mg eq/kg and 0.231 mg eq/kg, respectively. The extractabilities of the residues in all matrices ranged from 82 % (liver) to 97 % of TRR (kidney). The rate of identification amounted to 70 % to 89 % of the TRR. Prothioconazole-desthio was the predominant compound of the total residues in liver (31.2 % TRR - 5.7 mg eq/kg) and in kidney both under its free and glucuronide conjugated forms (32 % TRR – 6 mg eq/kg) whilst it was extensively metabolised as glucuronide conjugates of the hydroxylated related metabolites in milk, muscle and fat. Metabolite M3231 both under its free and glucuronide conjugated form was the predominant compound of the total residues in muscle (32 % TRR – 0.085 mg eq/kg), fat (27 % TRR – 0.063 mg eq/kg) and kidney (23 % TRR - 4.299 mg eq/kg). In milk, only prothioconazole-desthio under its glucuronide conjugated form was detected at a rather low level (6 % TRR – 0.017 mg eq/kg) whilst the sulphate conjugates of hydroxylated derivative prothioconazole-desthio metabolites (M14/M15/M16/M17/M2832/M3433/M3534) constituted the major part of the total residue in milk (44 % TRR, 0.126 mg eq/kg). All other compounds accounted for less than 10 % TRR.
Following prothioconazole administration to rats, metabolite 1,2,4-triazole was recovered in urine at minor amounts (2.3 % AR), whilst it was not recovered in goats. Therefore, meanwhile a harmonized approach on how to consider TDMs in the risk assessment, the general metabolic pathways in rodents and ruminants can be considered as comparable, mainly involving various types of hydroxylation affecting the chlorophenyl ring and leading to the formation of metabolites both under their free and glucuronide or sulphate conjugated forms. The metabolic pathway of prothioconazole-desthio depicted in ruminants can therefore be extrapolated to pigs.

Laying hens (EFSA, 2014)
Laying hens were dosed with 10 mg/kg bw per d of phenyl and triazole labelled prothioconazole, respectively. The major part of the total administered dose (AR) was recovered in excreta (66 % and 78 % AR for the triazole and phenyl labellings, respectively) and only trace amounts of radioactivity were detected both in eggs (0.01 % AR) and tissues (about 0.9 % AR).
The total radioactive residues accounted for 4.0 – 3.5 mg eq/kg in liver, 0.036 – 0.05 mg eq/kg in eggs, 0.45 – 0.29 mg eq/kg in subcutaneous fat and 0.089 – 0.12 mg eq/kg in muscle, respectively for the phenyl and triazole labellings. The extractability of the total radioactive residues ranged from 77 % TRR in eggs to 98 % TRR in fat.

Prothioconazole was the major compound of the total residues in liver (25 % - 31 % TRR, 1.0 - 1.1 mg/kg) and in fat (30 % - 16 % TRR, 0.14 - 0.046 mg/kg) for the phenyl and triazole labels, respectively. Prothioconazole-desthio (29 % - 27 % TRR, 0.13 - 0.08 mg eq/kg) and M0135 (20 % - 29 % TRR, 0.083 - 0.088 mg eq/kg) in fat as well as M0636 in liver (12 % - 15 % TRR, 0.48 - 0.53 mg eq/kg) were the only metabolites exceeding 10 % of the TRR in these commodities. In muscle, the major compounds were M4537 (28 % TRR, 0.035 mg eq/kg) and 1,2,4-triazole (19 % TRR, 0.023 mg eq/kg) specific to the triazole labelling, and M06 (16 % - 10 % TRR, 0.014 - 0.012 mg eq/kg) and parent prothioconazole (11 % - 2.5 % TRR, 0.01 - 0.003 mg eq/kg) for phenyl and triazole labelling, respectively. Prothioconazole-desthio accounted for only 7 % - 2.1 % TRR (0.006 - 0.003 mg eq/kg). In eggs, the major compounds of the total residues were M06 (24 % - 16 % TRR, 0.012 - 0.014 mg eq/kg) and prothioconazole-desthio (20 % - 6.2 % TRR, 0.007 - 0.003 mg eq/kg) for phenyl and triazole label, respectively. For the triazole labelling moiety, the metabolites M45 (15.6% TRR, 0.008 mg eq/kg) and 1,2,4-triazole (11 % TRR, 0.006 mg eq/kg) were also identified. Prothioconazole accounted for only 3.6 % - 3.4 % TRR (0.001 - 0.002 mg eq/kg), for phenyl and triazole label, respectively. All other metabolites identified were either glucuronic acid or sulphate conjugates of the hydroxylated prothioconazole and accounted for less than 10 % TRR.

Summary of new animal metabolism studies

Not relevant.

Conclusion on metabolism in livestock

It is noted that in poultry no study was performed with prothioconazole-desthio and that the fate of the triazole moiety in livestock was only investigated for prothioconazole. However, the available studies indicate similar metabolic patterns for the different compounds and moieties investigated. Additional studies addressing these requirements are therefore not expected to provide different results. It is also noted that no livestock metabolism study was performed with administration of all the metabolites included in the residue definition set for risk assessment in plants. Nevertheless, EFSA assumes that the administration of prothioconazole-desthio only in the livestock metabolism studies is acceptable since no different metabolic route of degradation would be expected if all the metabolites containing the moiety of the residue definition for risk assessment in plants were considered. Therefore, no additional metabolism data are deemed necessary (EFSA, 2014).

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2-8: Summary on the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	1-2 days in milk
	Eggs: not reached within test period of 53 hours
Animal residue definition for monitoring	Prothioconazole-desthio (sum of isomers) for all livestock matrices (Regulation (EU) 2019/552; EFSA, 2014)
Animal residue definition for risk assessment	Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers) (EFSA, 2007, EFSA, 2014). 1) Triazole parent compound and any other relevant metabolite exclusively linked to the parent compound;

	2) Sum of TA (triazole alanine) and TLA (triazole lactic acid), since these compounds share the same toxicity; 3) TAA (triazole acetic acid); 4) 1,2,4-T (1,2,4-triazole) (EFSA, 2018)
Conversion factor	2 for liver 9 for kidney
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Yes Log Pow for JAU 6476-desthio = 3.04

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 Summary of European data and new data supporting the intended uses

No new data are submitted in the framework of this application. All of the necessary studies to support the use of Protiokonazol 300 EC on cereals and oilseed rape have already been reviewed in the context of the DAR for prothioconazole and no further information is required.

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of Protiokonazol 300 EC and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Wheat grain (incl. triticale)	DAR, 2004 EFSA, 2007	N-EU	GAP on which EU a.s. assessment is based: 1-3 x 0.2 kg as/ha, BBCH 26-69, PHI 35d, outdoor E/RA: 10x <0.01	N/A				
	New trials	-	-					
	Overall supporting data for cGAP	N-EU	E/RA: 10x <0.01	E/RA: 0.01	E/RA: 0.01	-	0.1	Yes
Wheat straw	DAR, 2004 EFSA, 2007	N-EU	GAP on which EU a.s. assessment is based: 1-3 x 0.2 kg as/ha, BBCH 26-69, PHI 35d, outdoor E/RA: 0.08, 0.09, 0.11, 0.14, 0.15, 0.19, 0.20, 0.27, 0.31, 0.72	N/A				
	New trials	-	-					
	Overall supporting data for cGAP	N-EU	E/RA: 0.08, 0.09, 0.11, 0.14, 0.15, 0.19, 0.20, 0.27, 0.31, 0.72	E/RA: 0.17	E/RA: 0.72	-	NA	NA

Barley grain	DAR, 2004 EFSA, 2007	N-EU	GAP on which EU a.s. assessment is based: 1-3 x 0.2 kg as/ha, BBCH 26-69, PHI 35d, outdoor E/RA: 9x <0.01	N/A				
	New trials	-	-					
	Overall supporting data for cGAP	N-EU	E/RA: 9x <0.01	E/RA: 0.01	E/RA: 0.01	-	0.2	Yes
Barley straw	DAR, 2004 EFSA, 2007	N-EU	GAP on which EU a.s. assessment is based: 1-3 x 0.2 kg as/ha, BBCH 26-69, PHI 35d, outdoor E/RA: 0.05, 0.08, 2x 0.10, 2x 0.13, 2x 0.14, 0.30	N/A				
	New trials	-	-					
	Overall supporting data for cGAP	N-EU	E/RA: 0.05, 0.08, 2x 0.10, 2x 0.13, 2x 0.14, 0.30	E/RA: 0.13	E/RA: 0.30	-	NA	NA
Oilseed Rape (seed)	DAR, 2004 EFSA, 2007	N-EU	GAP on which EU a.s. assessment is based: 2 x 0.175 kg as/ha, BBCH 65-78, PHI 56d E/RA: 5x <0.01; 0.01; 2x 0.02	N/A				
	New trials	-	-					
	Overall supporting data for cGAP	N-EU	E/RA: 5x <0.01; 0.01; 2x 0.02	E/RA: 0.01	E/RA: 0.02	-	0.15	Yes

* Source of EU MRL: Regulation (EU) 2019/552

Table 7.2-8.1 Residue trials in N-EU used for support of wheat (incl. triticale) and rye registration (Draft Assessment Report for prothioconazole (DAR, United Kingdom, 2004))

No.	Crop	Country, year	Application rate (kg a.s./ha)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	Reference
1	Wheat	Germany, 1999	3x 0.20	69	Grain Straw	<0.01 0.20	RA-2003/99 R 1999 0266/2 0266-99 **DAR UK, 2004**
2	Wheat	Germany, 1999	3x 0.20	69	Grain Straw	<0.01 0.31	RA-2003/99 R 1999 0023/6 0023-99 **DAR UK, 2004**
3	Wheat	Germany, 1999	3x 0.20	69	Grain Straw	<0.01 0.72	RA-2003/99 R 1999 0025/2 0025-99 **DAR UK, 2004**
4	Wheat	N-France, 1998	3x 0.20	69	Grain Straw	<0.01 0.11	RA-2003/99 R 1999 0026/0 0026-99 **DAR UK, 2004**
5	Wheat	Great Britain, 1999	3x 0.20	69	Grain Straw	<0.01 0.19	RA-2003/99 R 1999 0027/9 0027-99 **DAR UK, 2004**
6	Wheat	Germany, 2000	3x 0.20	69	Grain Straw	<0.01 0.14	RA-2104/00 R 2000 0454/0 0454-00 **DAR UK, 2004**
7	Wheat	Germany, 2000	3x 0.20	69	Grain Straw	<0.01 0.09	RA-2104/00 R 2000 0457/5 0457-00 **DAR UK, 2004**
8	Wheat	N-France, 2000	3x 0.20	69	Grain Straw	<0.01 0.08	RA-2104/00 R 2000 0474/5 0474-00 **DAR UK, 2004**
9	Wheat	Great Britain, 2000	3x 0.20	69	Grain Straw	<0.01 0.27	RA-2104/00 R 2000 0475/3 0475-00 **DAR UK, 2004**
10	Wheat	Germany, 2000	3x 0.20	69	Grain Straw	<0.01 0.15	RA-2104/00 R 2000 0476/1 0476-00 **DAR UK, 2004**

Table 7.2-8.2 Residue trials in N-EU used for support of barley registration (Draft Assessment Report for prothioconazole (DAR, United Kingdom, 2004))

11	Barley	Germany, 1998	2x 0.20	61	Grain Straw	<0.01 0.14	RA-2140/98 R 1998 1580/2 1580-98 **DAR UK, 2004**
12	Barley	Germany, 1998	2x 0.20	61	Grain Straw	<0.01 0.13	RA-2140/98 R 1998 1247/1 1247-98 **DAR UK, 2004**
13	Barley	N-France, 1998	2x 0.20	61	Grain Straw	<0.01 0.13	RA-2140/98 R 1998 1581/0 1581-98 **DAR UK, 2004**
14	Barley	Great Britain, 1998	2x 0.20	61	Grain Straw	<0.01 0.10	RA-2140/98 R 1998 1582/9 1582-98 **DAR UK, 2004**

15	Barley	Sweden, 2000	2x 0.20	59-61	Grain Straw	<0.01 0.14	RA-2101/00 R 2000 0452/4 0452-00 **DAR UK, 2004**
16	Barley	Germany, 2000	2x 0.20	61	Grain Straw	<0.01 0.05	RA-2101/00 R 2000 0462/1 0462-00 **DAR UK, 2004**
17	Barley	N-France, 2000	2x 0.20	61	Grain Straw	<0.01 0.10	RA-2101/00 R 2000 0462/1 0462-00 **DAR UK, 2004**
18	Barley	Great Britain, 2000	2x 0.20	63	Grain Straw	<0.01 0.30	RA-2101/00 R 2000 0464/8 0464-00 **DAR UK, 2004**
19	Barley	Germany, 2000	2x 0.20	61	Grain Straw	<0.01 0.08	RA-2101/00 R 2000 0465/6 0465-00 **DAR UK, 2004**

Table 7.2-8.3 Residue trials in N-EU used for support of oilseed rape registration (Draft Assessment Report for prothioconazole (DAR, United Kingdom, 2004))

No.	Crop	Country, year	Application rate (kg a.s./ha)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	Reference
1	Rape seed	Germany, 2000	2x 0.175	69-71	seed	<0.01	RA-2088/00 R 2000 0079/0 0079-00 **DAR UK, 2004**
2	Rape seed	Sweden, 2000	2x 0.175	65-67	seed	<0.01	RA-2088/00 R 2000 0419/2 0419-00 **DAR UK, 2004**
3	Rape seed	N-France, 2000	2x 0.175	72	seed	0.02	RA-2088/00 R 2000 0420/6 0420-00 **DAR UK, 2004**
4	Rape seed	Great Britain, 2000	0.190 0.175	77	seed	0.01	RA--2088/00 R 2000 0421/4 0421- **DAR UK, 2004**
5	Rape seed	Germany, 2001	2x 0.175	69-70	seed	<0.01	RA-2178/01 R 2001 0515/0 0515-01 **DAR UK, 2004**
6	Rape seed	Great Britain, 2000	0.175 0.163	78	seed	<0.01	RA-2178/01 R 2001 0516/9 0516-01 **DAR UK, 2004**
7	Rape seed	N-France, 2001	2x 0.175	73	seed	<0.01	RA-2178/00 R 2001 0517/7 0517-01 **DAR UK, 2004**
8	Rape seed	N-France, 2001	0.190 0.175	73	seed	0.02	RA-2178/00 R 2001 0518/5 0518-01 **DAR UK, 2004**

7.2.3.2 Conclusion on the magnitude of residues in plants

Wheat
A total of 10 trials on wheat from N-EU zone are available. All trials were performed according to the

critical EU GAP from DAR (United Kingdom, 2005), which is more critical than the proposed GAP.
The residue data are valid with regard to storage stability and are sufficient to support the proposed use.
The residues arising from the proposed uses will not exceed the MRL of 0.1 mg/kg established for wheat (including triticale).

Barley
A total of 9 trials on barley from N-EU zone are available. All trials were performed according to the critical EU GAP from DAR (United Kingdom, 2005), which is more critical than the proposed GAP.
The residue data are valid with regard to storage stability and are sufficient to support the proposed use.
The residues arising from the proposed uses will not exceed the MRL of 0.2 mg/kg established for barley.

Rye
A total of 10 trials on wheat from N-EU zone are available for wheat. All trials were performed according to the critical EU GAP from DAR (United Kingdom, 2005), which is more critical than the proposed GAP.
The residue data are valid with regard to storage stability and are sufficient to support the proposed use.
The residues arising from the proposed uses will not exceed the MRL of 0.05 mg/kg established for rye.

Oilseed rape
A total of 8 trials on wheat from N-EU zone are available. All trials were performed according to the critical EU GAP from DAR (United Kingdom, 2005).
The residue data are valid with regard to storage stability and are sufficient to support the proposed use.
The residues arising from the proposed uses will not exceed the MRL of 0.15 mg/kg established for rapeseeds.

The uses are considered acceptable.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

Active substance prothioconazole is authorised in EU for use on crops that might be fed to livestock, so dietary burden calculation was performed in EFSA reasoned opinion on the review of the existing maximum residue levels for prothioconazole according to Article 12 of Regulation (EC) No 396/2005 (EFSA Journal 2014;12(5):3689) and Evaluation of confirmatory data following the Article 12 MRL review and modification of the existing maximum residue levels for prothioconazole in celeriacs and rapeseeds (EFSA Journal 2020;18(2):5999). In EFSA Journal 2020;18(2):5999 was stated: *due to the fact that existing EU MRLs for livestock and for various feed commodities are set on the basis of CXLs, instead of proposals made by the MRL review, the livestock dietary burden was calculated using Animal Model (OECD methodology), considering the actual existing EU MRLs for feed commodities. The input values for rapeseeds and carrots, swedes, turnips were as derived from the current assessment; for remaining feed commodities the input values were corresponding to the existing EU MRLs and were as reported in the MRL review, or in JMPR reports (in particular for cereals, cotton, maize, peanuts and soya beans, since for these crops the existing EU MRLs are set on the basis of CXLs) (FAO, 2009a,b, 2014, 2018) and in previous EFSA reasoned opinions (for sunflower seeds, EFSA, 2015b). Where residue data according to the risk assessment residue definition were not available, default conversion factors for risk assessment as derived by the MRL review, were applied.*

Dietary burden calculation for purpose of maintain authorisation of Protiokonazol 300 EC was performed by Excel spreadsheet Animal model 2017 regarding input values, for consistency, the same approach was used as in EFSA Journal 2020;18(2):5999. Input values (STMR and HR) used for dietary calculation are provided below in Table 7.2-8. Results of dietary burden calculation for Protiokonazol 300 EC are included in Table 7.2-9.

Table 7.2-10: Input values for the dietary burden calculation (considering the uses supported in this submission and all known EU uses according to the Article 12 review (EFSA, 2014 and EFSA, 2020))

Feed Commodity	Median dietary burden		Maximum dietary burden	
	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-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers)				
Rape seed meal	0.16	STMR x PF (2)[a] (EFSA, 2020)	0.16	STMR x PF (2)[a] (EFSA, 2020)
Sunflower seed meal	0.04	STMR x CF (2) x PF (2)[a] (EFSA, 2020)	0.04	STMR x CF (2) x PF (2)[a] (EFSA, 2020)
Head cabbage	0.02	STMR x CF (EFSA, 2020)	0.12	HR x CF (EFSA, 2020)
Maize silage	0.01	STMR (EFSA, 2020)	0.01	HR (EFSA, 2020)
Maize grain	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)
Maize, milled by-products[b] Maize, hominy meal[b] Maize gluten feed/ gluten meal[b] Distiller`s grain[b]	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)
Distiller's grain	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2020)
Barley grain	0.07	STMR (FAO, 2009) x CF (2) (EFSA, 2020)	0.07	STMR (FAO, 2009) x CF (2) (EFSA, 2020)
Brewer's grain	0.23	STMR barley grain x PF (3.3)[a] (EFSA, 2020)	0.23	STMR barley grain x PF (3.3)[a] (EFSA, 2020)
Oat grain	0.02	STMR (FAO, 2009) x CF (2) (EFSA, 2020)	0.02	STMR (FAO, 2009) x CF (2) (EFSA, 2020)
Wheat grain (including triticale)	0.02	STMR x CF (2)	0.02	STMR x CF (2)
Wheat gluten meal[b]	0.04	STMR wheat grain x PF (1.8)[a]	0.04	STMR wheat grain x PF (1.8)[a]
Wheat milled by-products[b]	0.14	STMR wheat grain x PF (7)[a]	0.14	STMR wheat grain x PF (7)[a]
Rye grain	0.02	STMR (FAO, 2009) x CF (2) (EFSA, 2020)	0.02	STMR (FAO, 2009) x CF (2) (EFSA, 2020)
Barley straw	1.96	STMR (FAO, 2009) x CF (3) (EFSA, 2020)	7.50	HR x CF (3) (EFSA, 2020)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Oat straw	1.26	STMR x CF (3) (EFSA, 2020)	7.50	HR x CF (3) (EFSA, 2020)
Wheat straw (including triticale)	1.22	STMR x CF (2.3)	2.30	HR x CF (2.3)
Rye straw	2.25	STMR x CF (3) (EFSA, 2020)	5.52	HR x CF (2.3) (EFSA, 2020)
Cotton seed	0.10	STMR (FAO, 2018) x CF (2) (EFSA, 2020)	0.10	STMR (FAO, 2018) x CF (2) (EFSA, 2020)
Cotton seed meal	0.13	STMR (FAO, 2018) x CF (2) x PF (1.3)[a] (EFSA, 2020)	0.13	STMR (FAO, 2018) x CF (2) x PF (1.3)[a] (EFSA, 2020)
Beans (dry)	0.02	STMR x CF (2) (EFSA, 2020)	0.02	STMR x CF (2) (EFSA, 2020)
Peas, lupins (dry)	0.10	STMR (FAO, 2009) x CF (2) (EFSA, 2020)	0.10	STMR (FAO, 2009) x CF (2) (EFSA, 2020)
Lupin seed meal	0.11	STMR (FAO, 2009) x CF (2) x PF (1.1)[a] (EFSA, 2020)	0.11	STMR (FAO, 2009) x CF (2) x PF (1.1)[a] (EFSA, 2020)
Potatoes	0.01	STMR (EFSA, 2020)	0.01	HR (EFSA, 2020)
Potato process waste[b] Potato dried pulp[b]	0.01	STMR potato x PF (1)[c] (EFSA, 2020)	0.01	HR potato x PF (1)[c] (EFSA, 2020)
Turnips, swedes, carrot culls	0.08	STMR (EFSA, 2020)	0.10	HR (EFSA, 2020)
Peanut meal	0.04	STMR (FAO, 2009) x CF (2) x PF (2) (EFSA, 2020)	0.04	STMR (FAO, 2009) x CF (2) x PF (2) (EFSA, 2020)
Linseed meal	0.12	STMR x CF (2) x PF (2)[a] (EFSA, 2020)	0.12	STMR x CF (2) x PF (2)[a] (EFSA, 2020)
Soybean seed	0.10	STMR (FAO, 2014) x CF (2) (EFSA, 2020)	0.10	STMR (FAO, 2014) x CF (2) (EFSA, 2020)
Soybean seed meal	0.13	STMR (FAO, 2014) x CF (2) x PF (1.3)[a] (EFSA, 2020)	0.13	STMR (FAO, 2014) x CF (2) x PF (1.3)[a] (EFSA, 2020)
Soybean hulls[b]	1.30	STMR (FAO, 2014) x CF (2) x PF (13)[a] (EFSA, 2020)	1.30	STMR (FAO, 2014) x CF (2) x PF (13)[a] (EFSA, 2020)

[a] For rape seed meal/sunflower seed meal, brewer's grain, wheat gluten meal, wheat milled by-products, cotton seed meal, lupin seed meal, soybean meal, lupin seed meal, and soybean hulls in the absence of processing factors supported by data, default processing factors of 2, 3.3, 1.8, 7, 1.3, 1.1, 1.3 and 13 were, respectively, included in the calculation to consider the potential concentration of residues in these commodities.
[b] New commodities (OECD methodology), not considered in MRL review.
[c] Default processing factors were not applied because prothioconazole and its metabolites were below LOQ both in maize and potatoes, indicating no-residue situation. Thus, concentration of residues in these commodities is therefore not expected.

Table 7.2-11: Results of the dietary burden calculation

Animal species	Median dietary burden	Maximum dietary burden	Median dietary burden	Maximum dietary burden	Most critical diet	Highest contributing commodity	Trigger 0.004 mg/kg bw/d exceeded (Y/N)
	mg/kg bw/d		mg/kg DM				
Cattle (all diets)	0.035	0.108	1.16	3.10	Dairy cattle	Barley straw	Y
Cattle (dairy only)	0.035	0.108	0.91	2.82	Dairy cattle	Barley straw	Y
Sheep (all diets)	0.075	0.236	1.77	5.55	Lamb	Barley straw	Y
Sheep (ewe only)	0.059	0.185	1.77	5.55	Ram/Ewe	Barley straw	Y
Swine (all diets)	0.016	0.019	0.54	0.69	Swine (finishing)	Soybean hulls	Y
Poultry (all diets)	0.028	0.049	0.41	0.72	Poultry layer	Barley straw	Y
Poultry (layer only)	0.028	0.049	0.41	0.72	Poultry layer	Barley straw	Y

The calculated dietary burdens were found to be above the trigger value of 0.004 mg/kg bw (0.1 mg/kg dry matter (DM) for all types of livestock. Further investigation on the nature of residues is therefore required.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

No new data were submitted in the framework of this application.

During the peer review under Directive 91/414/EEC, the magnitude of prothioconazole residues in ruminants was investigated in a feeding study with lactating cows (EFSA, 2007b; FAO, 2008a, 2008b; United Kingdom, 2004, 2007). Three groups of lactating cows, each consisting of three animals, were dosed for 28 consecutive days with prothioconazole-desthio at levels of 4, 25, and 100 mg/kg in the diet (equivalent to 0.145, 0.909 and 3.636 mg/kg bw per d, respectively). The samples were analysed for prothioconazole-desthio, M14 and M15. In milk, a plateau level was reached after 1 or 2 days of exposure, according to the dose level group. Since neither the metabolites (free and conjugated) containing the common moiety and included in the residue definition for risk assessment nor the glucuronide conjugates of prothioconazole-desthio were analysed, EFSA reported the residue levels for enforcement only (prothioconazole-desthio) and considered the conversion factors for enforcement to risk assessment of 2 and 9 respectively for liver and kidney based on the goat metabolism study with administration of prothioconazole-desthio. No tentative CF was derived for milk, muscle and fat since the residue levels in these matrices are expected to be negligible (<0.01 mg/kg) at the calculated dietary burden. However, conversion factors reported above should in principle be covered by a new feeding study to estimate prothioconazole metabolites containing the common moiety in accordance with the residue definition for risk assessment.
Furthermore, in the framework of the reported feeding study, the storage stability of prothioconazole-desthio, M14 and M15 was demonstrated in all matrices for up to 1 month when stored deep frozen and was shown to cover the storage time interval of the residue samples of the feeding study. Degradation of prothioconazole-desthio residues during storage of the feeding study residue samples is therefore not expected.
Consequently, the available data allow deriving tentative MRLs in ruminants and pigs. These MRLs were derived in compliance with the latest recommendations on this matter (FAO, 2009b). Tentative MRLs in all commodities are established at the LOQ, except in liver and kidney of ruminants, where MRLs of 0.05 and 0.02 mg/kg respectively are proposed. EFSA notes that all the MRLs in ruminant and pig matrices can only be derived on a tentative basis, leading to a provisional dietary burden calculation and the miss-

ing livestock feeding study (EFSA, 2014).

Conclusion on metabolism in livestock

Although the maximum dietary burden for poultry exceeds the threshold of 0.1 mg/kg DM, no appropriate feeding study is available and is required, since based on the metabolism study, no residues above the LOQ are expected in poultry matrices at the calculated dietary burden. Therefore, tentative MRLs can be established at the LOQ in all poultry commodities and no default conversion factors for risk assessment need to be derived. These MRLs can only be tentatively derived due to the tentative dietary burden calculations and the required validated analytical method for enforcement in eggs. (EFSA, 2014).

Table 7.2-12: Overview of the values derived from livestock feeding studies

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)[b]	Highest residue (mg/kg)[c]	Calculated MRL (mg/kg)	CF for RA[d]
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)[a]	No	Result for enforce-ment		Result for RA					
					Mean (mg/kg)	Max. (mg/kg)	Mean (mg/kg)	Max. (mg/kg)				
EU data (EFSA, 2014)												
Enforcement residue definition: prothioconazole-desthio (sum of isomers). Risk assessment residue definition: sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers).												
Pig muscle	0.017	0.031	0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	1.0
			0.91	3	<0.01	<0.01	n.a.	n.a.				
			3.64	3	<0.01	<0.01	n.a.	n.a.				
Pig fat			0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	1.0
			0.91	3	<0.01	0.01	n.a.	n.a.				
			3.64	3	0.02	0.04	n.a.	n.a.				
Pig liver			0.15	3	0.02	0.03	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	2.0
			0.91	3	0.14	0.18	n.a.	n.a.				
			3.64	3	0.68	1.20	n.a.	n.a.				
Pig kidney			0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	9.0
			0.91	3	0.03	0.03	n.a.	n.a.				
			3.64	3	0.13	0.24	n.a.	n.a.				
Milk	0.028	0.086	0.15	42	<0.005[f]	N/A	n.a.	n.a.	<0.005	<0.005	0.005* (tentative)	1.0
			0.91	42	<0.005[f]	N/A	n.a.	n.a.				

			3.64	39	0.005[f]	N/A	n.a.	n.a.				
Ruminant meat	0.069	0.208	0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	1.0
			0.91	3	<0.01	<0.01	n.a.	n.a.				
			3.64	3	<0.01	<0.01	n.a.	n.a.				
Ruminant fat			0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	<0.01	0.01* (tentative)	1.0
			0.91	3	<0.01	0.01	n.a.	n.a.				
			3.64	3	0.02	0.04	n.a.	n.a.				
Ruminant liver			0.15	3	0.02	0.03	n.a.	n.a.	0.01	0.042	0.05 (tentative)	2.0
			0.91	3	0.14	0.18	n.a.	n.a.				
			3.64	3	0.68	1.20	n.a.	n.a.				
Ruminant kidney			0.15	3	<0.01	<0.01	n.a.	n.a.	<0.01	0.012	0.02 (tentative)	9.0
			0.91	3	0.03	0.03	n.a.	n.a.				
			3.64	3	0.13	0.24	n.a.	n.a.				

N/A: Not applicable.
n.a.: Not analysed.
(a): Based on a 560 kg animal consuming approximately 20 kg feed DM/day.
(b): In the feeding study, residues were not determined according to the residue definition for risk assessment. Indeed, only prothioconazole-desthio, M14 and M15 were analysed.
(c): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009b).
(d): Highest residue value (tissues) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009b).
(e): The tentative conversion factors for enforcement to risk assessment in liver and kidney were derived on the basis of the available metabolism study on ruminants. For muscle, fat and milk, no CF was derived as residue levels are expected at the maximum meat ruminant dietary burden in these matrices are negligible (<0.01 mg/kg).
(f): Mean residue level from day 1 or 4 until day 29 (3 cows, 13 or 14 sampling days).
(*): Indicates that the MRL is set at the limit of analytical quantification.

7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.2.5.1 Available data for all crops under consideration

No new data submitted in the framework of this application.

The effect of processing on the nature of prothioconazole residues was not investigated in the framework of the peer review. Nevertheless, studies were assessed by the JMPR (FAO, 2008a, 2008b), simulating representative hydrolytic conditions for pasteurisation (20 minutes at 90°C, pH 4), boiling/brewing/baking (60 minutes at 100°C, pH 5) and sterilisation (20 minutes at 120°C, pH 6). From these studies, it was concluded that parent compound prothioconazole is stable under processing by pasteurisation and baking/brewing/boiling. However, under sterilisation, prothioconazole slightly degrades (≤ 11 %) to prothioconazole-desthio (EFSA, 2014).
Residues of prothioconazole exceeding 0.1 mg/kg are not expected in the treated crops.

7.2.5.2 Conclusion on processing studies

Please refer to point 7.2.5.1.

7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

No new data submitted in the framework of this application.

Considering available data dealing with nature of residues, no study dealing with magnitude of residues in succeeding crops is needed.

Conclusion on rotational crops studies

Based on the confined rotational crop study, considering that the application rate of prothioconazole within the EU ranges between 0.009 - 0.600 kg a.s./ha and due to the fact that prothioconazole was applied to bare soil in the metabolism study (interception of prothioconazole by the plants is expected in practice), it can be concluded that prothioconazole residue levels in food and feed rotational commodities are expected to be covered by the residue levels in primary crops. Therefore, no risk mitigation measures (plant back restrictions) need to be proposed (EFSA, 2014).

7.2.7 Other / special studies (KCA6.10, 6.10.1)

If residues in honey are expected considering the proposed uses and the properties of the active substance, then further data on crop or field/tunnel trials are required.
One of the proposed uses (oilseed rape) is classified as a melliferous crop according to SANTE/11956/2016 rev. 9 (14 September 2018). Also, prothioconazole is an active substance with systemic

properties and is applied during the flowering stage. Regarding above is highly possible that residues in honey can occur.

Four new studies (2 NEU and 2 SEU trials) have been performed on phacelia crop to investigate the magnitude of prothioconazole residues in honey. These studies consider a "worst case" situation (the most critical scenario was used on a crop (phacelia) representing a worst case in terms of residues in honey). The results of these studies are summarized in the table below. The details are presented in Appendix 2.

Table 7.2-13: Summary of new data on honey supporting the intended uses of Protiokonazol 300 EC and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Phacelia (worst case) - residues in honey	New trials (22SGS46-01, 22SGS46-02, 1147.F.SAG22/r, 1198.F.SAG22/r	N-EU S-EU	Trial GAP: 1 x 0.390 kg as/ha, BBCH 65, outdoor E/RA: 4x <LOD (0.002)	N/A				
	Overall supporting data for honey	N-EU S-EU	E/RA: 4x <LOD (0.002)	E/RA: 0.002	E/RA: 0.002	-	0.05	Yes

*Source of EU MRL: Reg. (EU) 2019/552

The intended GAP for oilseed rape is 2x 180 g as/ha, BBCH 61-72, outdoor.
In four honey trials Protiokonazol 300 EC was applied at a rate 390 g as/ha at a flowering phase (BBCH 65), representing worst case scenario. In these trials all residues of prothioconazole in honey were below LOD (<0.002 mg/kg).
All samples were analysed within 30 days from sampling (23 days), therefore there is no need to perform studies on the stability of residues during storage.
The residues will not exceed the MRL of 0.05 mg/kg established for honey (Regulation (EU) 2019/552).

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.2.8.1 Input values for the consumer risk assessment

Table 7.2-14: 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: Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2- chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety) expressed as prothioconazole-desthio.				
Intended/relevant uses				
Wheat (incl. triticale)	0.1	existing EU MRL* ~~x CF~~	0.1	existing EU MRL* ~~x CF~~
Barley	0.2	existing EU MRL* ~~x CF~~	0.2	existing EU MRL* ~~x CF~~
Rye	0.05	existing EU MRL* ~~x CF~~	0.05	existing EU MRL* ~~x CF~~
Rape seeds	0.15	existing EU MRL* ~~x CF~~	0.15	existing EU MRL* ~~x CF~~
Further uses				
Other commodities of plant and animal origin	variable	existing EU MRL* ~~x CF~~ (where relevant)	Not relevant. Acute risk assessment was performed only for relevant uses.	

* Source of EU MRL: Regulation (EU) 2019/552

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.2-15: Consumer risk assessment

ADI	0.01 mg/kg bw/d (prothioconazole-desthio)
TMDI (% ADI) according to EFSA PRIMo rev. 3.1	~~45~~ 29 % (based on NL toddler diet)
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	Not relevant. TMDI< 100%
ARfD	0.01 mg/kg bw/d (prothioconazole-desthio)
IESTI (% ARfD) according to EFSA PRIMo rev. 3.1	Unprocessed commodities - children Wheat: ~~29~~ 14 % (based on UK 4-6 years diet) Barley: ~~22~~ 11 % (based on UK 7-10 years diet) Rapeseed/canola: ~~4~~ 2 % (based on DE child diet) Unprocessed commodities - adult Wheat: ~~19~~ 10 % (based on UK 15-18 years diet) Barley: ~~17~~ 8 % (based on DE general population diet) Rapeseed/canola: ~~2~~ 0.8 % (based on DE women 14-50 diet) Processed commodities - children Wheat / milling (flour): ~~24~~ 12 % (based on DE child diet) Barley / cooked: ~~15~~ 7 % (based on NL child diet) Wheat / milling (wholemeal)-baking: ~~11~~ 6 % (based on NL child diet) Barley / milling (flour): ~~7~~ 4 % (based on NL child diet) Rapeseeds / oils: ~~2~~ 0.9 % (based on NL toddler diet) Processed commodities - adult

	Barley / beer: ~~29~~ 14 % (based on NL general population diet) Wheat / bread/pizza: ~~9~~ 4 % (based on IT adult diet) Wheat / pasta: ~~8~~ 4 % (based on NL general population diet) Wheat / bread (wholemeal): ~~7~~ 3 % (based on NL general population diet)
NTMDI (% ADI)	Not relevant.
NEDI (% ADI)	Not relevant.
NESTI (% ARfD)	Not relevant.

Chronic and acute exposure calculations were performed using revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo rev. 3.1; calculation version 06/01/2021) provided on the internet homepage of EFSA (https://www.efsa.europa.eu/). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population. The model was developed to calculate simultaneously the short-term (acute) and long-term (chronic) dietary exposure to pesticide residue in food according to internationally agreed methodologies. The exposure is compared to the toxicological reference values (i.e., the ADI and the ARfD).
The potential chronic dietary exposure was compared to the ADI and TMDI values were achieved. Input values for all commodities were derived from existing EU MRL (Reg. (EU) 2019/552), representing a worst-case scenario. The highest chronic exposure was calculated for NL toddler diet, representing ~~45~~ 29% of the ADI. For this diet the highest contributors were maize/corn (~~14~~ 7% of ADI), wheat (~~8~~ 5 % of ADI) and milk: cattle (~~6~~ 2 % of ADI). Since TMDI values are below 100%, there is no need to perform higher tier/refined chronic exposure calculation.

The potential acute dietary exposure was compared to the ARfD and IESTI values were achieved. Input values only for intended uses were derived from existing EU MRL (Reg. (EU) 2019/552), representing a worst-case scenario. With regard to the acute exposure, no exceedance was identified. The % of ARfD for wheat, barley and rapeseed was ~~29~~ 14%, ~~22~~ 11% and ~~4~~ 2% respectively for unprocessed commodities. In view of the above, there is no need to perform a higher tier exposure calculation for acute exposure.

The proposed uses of prothioconazole in the formulation Protiokonazol 300 EC does not represent unacceptable chronic and acute risks for the consumer.

zRMS:

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day): **0,01** ARfD (mg/kg bw): **0,01**

Source of ADI: Source of ARfD:

Year of evaluation: Year of evaluation:

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
29%	NL toddler	2,93	7%	Maize/corn	6%	Milk: Cattle	4%	Wheat		
19%	GEMS/Food G11	1,95	7%	Soybeans	4%	Wheat	2%	Barley		
19%	GEMS/Food G10	1,91	7%	Soybeans	4%	Wheat	1%	Barley		
19%	GEMS/Food G15	1,86	5%	Wheat	3%	Soybeans	2%	Barley		
19%	GEMS/Food G06	1,86	7%	Wheat	2%	Soybeans	1%	Maize/corn		
18%	GEMS/Food G07	1,84	4%	Wheat	4%	Soybeans	1%	Barley		
18%	GEMS/Food G08	1,82	4%	Wheat	4%	Soybeans	2%	Barley		
15%	NL child	1,46	4%	Wheat	2%	Milk: Cattle	0,8%	Sugar beet roots		
15%	FR child 3 15 yr	1,46	5%	Wheat	2%	Milk: Cattle	2%	Lentils		
14%	IE adult	1,38	3%	Peas	2%	Wheat	1%	Lentils		
13%	UK infant	1,31	4%	Milk: Cattle	3%	Wheat	1%	Carrots		
13%	ES child	1,28	4%	Wheat	2%	Lentils	1%	Milk: Cattle		
13%	RO general	1,28	5%	Wheat	1%	Sunflower seeds	1%	Head cabbages		
13%	DE child	1,28	4%	Wheat	2%	Milk: Cattle	1%	Apples		
13%	DK child	1,28	4%	Wheat	3%	Rye	1%	Carrots		
12%	FR toddler 2 3 yr	1,20	3%	Wheat	3%	Milk: Cattle	1,0%	Lentils		
10%	UK toddler	1,03	4%	Wheat	2%	Milk: Cattle	0,7%	Potatoes		
9%	SE general	0,91	3%	Wheat	1%	Milk: Cattle	0,8%	Carrots		
9%	PT general	0,87	4%	Wheat	1%	Potatoes	0,7%	Carrots		
9%	IT toddler	0,85	7%	Wheat	0,4%	Lentils	0,2%	Carrots		
8%	NL general	0,79	2%	Wheat	0,8%	Milk: Cattle	0,6%	Barley		
8%	DE general	0,79	2%	Wheat	1%	Milk: Cattle	1%	Barley		
8%	ES adult	0,77	2%	Wheat	1%	Lentils	1,0%	Barley		
7%	DE women 14-50 yr	0,75	2%	Wheat	1%	Milk: Cattle	0,5%	Sugar beet roots		
7%	FR adult	0,66	2%	Wheat	0,7%	Lentils	0,4%	Milk: Cattle		
6%	FR infant	0,59	2%	Milk: Cattle	1%	Carrots	0,8%	Wheat		
6%	FI 3 yr	0,58	1%	Wheat	0,9%	Potatoes	0,8%	Carrots		
6%	IT adult	0,56	4%	Wheat	0,2%	Lentils	0,1%	Carrots		
5%	FI adult	0,53	3%	Coffee beans	0,4%	Peas	0,4%	Rye		
5%	FI 6 yr	0,50	1,0%	Wheat	0,8%	Potatoes	0,7%	Peas		
5%	UK vegetarian	0,49	2%	Wheat	0,4%	Lentils	0,3%	Milk: Cattle		
4%	LT adult	0,43	1%	Wheat	0,6%	Potatoes	0,5%	Rye		
4%	UK adult	0,40	2%	Wheat	0,3%	Milk: Cattle	0,3%	Potatoes		
4%	DK adult	0,39	1%	Wheat	0,5%	Milk: Cattle	0,5%	Carrots		
3%	PL general	0,26	0,7%	Potatoes	0,3%	Head cabbages	0,3%	Carrots		
2%	IE child	0,22	1%	Wheat	0,4%	Milk: Cattle	0,2%	Carrots		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment /children | **Acute risk assessment / adults / general population** | **Acute risk assessment /children** | **Acute risk assessment / adults / general population**

Details - acute risk assessment /children | Details - acute risk assessment/adults | Hide IESTI new calculations | Show IESTI new calculations

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the Eu

The calculation is based on the large portion of the most critical consumer group.

IESTI new calculations:
The calculation is performed with the MRL and the peeling/processing factor (PF), taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.
Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Wheat	0,1 / 0,1	1,4
11%	Barley	0,2 / 0,2	1,1
2%	Rapeseeds/canola	0,15 / 0,15	0,21

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
10%	Barley	0,2 / 0,2	0,97
8%	Wheat	0,1 / 0,1	0,84
0,8%	Rapeseeds/canola seeds	0,15 / 0,15	0,08

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI new

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Wheat	0,1 / 0,1	1,4
11%	Barley	0,2 / 0,2	1,1
2%	Rapeseeds/canola	0,15 / 0,15	0,21

Total number of commodities found exceeding the ARfD/ADI in children and adult diets (IESTI new calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI new

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
10%	Barley	0,2 / 0,2	0,97
8%	Wheat	0,1 / 0,1	0,84
0,8%	Rapeseeds/canola seeds	0,15 / 0,15	0,08

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
12%	Wheat / milling (flour)	0,1 / 0,1	1,2
7%	Barley / cooked	0,2 / 0,2	0,73
6%	Wheat / milling (wholemea	0,1 / 0,1	0,55
4%	Barley / milling (flour)	0,2 / 0,2	0,36
0,9%	Rapeseeds / oils	0,15 / 0,3	0,09

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Barley / beer	0,2 / 0,04	1,4
4%	Wheat / bread/pizza	0,1 / 0,1	0,44
4%	Wheat / pasta	0,1 / 0,1	0,38
3%	Wheat / bread	0,1 / 0,1	0,35

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI new

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
12%	Wheat / milling (flour)	0,1 / 0,1	1,2
7%	Barley / cooked	0,2 / 0,2	0,73
6%	Wheat / milling	0,1 / 0,1	0,55
4%	Barley / milling (flour)	0,2 / 0,2	0,36
0,9%	Rapeseeds / oils	0,15 / 0,3	0,09

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI new): ---

IESTI new

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Barley / beer	0,2 / 0,04	1,4
4%	Wheat / bread/pizza	0,1 / 0,1	0,44
4%	Wheat / pasta	0,1 / 0,1	0,38
3%	Wheat / bread (wholemeal)	0,1 / 0,1	0,35

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

7.3 Triazole derivative metabolites (TDMs)

Prothioconazole is one of a triazole pesticide active substance (triazole-containing fungicide). The triazole derivative metabolites, triazole acetic acid (TAA), triazole alanine (TA), 1,2,4-triazole (1,2,4-T) and triazole lactic acid (TLA), are common metabolites of the triazole-containing fungicides.
During the second and third stage of the European Commission's pesticides review program data gaps and confirmatory data requirements were identified for a number of triazole fungicides. A group of manufactures of the triazole-containing fungicides formed an industry taskforce, known as the Triazole Derivative Metabolite Group (TDMG) which made a joint submission of new toxicological, metabolism and residues data to meet these data requirements (Confirmatory Data dossier). These data were assessed by the United Kingdom (UK, 2018) as a Confirmatory Data and approved by EFSA as a conclusion in June 2018 (amended in April 2019): **Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted** (EFSA Journal 2018;16(7):5376). Confirmatory Data dossier is not subject to data protection and have therefore been used to support this registration.

7.3.1 Stability of residues during storage of samples

Available data

New data has been generated for TDMs. Please refer to the data to which the applicant has been granted access under the LoA.

Table 7.3-1: Summary of stability data achieved at ≤ - 18°C

Matrix	Characteristics of the matrix	Storage stability				Reference
		1,2,4 T	TA	TAA	TLA	
Data relied on in EU						
Plant products						
Apples, tomatoes, mustard leaves, wheat forage, radishes tops/roots, turnips roots, sugar beet roots, cabbages, lettuces	High water content	6 months	53 months	53 months	48 months (lettuce only)	EFSA, 2018
Barley, wheat, rye	High starch content	12 months	26 months	26 months	48 months	
Rapeseeds, soya beans	High oil content	12 months (soya bean only; not stable in rape seed)	26 months (soya bean only; not stable in rape seed)	53 months	48 months	
Peas, dry; Navy beans	High protein content	No data	15 months	25 months	48 months	
Oranges	High acid content	No data	No data	No data	48 months	
Barley, wheat, rye	Cereal straw	12 months	53 months	40 months	No data	
Animal products						
Ruminant	Milk	18 months	No data	No data	No data	EFSA, 2018
Poultry	Eggs	12 months	No data	No data	No data	
Ruminant/poultry	Liver	12 months	No data	No data	No data	
	Muscle	12 months	No data	No data	No data	
	Fat	12 months	No data	No data	No data	
New studies: TDMs (triazole Derived Metabolites)						
Plant products						

Matrix	Characteristics of the matrix	Storage stability				Reference
		1,2,4 T	TA	TAA	TLA	
Data relied on in EU						
Please refer to the data to which the applicant has been granted access under the LoA attached to this application.						

Conclusion on stability of residues during storage

According to EFSA Journal 2018;16(7):5376:
"From the submitted storage stability data, it can be concluded that the residue trials analysing TA, TAA and TLA residues in high water-, high oil-, high protein- and high starch content commodities were supported by acceptable storage stability data on these compounds, except for TA (raspberries, peas, rapeseeds) and TAA (raspberries). The residue trials analysed 1,2,4-T residues in most of the crops within a time interval for which acceptable storage stability of this compound could not be demonstrated, except for stone fruit, stem vegetables, soya beans and oats grain. Storage stability data were not provided and are required for 1,2,4-T, TA and TAA in high acid-content commodities, for 1,2,4-triazole in high protein-content commodities and for TLA in cereal straw to cover the maximum storage time interval of all residue trials in primary and rotational crops (data gap). For products of animal origin, the available storage stability data demonstrated acceptable freezer storage stability of 1,2,4-T in milk for 18 months and in eggs, liver, muscle and fat for 12 months. Additional storage stability data analysing for the residues of TA and TAA in milk and eggs were also provided but were not considered as acceptable since the homogenised samples of milk and eggs were fortified with a mixture of TA and TAA and not with the individual compound, respectively."

zRMS:
Applicant has LoA from Indofil Industries (Netherlands) B.V. to following study:
Longhi, D., 2022. *Storage stability of Triazole Derivative Metabolites (TDM) in wheat forage, wheat grain, rapeseed seeds, wheat straw, apple, tomato, carrot. Final Report No. GLP-STUDY-21-124.*
The applicant does not have access to a copy of the study.
Part of the study for which the access is granted:
Storage stability of TDM (TRZ, TA, TLA, TAA) in matrices:
- high water (green forage wheat)
- high starch (wheat grain)
- dry (wheat straw)

The storage stability was evaluated over a period of 7 months.
The study demonstrated the stability of all tested metabolites in all tested matrices for 7 months.
The study was found to be acceptable.
The study was accepted by zRMS (PL) in *Prothioconazole_fRR Part B7_INDOFIL Prothio 250 EC_Indofil Industries_PL_rev 02.2024.*

7.3.1.1 Stability of residues in sample extracts (KCA 6.1)

Conclusion on stability of residues in sample extracts

Please refer to the data to which the applicant has been granted access under the LoA.

7.3.2 Nature of residues in plants, livestock and processed commodities

7.3.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

No new data submitted in the framework of this application.

Summary of plant metabolism studies reported in the EU

According to Confirmatory Data - Triazole Derivative Metabolites, 2018:
"Plant metabolism studies have not been conducted where the triazole derivative metabolites have been directly applied, but plant metabolism studies using the parent triazole fungicides have all been previously submitted as part of the EU review process under 91/414/EEC (and actives deemed approved under Regulation (EC) 1107/2009). These studies provide information on which of the triazole derivative metabolites are formed and an indication of the level at which they are present."
"*In general, the triazole fungicides follow a common pathway in crops with regard to the formation of the triazole derivative metabolites. In a first step, the parent active (or closely related metabolites) are cleaved in plants or soil resulting in 1,2,4-triazole. In a second step, 1,2,4-triazole is enzymatically conjugated resulting in triazole alanine which is then further converted into triazole acetic acid and triazole lactic acid. Whereas 1,2,4-triazole occurs only in few crop matrices (cereal grain and oilseeds), triazole alanine and triazole acetic acid formed major parts of the polar radioactivity identified (cereal grain, oilseeds, root and tuber and fruiting crops). Compared with triazole alanine and triazole acetic acid the metabolite triazole lactic acid was identified in fewer matrices (cereal grain). Triazole pyruvic acid, a potential intermediate between triazole alanine and triazole lactic acid was not detected in any of the crop studies.*"

Conclusion on metabolism in primary crops

Sufficient data regarding the metabolism of TDMs have been provided. The residue definition for risk assessment of active substances belonging to the class of triazole fungicides was proposed as "Parent compound and any other relevant metabolite exclusively linked to the parent compound; triazole alanine (TA) and triazole lactic acid (TLA); triazole acetic acid (TAA); and 1,2,4-triazole. No further data is required or submitted in the framework of this application.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data is required or submitted in the framework of this application.

According to EFSA Journal 2018;16(7):5376:
"Based on the metabolism data in primary and rotational crops that were compiled from the assessment of the 18 triazole active substances the triazole active substances were shown to degrade into the common metabolites 1,2,4-T, TA, TLA and TAA, known as TDMs (…) Similar metabolic patterns were depicted both in primary and in rotational crops."

Conclusion on metabolism in rotational crops

Sufficient data regarding metabolism of TDMs in rotational crops have been provided. Specific residue definition for rotational crops is not deemed necessary.
No further data is required or submitted in the framework of this application.

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data is required or submitted in the framework of this application.

According to EFSA Journal 2018;16(7):5376:
"The TDMs remained stable under the standard hydrolysis conditions simulating processing of pasteurisation, baking, brewing and boiling and sterilisation".

Conclusion on nature of residues in processed commodities

Sufficient data regarding the nature of residues in processed commodities of TDMs have been provided. No further data is required or submitted in the framework of this application.

7.3.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.3-2: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Fruit crops Cereals (straw and grain) Pulses and oilseeds Root crops.
Rotational crops covered	Leafy vegetables (swiss chard) Root and tuber vegetables (turnip) Cereals (wheat)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	N/A
Residue pattern in processed commodities similar to pattern in raw commodities?	N/A
Plant residue definition for monitoring	Triazole parent compound only : Prothioconazole-desthio (sum of isomers) (Regulation (EU) 2019/552, EFSA, 2014)
Plant residue definition for risk assessment	1) Triazole parent compound and any other relevant metabolite exclusively linked to the parent compound; 2) Sum of TA (triazole alanine) and TLA (triazole lactic acid), since these compounds share the same toxicity; 3) TAA (triazole acetic acid); 4) 1,2,4-T (1,2,4-triazole) (EFSA, 2018)
Conversion factor from enforcement to RA	2 (cereal grain, pulses and oilseeds, leafy vegetables and root and tuber vegetables) 3 (cereal straw)

7.3.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

According to EFSA Journal 2018;16(7):5376:
"The compilation of the poultry and ruminant metabolism studies conducted with the triazole pesticide active substances with the ^{14}C labelling on the triazole moiety showed that besides the parent compound that was detected in significant proportions in all animal matrices ranging between 27% and 81% TRR in milk, eggs and tissues, 1,2,4-T was also found to be a predominant compound of the total residues with levels ranging from 31% to 86% TRR in those matrices. TA was identified at very low levels in poultry muscle only (< 10% TRR) and at levels between 22% and 39% TRR in ruminant matrices.
Since TA is a major component in feed items, the potential transfer of this compound in poultry and ruminant matrices was further investigated in a metabolism study conducted with ^{14}C-TA. TA remains the major compound of the total residues in all poultry matrices (84–97.2% TRR) and in ruminant tissues (56–76% TRR) while TA and 1,2,4-T accounted for 8% and 86% TRR, respectively, in milk. TLA and TAA were detected in very low levels in all matrices (< 1% TRR). The potential transfer of TAA, TLA and 1,2,4-T present in feed items to the animal matrices was not further investigated. Although there are indications from the ruminant metabolism study conducted with the ^{14}C-TA, that there is no accumulation of TAA and TLA (4.2% and < 1% of the total administered dose in urine, respectively), these metabolites were however detected in the ruminant matrices from the feeding study conducted with TA."

Conclusion on metabolism in livestock

Sufficient data regarding metabolism in livestock of TDMs have been provided. No further data is required or submitted in the framework of this application.

7.3.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.3-3: Summary on the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	1-2 days in milk
	Eggs: 4-8 days
Animal residue definition for monitoring	Triazole parent compound only: Prothioconazole-desthio (sum of isomers) for all livestock matrices (Regulation (EU) 2019/552; EFSA, 2014)
Animal residue definition for risk assessment	1) Triazole parent compound and any other relevant metabolite exclusively linked to the parent compound; 2) Sum of TA (triazole alanine) and TLA (triazole lactic acid), since these compounds share the same toxicity; 3) TAA (triazole acetic acid); 4) 1,2,4-T (1,2,4-triazole) (EFSA, 2018)
Conversion factor	2 for liver 9 for kidney
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No

7.3.3 Magnitude of residues in plants (KCA 6.3)

7.3.3.1 Summary of European data and new data supporting the intended uses

New data has been generated for TDMs. Please refer to the data to which the applicant has been granted access under the LoA.

zRMS:
Applicant has LoA from Indofil Industries (Netherlands) B.V. to following study:

Sala, A.2021. *Determination of difenoconazole and prothioconazole residues in winter or spring wheat raw and processed commodities (white flour and white bread) following two applications of IN233C1560 Northern and Southern Europe – 16 trials. GLP-STUDY-21-24*.
The applicant does not have access to a copy of the study.
Part of the study for which the access is granted:
Determination of the residues level of the following analytes in wheat samples (whole plant, straw, grain) and processed commodities (white flour and white bread):

- prothioconazole-desthio
- tiazole derivative metabolites (TDMs)
- Prothioconazole-desthio-3-hydroxy
- Prothioconazole-desthio-4-hydroxy
- Prothioconazole-desthio-5-hydroxy
- Prothioconazole-desthio-6-hydroxy
- Prothioconazole-desthio-alpha-hydroxy

The study was accepted by zRMS (PL) in *Prothioconazole_fRR Part B7_INDOFIL Prothio 250 EC_Indofil Industries_PL_rev 02.2024.*

No data were provided on residues in rapeseed (data gap).

7.3.3.2 Conclusion on the magnitude of residues in plants

New data has been generated for TDMs. Please refer to the data to which the applicant has been granted access under the LoA.

7.3.4 Magnitude of residues in livestock

Available data

No new data is required or submitted in the context of this application.

According to Confirmatory Data – Triazole Derivative Metabolites, 2018:
"The dietary burdens for all four TDM were determined. As outlined above for plant residues, the studies on the nature of the residue on processing demonstrated that all four TDM are hydrolytically stable. The magnitude of the TDM in processed commodities relevant to animal feed items was investigated. Where appropriate the processing factors derived for feed items as detailed at section B.7.5.3 were used in the dietary intake assessments.

For all four TDM the dietary burden on a DM (dry matter) basis exceeds 0.1 mg/kg. On consideration of the trigger outlined in Regulation (EC) 283/2013 then residues of all four TDM in the diets of livestock are also above 0.004 mg/kg bw/day.
Residues of the parent triazole pesticides in animal feed items could also give rise to TDM residues in products of animal origin. Livestock metabolism studies for the triazole pesticides demonstrate that T can occur in products of animal origin. For the 14 triazole pesticides supported by the TDMG an estimation of the residue levels of T in products of animal origin has been made.
In most cases the metabolism data demonstrate that for the dietary burdens of the parent triazoles considered in this assessment, residues of T in products of animal origin will be <0.01 mg/kg. Hence a further consideration is not required. Where residues may occur then the residues levels of T have been estimated using the animal metabolism studies as no feeding studies with the parent triazole pesticides, in which T is determined, have been undertaken. T residue levels in products of animal origin have been estimated from the metabolism studies assessed for the approvals of the actives.
The sum of each TDM arising in products of animal origin (from TDM residues in crops and the parent triazole in crops) has been determined and these levels included in the consumer intake assessments. Ideally feeding studies would be available to estimate residues of T in products of animal origin arising from the parent triazole in animal feed items. However, given the outcome of the consumer risk assessments and the fact that the available metabolism data indicate the contribution of T from the parent triazoles is low then further feeding studies are not deemed necessary. The consideration of additional GAPs where the NEDIs and NESTIs increase significantly may require further data to ensure consumers are adequately protected."

Table 7.3-4: Dietary burden results for parent triazole pesticides – prothioconazole (Confirmatory – Data Triazole Derivative Metabolites; 2018

Parent triazole pesticide	Dairy ruminants		Meat Ruminants		Poultry		Pigs		Residue levels of T* (mg/kg)
	Maximum dietary burden (mg/kg bw/day)	Median dietary burden (mg/kg bw/day)	Maximum dietary burden (mg/kg bw/day)	Median dietary burden (mg/kg bw/day)	Maximum dietary burden (mg/kg bw/day)	Median dietary burden (mg/kg bw/day)	Maximum dietary burden (mg/kg bw/day)	Median dietary burden (mg/kg bw/day)	
Prothioconazole	0.086	0.028	0.208	0.069	0.018	0.011	0.031	0.071	Residues not expected

* 1,2,4-triazole

According to Confirmatory Data – Triazole Derivative Metabolites, 2018 (Appendix E – Estimation of the potential and actual exposure through the diet):
"Lactating goat and laying hen metabolism studies were evaluated for the approval of the active. In the article 12 RO reference is also made to goat metabolism studies assessed by the JMPR. These studies were conducted at a feeding rate of 10 mg/kg bw/day (representing 116N and 556 N for the maximum dietary burdens of ruminants and poultry outlined in table 7.4.5-9). According to the article 12 RO the only identified triazole related metabolite was the thiocyanate metabolite found in the goat metabolism studies: 41 % TRR (0.061 mg eq/kg) in milk, 30 % TRR (0.035 mg eq/kg) in muscle, 12 % TRR (0.022 mg eq/kg) in fat, 9 % TRR (0.41 mg eq/kg) in kidney and 2 % TRR (0.13 mg eq/kg) in liver. At the maximum dietary burden of meat ruminants, this metabolite is expected to occur at a trace level in all matrices (up to 0.004 mg eq/kg in kidney).

It was concluded that there was no need to further address its toxicological properties. Due to the fact that none of the TDMs were identified then further consideration is not required."

Regarding above, it is not expected that the proposed uses of Protiokonazol 300 EC will increase the dietary burden of TDMs.

7.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.3.5.1 Available data for all crops under consideration

New data has been generated for TDMs. Please refer to the data to which the applicant has been granted access under the LoA.

zRMS: The TDMs remained stable under the standard hydrolysis conditions simulating processing of pasteurisation, baking, brewing and boiling and sterilisation (EFSA Journal 2018;16(7):5376). No further data is required.

7.3.6 Magnitude of residues in representative succeeding crops

7.3.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

No new data is submitted in the framework of this application.

Conclusion on rotational crops studies

According to EFSA Journal 2018;16(7):5376:
"The magnitude of the TDMs have been determined in numerous residue trials conducted on crops covering most of the crop categories and for different triazole active substances both in primary and rotational crops. These trials were submitted in the framework of the confirmatory data (United Kingdom, 2015). The submitted residue trials were performed according to specific good agricultural practices (GAPs) authorised for the triazole active substances and residue trials conducted outside Europe were also available. In some cases, these residue trials were compliant with the representative uses of triazole active substances that were approved at EU level."
"Residue trials analysing for all TDMs and compliant with the representative uses on cereals (wheat, rye, barley, oats, triticale) and on rapeseeds together with rotational crops residue field trials were submitted in the framework of this confirmatory data assessment but were not supported by acceptable storage stability data for 1,2,4-T in cereal grain, straw and rapeseeds and for TLA in straw. Sufficient residue trials in primary and rotational crops and supported by acceptable storage stability data are therefore required (data gap)."
However, above mentioned rotational crops studies were used in the TDMs consumer risk assessment (EFSA Journal 2018;16(7):5376 and Confirmatory Data – Triazole Derivative Metabolites, Addendum; Rapporteur Member State: United Kingdom; May 2016, amended February 2018). No further data is required or submitted.

7.3.7 Other / special studies (KCA 6.10, 6.10.1)

Please refer to point 7.2.7.

7.3.8 Estimation of exposure through diet and other means (KCA 6.9)

Potential exposure to TDMs residues arising from the proposed uses of Protiokonazol 300 EC has been estimated using residues data available from unprotected Confirmatory Data dossier, 2018.

7.3.8.1 Input values for the consumer risk assessment

Table 7.3-5: Input values for the consumer risk assessment Triazole alanine (TA) and triazole lactic acid (TLA)

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Risk assessment residue definition 2: Triazole alanine (TA) and triazole lactic acid (TLA)				
Citrus fruit	0.36	(STMR TA + STMR TLA)*	-	-
Pome fruit	0.069	(STMR TA + STMR TLA)*	-	-
Stone fruit	0.358	(STMR TA + STMR TLA)*	-	-
Berries	0.10	(STMR TA + STMR TLA)*	-	-
Banana	0.05	(STMR TA + STMR TLA)*	-	-
Root & tuber vegetables	0.41	(STMR TA + STMR TLA)* x CF	-	-
Bulb vegetables	0.07	(STMR TA + STMR TLA)*	-	-
Fruiting vegetables	0.24	(STMR TA + STMR TLA)*	-	-
Brassica vegetables	0.18	(STMR TA + STMR TLA)*	-	-
Leafy vegetables	0.254	(STMR TA + STMR TLA)* x CF	-	-
Legume vegetables	0.10	(STMR TA + STMR TLA)*	-	-
Stem vegetables	0.10	(STMR TA + STMR TLA)*	-	-
Pulses	0.26	(STMR TA + STMR TLA)* x CF	-	-
Oilseeds	2.208	(STMR TA + STMR TLA)* x CF	-	-
Oilseed rape (intended use)	**2.208**	**(STMR TA + STMR TLA)* x CF**	**6.036**	**(HR TA + HR TLA)* x CF**
Oilfruits	1.104	(STMR TA + STMR TLA)*	-	-
Cereals	1.286	(STMR TA + STMR TLA)* x CF	-	-
Wheat incl. triticale, rye (intended uses)	**1.286**	**(STMR TA + STMR TLA)* x CF**	**4.72**	**(HR TA + HR TLA)* x CF**
Barley (intended uses)	**1.286**	**(STMR TA + STMR TLA)* x CF**	**4.72**	**(HR TA + HR TLA)* x CF**
Sugarplants	0.06	(STMR TA + STMR TLA)*	-	-
Ruminant meat	0.50	(STMR TA + STMR TLA)*	-	-
Ruminant fat	0.29	(STMR TA + STMR TLA)*	-	-

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Ruminant liver	1.05	(STMR TA + STMR TLA)*	-	-
Ruminant kidney	0.58	(STMR TA + STMR TLA)*	-	-
Ruminant milk	0.08	(STMR TA + STMR TLA)*	-	-
Sheep meat	0.55	(STMR TA + STMR TLA)*	-	-
Sheep fat	0.30	(STMR TA + STMR TLA)*	-	-
Sheep liver	1.17	(STMR TA + STMR TLA)*	-	-
Sheep kidney	0.64	(STMR TA + STMR TLA)*	-	-
Sheep milk	0.08	(STMR TA + STMR TLA)*	-	-
Swine meat	0.25	(STMR TA + STMR TLA)*	-	-
Swine fat	0.16	(STMR TA + STMR TLA)*	-	-
Swine liver	0.54	(STMR TA + STMR TLA)*	-	-
Swine kidney	0.27	(STMR TA + STMR TLA)*	-	-
Poultry meat	0.15	(STMR TA + STMR TLA)*	-	-
Poultry fat	0.14	(STMR TA + STMR TLA)*	-	-
Poultry liver	0.31	(STMR TA + STMR TLA)*	-	-
Poultry eggs	0.10	(STMR TA + STMR TLA)*	-	-

* Confirmatory Data; Triazole Derivative Metabolites; February 2018 – Appendix E – Estimation of the potential and actual exposure through the diet

Table 7.3-6: Input values for the consumer risk assessment Triazole acetic acid (TAA)

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition 3: Triazole acetic acid (TAA)				
Citrus fruit	0.050	STMR*	-	-
Pome fruit	0.030	STMR*	-	-
Stone fruit	0.020	STMR*	-	-
Berries	0.050	STMR*	-	-
Banana	0.050	STMR*	-	-
Root & tuber vegetables	0.020	STMR* x CF	-	-
Bulb vegetables	0.010	STMR*	-	-
Fruiting vegetables	0.010	STMR*	-	-
Brassica vegetables	0.010	STMR*	-	-
Leafy vegetables	0.046	STMR* x CF	-	-
Legume vegetables	0.010	STMR*	-	-
Stem vegetables	0.020	STMR*	-	-
Pulses	0.10	STMR* x CF	-	-

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Oilseeds	0.24	STMR* x CF	-	-
Oilseed rape (intended uses)	**0.24**	**STMR* x CF**	**1.36**	**HR* x CF**
Oilfruits	0.120	STMR*	-	-
Cereals	1.58	STMR* x CF	-	-
Wheat incl. triticale, rye (intended uses)	**1.58**	**STMR* x CF**	**3.46**	**HR* x CF**
Barley (intended uses)	**1.58**	**STMR* x CF**	**3.46**	**HR* x CF**
Sugarplants	0.050	STMR*	-	-
Ruminant meat	0.04	STMR*	-	-
Ruminant fat	0.05	STMR*	-	-
Ruminant liver	0.05	STMR*	-	-
Ruminant kidney	0.15	STMR*	-	-
Ruminant milk	0.04	STMR*	-	-
Sheep meat	0.04	STMR*	-	-
Sheep fat	0.06	STMR*	-	-
Sheep liver	0.05	STMR*	-	-
Sheep kidney	0.18	STMR*	-	-
Sheep milk	0.04	STMR*	-	-
Swine meat	0.04	STMR*	-	-
Swine fat	0.04	STMR*	-	-
Swine liver	0.04	STMR*	-	-
Swine kidney	0.11	STMR*	-	-
Poultry meat	0.04	STMR*	-	-
Poultry fat	0.04	STMR*	-	-
Poultry liver	0.05	STMR*	-	-
Poultry eggs	0.04	STMR*	-	-

* Confirmatory Data; Triazole Derivative Metabolites; February 2018 – Appendix E – Estimation of the potential and actual exposure through the diet

Table 7.3-7: Input values for the consumer risk assessment 1,2,4-triazole

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Risk assessment residue definition 4: 1,2,4-triazole				
Citrus fruit	0.050	STMR*	-	-
Pome fruit	0.010	STMR*	-	-
Stone fruit	0.010	STMR*	-	-

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Berries	0.010	STMR*	-	-
Banana	0.050	STMR*	-	-
Root & tuber vegetables	0.02	STMR* x CF	-	-
Bulb vegetables	0.010	STMR*	-	-
Fruiting vegetables	0.010	STMR*	-	-
Brassica vegetables	0.039	STMR*	-	-
Leafy vegetables	0.030	STMR* x CF	-	-
Legume vegetables	0.010	STMR*	-	-
Stem vegetables	0.010	STMR*	-	-
Pulses	0.10	STMR* x CF	-	-
Oilseeds	0.10	STMR* x CF	-	-
Oilseed rape (intended uses)	**0.10**	STMR* x CF	**0.20**	**HR* x CF**
Oilfruits	0.050	STMR*	-	-
Cereals	0.10	STMR* x CF	-	-
Wheat incl. triticale, rye (intended uses)	**0.10**	**STMR* x CF**	**0.16**	**HR* x CF**
Barley (intended uses)	**0.10**	**STMR* x CF**	**0.16**	**HR* x CF**
Sugarplants	0.050	STMR*	-	-
Ruminant meat	0.27	STMR*	-	-
Ruminant fat	0.18	STMR*	-	-
Ruminant liver	0.31	STMR*	-	-
Ruminant kidney	0.32	STMR*	-	-
Ruminant milk	0.30	STMR*	-	-
Sheep meat	0.29	STMR*	-	-
Sheep fat	0.19	STMR*	-	-
Sheep liver	0.34	STMR*	-	-
Sheep kidney	0.34	STMR*	-	-
Sheep milk	0.32	STMR*	-	-
Swine meat	0.13	STMR*	-	-
Swine fat	0.10	STMR*	-	-
Swine liver	0.13	STMR*	-	-
Swine kidney	0.14	STMR*	-	-
Poultry meat	0.04	STMR*	-	-
Poultry fat	0.04	STMR*	-	-
Poultry liver	0.04	STMR*	-	-
Poultry eggs	0.04	STMR*	-	-

* Confirmatory Data; Triazole Derivative Metabolites; February 2018 – Appendix E – Estimation of the potential and actual exposure through the diet

7.3.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.3-8: Consumer risk assessment – Triazole alanine (TA) and triazole lactic acid (TLA)

ADI	0.3 mg/kg bw/d
TMDI (% ADI) according to EFSA PRIMo rev. 3.1	11% (based on NL toddler diet)
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	Not relevant. TMDI< 100%
ArfD	0.3 mg/kg bw
IESTI (% ArfD) according to EFSA PRIMo rev. 3.1	Unprocessed commodities – children Wheat: 6% (based on UK 4-6 years diet) Barley: 2% (based on UK 7-10 years diet) Rapeseed/canola: 1% (based on DE child diet) Unprocessed commodities – adult Wheat: 4% (based on UK 15-18 years diet) Barley: 2% (based on DE general population diet) Rapeseed/canola: 0.4% (based on DE women 14-50 diet) Processed commodities – children Wheat / milling (flour): 5% (based on DE child diet) Wheat / milling (wholemeal)-baking: 2% (based on NL child diet) Barley / cooked: 2% (based on NL child diet) Barley / milling (flour): 0.8% (based on NL child diet) Rapeseeds / oils: 0.4% (based on NL toddler diet) Processed commodities – adult Barley / beer: 3% (based on NL general population diet) Wheat / bread/pizza: 2% (based on IT adult diet) Wheat / pasta: 2% (based on NL general population diet) Wheat / bread (wholemeal): 1% (based on NL general population diet)
NTMDI (% ADI)	Not relevant.
NEDI (% ADI)	Not relevant.
NESTI (% ArfD)	Not relevant.

Table 7.3-9: Consumer risk assessment – Triazole acetic acid (TAA)

ADI	1 mg/kg bw/d
TMDI (% ADI) according to EFSA PRIMo rev. 3.1	2% (based on NL toddler diet)
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	Not relevant. TMDI< 100%
ArfD	1 mg/kg bw
IESTI (% ArfD) according to EFSA PRIMo rev. 3.1	Unprocessed commodities – children Wheat: 2% (based on UK 4-6 years diet) Barley: 0.9% (based on UK 7-10 years diet) Rapeseed/canola: 0.03% (based on DE child diet)

	Unprocessed commodities – adult Wheat: 1% (based on UK 15-18 years diet) Barley: 0.8% (based on DE general population diet) Rapeseed/canola: 0.01% (based on DE women 14-50 diet) Processed commodities – children Wheat / milling (flour): 2% (based on DE child diet) Wheat / milling (wholemeal)-baking: 0.9% (based on NL child diet) Barley / cooked: 0.6% (based on NL child diet) Barley / milling (flour): 0.3% (based on NL child diet) Rapeseeds / oils: 0.0% (based on NL toddler diet) Processed commodities – adult Barley / beer: 1% (based on NL general population diet) Wheat / bread/pizza: 0.7% (based on IT adult diet) Wheat / pasta: 0.6% (based on NL general population diet) Wheat / bread (wholemeal): 0.6% (based on NL general population diet)
NTMDI (% ADI)	Not relevant.
NEDI (% ADI)	Not relevant.
NESTI (% ArfD)	Not relevant.

Table 7.3-10: Consumer risk assessment – 1, 2, 4-triazole (1,2,4-T)

ADI	0.023 mg/kg bw/d
TMDI (% ADI) according to EFSA PRIMo rev. 3.1	91% (based on NL toddler diet)
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	Not relevant. TMDI< 100%
ArfD	0.1 mg/kg bw
IESTI (% ArfD) according to EFSA PRIMo rev. 3.1	Unprocessed commodities – children Wheat: 1% (based on UK 4-6 years diet) Barley: 0.6% (based on UK 7-10 years diet) Rapeseed/canola: 0.1% (based on DE child diet) Unprocessed commodities – adult Wheat: 0.8% (based on UK 15-18 years diet) Barley: 0.5% (based on DE general population diet) Rapeseed/canola: 0.05% (based on DE women 14-50 diet) Processed commodities – children Wheat / milling (flour): 1% (based on DE child diet) Wheat / milling (wholemeal)-baking: 0.6% (based on NL child diet) Barley / cooked: 0.4% (based on NL child diet) Barley / milling (flour): 0.2% (based on NL child diet) Rapeseeds / oils: 0.1% (based on NL toddler diet) Processed commodities – adult Barley / beer: 0.7% (based on NL general population diet) Wheat / bread/pizza: 0.4% (based on IT adult diet) Wheat / pasta: 0.4% (based on NL general population diet)

	Wheat / bread (wholemeal): 0.3% (based on NL general population diet)
NTMDI (% ADI)	Not relevant.
NEDI (% ADI)	Not relevant.
NESTI (% ArfD)	Not relevant.

Chronic and acute exposure calculations were performed using revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo rev. 3.1; calculation version 06/01/2021) provided on the internet homepage of EFSA (https://www.efsa.europa.eu/). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population. The model was developed to calculate simultaneously the short-term (acute) and long-term (chronic) dietary exposure to pesticide residue in food according to internationally agreed methodologies. The exposure is compared to the toxicological reference values (i.e., the ADI and the ArfD).

The potential chronic and acute dietary exposure was compared to the appropriate ADI and ArfD values. The TMDI and IESTI values were achieved. Input values for all commodities were derived from existing STMR and HR values (Confirmatory Data; Triazole Derivative Metabolites; February 2018 – Appendix E – Estimation of the potential and actual exposure through the diet). Chronic dietary exposure was performed for all crops and acute dietary exposure was performed only for intended uses.

Triazole alanine (TA) and triazole lactic acid (TLA):
Chronic risk assessment has been conducted for sum of triazole alanine (TA) and triazole lactic acid (TLA). The highest chronic exposure was calculated for NL toddler diet, representing 11% of the ADI. For this diet the highest contributors were maize/corn (3% of ADI), wheat (2% of ADI) and milk: cattle (2% of ADI). Since TMDI values are below 100%, there is no need to perform higher tier/refined chronic exposure calculation.
With regard to the acute exposure, no exceedance was identified. The calculated % of ArfD was 6%, 2% and 1% for wheat, barley, rye and rapeseed/canola, respectively in unprocessed commodities.
In view of the above, there is no need to perform a higher tier/refined acute exposure calculation.
Triazole acetic acid (TAA)
The highest chronic exposure was calculated for NL toddler diet, representing 2% of the ADI. For this diet the highest contributors were maize/corn (1% of ADI), wheat (0.6% of ADI) and milk: cattle (0.2% of ADI). Since TMDI values are below 100%, there is no need to perform higher tier/refined chronic exposure calculation.
With regard to the acute exposure, no exceedance was identified. The calculated % of ArfD was 2%, 0.9% and 0.03% for wheat, barley, rye and rapeseed/canola, respectively in unprocessed commodities.
In view of the above, there is no need to perform a higher tier/refined acute exposure calculation.
1, 2, 4-triazole (1,2,4-T)
The highest chronic exposure was calculated for NL toddler diet, representing 91% of the ADI. For this diet the highest contributors were milk: cattle (78% of ADI), maize/corn (3% of ADI) and wheat (2% of ADI). Since TMDI values are below 100%, there is no need to perform higher tier/refined chronic exposure calculation.
With regard to the acute exposure, no exceedance was identified. The calculated % of ArfD was 1%, 0.6% and 0.1% for wheat, barley, rye and rapeseed/canola, respectively in unprocessed commodities.
In view of the above, there is no need to perform a higher tier/refined acute exposure calculation.

The representative uses of Protiokonazol 300 EC do not represent unacceptable acute and chronic risks for the consumer with regard to TDMs even using extreme worst-case scenario.

7.4 Combined exposure and risk assessment

From a scientific point of view it is regarded necessary to take into account potential combination effects.

However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised "scientific methods accepted by the Authority to assess such effects are available."
Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

The product contains only one active substance. However, prothioconazole is one of a triazole pesticide active substance (triazole-containing fungicide) and its use can cause formation the triazole derivative metabolites (TDMs): triazole acetic acid (TAA), triazole alanine (TA), 1,2,4-triazole (1,2,4-T) and triazole lactic acid (TLA). These metabolites are part of the residue definition and acute toxicological reference values have been derived for them. Therefore, combined acute exposure can be considered.

7.4.1 Acute consumer risk assessment from combined exposure

In a first step, dose-addition of residues of the individual active substances is assumed by making use of the Hazard Index (HI) concept. The Hazard Quotient (HQ) is calculated for all active substances in the PPP that are acutely toxic by performing deterministic IESTI/NESTI calculations with the calculation models EFSA PRIMo (rev.3.1) and appropriate national models, if required, and dividing the individual exposure levels by the respective ArfD. Addition of the individual HQs irrespective of any considerations on phenomenological effects or mode(s)/mechanisms of action results in the HI. The results of the HQ/HI calculations are summarized in the following table.

Table 7.4-1: Acute consumer risk assessment from combined exposure

Crop	Active Ingredient	HQ (based on IESTI according to EFSA PRIMo)
Wheat incl. triticale, rye	Prothioconazole	~~0.29~~ 0.14
	TA + TLA	0.06
	TAA	0.02
	1,2,4-T	0.01
	Cumulative risk wheat incl. triticale (HI)	**~~0.38~~ 0.23**
Barley	Prothioconazole	~~0.22~~ 0.11
	TA + TLA	0.02
	TAA	0.009
	1,2,4-T	0.006
	Cumulative risk barley (HI)	**~~0.255~~ 0.145**
Rapeseed/canola	Prothioconazole	~~0.04~~ 0.02
	TA + TLA	0.01
	TAA	0.0003
	1,2,4-T	0.001
	Cumulative risk rapeseed/canola (HI)	**~~0.0513~~ 0.0313**

The Hazard Index is <1. Thus, combined exposure to all active ingredients in Protiokonazol 300 EC is not

expected to present a consumer risk. No further refinement of the assessment is required.

7.4.2 Chronic consumer risk assessment from combined exposure

The uses under consideration provide only a minor contribution to the overall chronic exposure of consumers to pesticide residues. The issue requires a more universal consideration and possibly the generic usage of monitoring data. A harmonised approach is not yet available.

7.5 References

EC (European Commission), 2017. Animal model. Downloaded at https://ec.europa.eu/food/plant/pesticides/max_residue_levels/guidelines_en (26/06/2019)

EFSA (European Food Safety Authority), 2007b. Conclusion on the peer review of the pesticide risk assessment of the active substance prothioconazole. The EFSA Journal 2007, 106r, 1-98. doi:10.2903/j.efsa.2007.106r

EFSA (European Food Safety Authority), 2009. Reasoned opinion on the modification of the existing MRL(s) for prothioconazole in head cabbage and Brussels sprouts. The EFSA Journal 2009, 261r, 1-24. doi:10.2903/j.efsa.2009.261r

EFSA (European Food Safety Authority), 2010a. Reasoned opinion on the modification of the existing MRLs for prothioconazole in cauliflower and broccoli. EFSA Journal 2010;8(4):1577, 22 pp. doi:10.2903/j.efsa.2010.1577

EFSA (European Food Safety Authority), 2010b. Reasoned opinion on the modification of the existing MRLs for prothioconazole in various root vegetables. EFSA Journal 2010;8(7):1675, 28 pp. doi:10.2903/j.efsa.2010.1675

EFSA (European Food Safety Authority), 2012. Reasoned opinion on the modification of the existing MRLs for prothioconazole in rapeseed, linseed, poppy seed and mustard seed. EFSA Journal 2012;10(11):2952, 35 pp. doi:10.2903/j.efsa.2012.2952

EFSA (European Food Safety Authority), 2014. 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 Journal 2014;12(5):3689, 72 pp. doi: 10.2903/j.efsa.2014.3689

FAO (Food and Agriculture Organization of the United Nations), 2008a. Prothioconazole. In: Pesticide residues in food – 2008. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. FAO Plant Production and Protection Paper 193.

FAO (Food and Agriculture Organization of the United Nations), 2008b. Prothioconazole. In: Pesticide residues in food – 2008. Evaluations. Part I. Residues. FAO Plant Production and Protection Paper 194.

United Kingdom, 2004. Draft assessment report on the active substance Prothioconazole prepared by the rapporteur Member State United Kingdom in the framework of Council Directive 91/414/EEC, October 2004.

United Kingdom, 2007. Final addendum to the additional report and the draft assessment report on the active substance prothioconazole prepared by the rapporteur Member State United Kingdom in the framework of Council Regulation (EC) No 33/2008, compiled by EFSA, May 2007.

EFSA (European Food Safety Authority), 2018b. Conclusion on the peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted. EFSA Journal 2018;16(7):5376, 20 pp. https://doi.org/10.2903/j.efsa.2018.5376

United Kingdom, 2015. Triazole Derivate Metabolites, addendum – confirmatory data prepared by the rapporteur Member State, the United Kingdom in the framework of Regulation (EC) No 1107/2009, revised version of 2015. Available online: www.efsa.europa.eu

United Kingdom, 2018. Triazole Derivate Metabolites, addendum – confirmatory data prepared by the rapporteur Member State, the United Kingdom in the framework of Regulation (EC) No 1107/2009, revised version of February 2018. Available online: www.efsa.europa.eu

Appendix 1 Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.10/01a	Peda T.	2022	Magnitude of residue of prothioconazole and metabolites prothioconazole-desthio, triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole acetic acid (TAA) and triazole lactic acid (TLA) in honey after one application of Protiokonazol 300 EC on phacelia (Raw agricultural Commodity) – two harvest study trials in Poland. Company Report No.: 22SGS46 SGS Polska Sp. z o. o. GLP Unpublished	N	Pestila Sp. z o.o.* ProAgri Sp. z o.o.**
KCA 6.10/01b	Peda T.	2022	ANALYTICAL PHASE REPORT: Magnitude of residue of prothioconazole and metabolites prothioconazole-desthio, triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole acetic acid (TAA) and triazole lactic acid (TLA) in honey after one application of Protiokonazol 300 EC on phacelia (Raw agricultural Commodity) – two harvest study trials in Poland. Company Report No.: 22SGS46; LBN-0044-2022 SGS Polska Sp. z o. o.; LabAnalysis s.r.l. GLP Unpublished	N	Pestila Sp. z o.o.* ProAgri Sp. z o.o.**
KCA 6.10/02a	Rovetto I.	2023	Magnitude of the residue of prothioconazole, prothioconazoledesthio and triazole-derivative metabolites (TDMs) in honey after one application of PROTIOKONAZOL 300 EC on Phacelia crop under semi field conditions in two trials in Southern Europe – 2022 Company Report No.: 1147.2F.SAG22 SAGEA Centro di Saggio s.r.l.	N	Pestila Sp. z o.o.* ProAgri Sp. z o.o.**

Data point	Author(s)	Year	**Title** **Company Report No.** **Source (where different from company)** **GLP or GEP status** **Published or not**	**Vertebrate study Y/N**	**Owner**
			GLP Unpublished		
KCA 6.10/02b	Rovetto I.	2022	ANALYTICAL PHASE REPORT: Magnitude of the residue of prothioconazole, prothioconazole-desthio and triazole-derivative metabolites (TDMs) in honey after one application of PROTIOKONAZOL 300 EC on Phacelia crop under semi field conditions in two trials in Southern Europe – 2022 Company Report No.: 1147.2F.SAG22; LBN-0045-2022 SAGEA Centro di Saggio s.r.l.; LabAnalysis s.r.l. GLP Unpublished	N	Pestila Sp. z o.o.* ProAgri Sp. z o.o.**
	Longhi, D.	2022b	Storage stability of Triazole Derivative Metabolites (TDM) in wheat forage, wheat grain, rapeseed seeds, wheat straw, apple, tomato, carrot Report No. : GLP-STUDY-21-124 LabAnalysis s.r.l., Casanova Lonati -Italy GLP :Yes Unpublished Part of the study for which the access is granted: Storage stability of TDM (TRZ, TA, TLA, TAA) in below Matrices: - high water (green forage wheat) - high starch (wheat grain) - dry matrix (wheat straw)	No	Indofil Letter of Access
	Longhi, D.	2022c	Storage stability of prothioconazole-desthio-3-hydroxy, prothioconazole-desthio-4-hydroxy, prothioconazole-desthio-5-hydroxy, prothioconazole-desthio-6-hydroxy and prothioconazole-desthio-alpha-hydroxy in cereal straw Report No. : GLP-STUDY-21-125 LabAnalysis s.r.l., Casanova Lonati -Italy GLP :Yes Unpublished	No	Indofil Letter of Access

Data point	Author(s)	Year	**Title** **Company Report No.** **Source (where different from company)** **GLP or GEP status** **Published or not**	**Vertebrate study Y/N**	**Owner**
	Sala, A.	2021a	Determination of difenoconazole and prothioconazole residues in winter or spring wheat raw and processed commodities (white flour and white bread) following two applications of IN233C1560 Northern and Southern Europe – 16 trials Report No. : GLP-study-21-24 Staphyt, Inchy en Artois – France GLP : Yes Unpublished Part of the study for which the access is granted: Determination of the residues level of the following analytes in wheat samples (whole plant, straw, grain) and processed commodities (white flour and white bread): - prothioconazole-desthio - Triazole derivative metabolites (TDMs): o 1H-1,2,4-triazole (TRZ) o 1H-1,2,4-triazole alanine (TA) o Triazole lactic acid (TLA) o Triazole acetic acid (TAA). In addition to the above mentioned analytes, the following metabolites were quantified in wheat (straw) samples: o prothioconazole-desthio-3-hydroxy o prothioconazole-desthio-4-hydroxy o prothioconazole-desthio-5-hydroxy o prothioconazole-desthio-6-hydroxy o prothioconazole-desthio-alphahydroxy after 2 foliar applications in Northern Europe (4HS +4 DCS).	No	Indofil Letter of Access

*Pestila Spółka z ograniczoną odpowiedzialnością (short name: Pestila Sp. z o. o.)
** ProAgri Spółka z ograniczoną odpowiedzialnością (short name: ProAgri Sp. z o.o.)

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

The following tables are to be completed by MS.

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

List of data relied on and not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Prothioconazole

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

A 2.1.1.1.1 Storage stability of residues in plant products

Not relevant. No new studies are submitted with this application.

A 2.1.1.1.2 Storage stability of residues in animal products

Not relevant. No new studies are submitted with this application.

A 2.1.2 Nature of residues in plants, livestock and processed commodities

A 2.1.2.1 Nature of residue in plants

A 2.1.2.1.1 Nature of residue in primary crops

Not relevant. No new studies are submitted with this application.

A 2.1.2.1.2 Nature of residue in rotational crops

Not relevant. No new studies are submitted with this application.

A 2.1.2.1.3 Nature of residues in processed commodities

Not relevant. No new studies are submitted with this application.

A 2.1.2.2 Nature of residues in livestock

Not relevant. No new studies are submitted with this application.

A 2.1.3 Magnitude of residues in plants

Not relevant. No new studies are submitted with this application.

A 2.1.4 Magnitude of residues in livestock

A 2.1.4.1 Livestock feeding studies

Not relevant. No new studies are submitted with this application.

A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.1.5.1 Distribution of the residue in peel/pulp

Not relevant. No new studies are submitted with this application.

A 2.1.5.2 Processing studies on a core set of representative processes

Not relevant. No new studies are submitted with this application.

A 2.1.6 Magnitude of residues in representative succeeding crops

Not relevant. No new studies are submitted with this application.

A 2.1.7 Other/Special Studies

A 2.1.7.1 Residues in honey

A 2.1.7.1.1 Study 1

Comments of zRMS:	Study is accepted

Reference:	KCA 6.10/01a KCA 6.10/01b
Report	Magnitude of residue of prothioconazole and metabolites prothioconazole-desthio, triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole acetic acid (TAA) and triazole lactic acid (TLA) in honey after one application of Protiokonazol 300 EC on phacelia (Raw agricultural Commodity) – two harvest study trials in Poland; Company Report No.: 22SGS46; LBN-0044-2022, Peda. T, 2022 (Field and Analytical Report)

Guideline(s): Reg. (EC) no. 1107/2009, Reg. (EU) 283/2013 and 284/2013; 7029/VI/95 rev.5; OECD TG 509; SANTE/2020/12830 rev.1; SANTE/11956/2016 rev.9;

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods

This study was conducted to generate specimens of honey after one application of Protiokonazol 300 EC under cultural practice typical for phacelia production to quantify residues of prothioconazole and metabolites prothioconazole-desthio, triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole acetic acid (TAA) and triazole lactic acid (TLA).

Table A 1: Test item data

Name	Protiokonazol 300 EC
Code	Protiokonazol 300 EC
Batch No.	01/PRO/2022
Active substance	prothioconazole
CAS	178928/70-6
Formulation	Emulsifiable concentrate (EC)
Density	1.031 g/cm^3
Content of a.s.	Nominal: 300 g/L Analysed: 306 g/L
Expiration date	24/03/2025

Table A 2: Test system

Crop	Phacelia (*Phacelia tanacetifolia* Benth)
Variety, planting date	Stala, 03/06/2022 Stala, 01/06/2022
RACs harvested	Honey

Study Design and Methods

Table A 3: Test facilities

Field Phase	SGS Polska Sp. z o.o., ul. Jana Kazimieraz 3, 01-248 Warszawa, Poland
Analytical Phase	LabAnalysis s.r.l., GLP Studies Department, Via Europa 5, 27041 Casanova Lonati (PV), Italy

Field phase

Two trials were established in Poland (NEU) in 2022. Each trial consists of one control tunnel and one treated tunnel with phacelia with an insect-proof net without possibility to foraging on another nectar source. Also covered tunnel area was empty of melliferous plants but with regular access to water. Each tunnel consists at least 120 m^2 required.

Beehives were placed in tunnels (one colony per tunnel) on the same day before application. During application hives were covered and closed.

One application was performed at each trial with boom sprayer on the treated plot at a target dose rate 1,3 L/ha of formulated product at BBCH 65.

After application, when the spray solution was dry, the beehives were opened until the honey was ripe or honey cell-closured.

Quality control measures were taken to maintain specimen integrity and to avoid contamination at the trial site.

Honey was taken at 3 different spots on one pooled sample per colony with a tool such as a spoon or by extraction of the de-capped broods (manual honey extractor).

Table A 4: Identification of the field trials

Trial no.	Study type	Country (region)	Trial site	Zip code
22SGS46-01	HS	Poland (Dolnośląskie)	Stoszowice	57-213
22SGS46-02	HS	Poland (Dolnośląskie)	Chwastnica	55-216

Table A 5: Soil characterization

Trial number	Soil texture	Organic matter content	pH
22SGS46-01	Silt Loam	1,3	6,9 (KCl)
22SGS46-02	Silt Loam	1,8	5,6 (KCl)

Table A 6: Application equipment

Trial no.	Plot ID	Application No.	Sprayer configuration	Nozzle type	No. Of nozzles	Nozzle spacing (cm)
22SGS46-01	T	A1	Boom sprayer	TEEJET AIXR 11002	6	50
22SGS46-02	T	A1	Boom sprayer	TEEJET AIXR 11002	6	50

Protiokonazol 300 EC was mixed only with water. No adjuvant was added to the spray mixture. The target dose rate of the test item per application was 1.3 L/ha, equivalent to 390 g a.s./ha and target water volume was 100-400 L/ha according to GAP.

Table A 7: Application data

Trial no.	Application date	Application timing	Actual rate [l/ha]	Actual rate [g a.s./ha]	Deviaton [%]	Spray volume applied [l/ha]	Treated area [m^2]	Total spray mixture [g]	Test item added to spray mixture [g]	Spray mixture remaining [g]	Spray mixture applied to plot area [g]
22SGS46-01	09/08/2022	BBCH 65	1,286	385,8	-1,1	296,7	180	7000	31,274	1660	5340
22SGS46-02	12/08/2022	BBCH 65	1,276	385,8	-1,8	294,4	180	7000	31,274	1700	5300

RAC specimens were put in deep freezing conditions at a target temperature of ≤ -18°C on the day of sampling, within 6 hours after sampling.

Table A 8: Sampling procedures and shipment of RAC specimens - trial 22SGS46-01

Specimen no.	Plot ID	Actual sampling date	Growth stage	Sampling event	Actual DALA	Matrix	Specimen weight [g]	Specimens water content [%]	Starting time of spenimens collection	Time in freezer	Condition during transport	Target storage temp. [°C]	Shipment data*	Specimens delivered to laboratory
22SGS46-01 1	U	30/08/2022	BBCH 69	S1-end of flowering	21	Honey	109	16	11:06	13:00	Gel packs	< - 18	07/09/2022	08/09/2022
22SGS46-01 1R							103						-	-
22SGS46-01 2	T						104	17	11:41	13:00	Gel packs		07/09-2022	08/09/2022
22SGS46-01 2R							104						-	-

* only a part of specimens were shipped. The other part are spare specimens that were retained deep-frozen, unless required for analysis

Table A 9: Sampling procedures and shipment of RAC specimens - trial 22SGS46-02

Specimen no.	Plot ID	Actual sampling date	Growth stage	Sampling event	Actual DALA	Matrix	Specimen weight [g]	Specimens water content [%]	Starting time of spenimens collection	Time in freezer	Condition during transport	Target storage temp. [°C]	Shipment data*	Specimens delivered to laboratory
22SGS46-02 1	U	30/08/2022	BBCH 69	S1-end of flowering	18	Honey	106	17	13:20	15:05	Gel packs	< - 18	07/09/2022	08/09/2022
22SGS46-02 1R							105						-	-
22SGS46-02 2	T						103	18	14:02	15:05	Gel packs		07/09-2022	08/09/2022
22SGS46-02 2R							102						-	-

* only a part of specimens were shipped. The other part are spare specimens that were retained deep-frozen, unless required for analysis

Analytical phase

The objective of this analytical phase (of the SGS study 22SGS46) is to analyse honey specimens to determine the magnitude of residues of prothioconazole, its metabolite prothioconazole-desthio, and the triazole derivative metabolites (TDMs) 1,2,4-triazole (1,2,4-T), triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA).

The analytical method for the determination of Prothioconazole and Prothioconazole-desthio in honey consisted in a dissolution of the honey sample in a mixture of acetonitrile/water 80:20 containing 5 g/L of L-cysteine hydrochloride. Then, the separation of the acetonitrile layer was achieved by the addition of sodium chloride. After centrifugation and filtration, the acetonitrile extract was analysed using a HPLC-MS/MS (high-performance liquid chromatography + triple-quadrupole mass spectrometry), acquiring 2 simultaneous MRM transitions (primary and confirmatory) for each analyte.

The analytical method was validated under GLP compliance according to SANTE/2020/12830 Rev.1 guideline.

The analytical method for the determination of the TDM (triazole-derivative metabolites) 1,2,4-triazole, triazole-alanine, triazole-lactic acid and triazole-acetic acid (TAA) consisted in the addition of a proper amount of ILIS (isotope-labelled internal standards) and in a dissolution of the honey sample in deionised water. After that, methanol with 1 % formic acid was added. The mixture was then filtered and analysed using a HPLC-MS/MS system (high-performance liquid chromatography + triple quadrupole mass spectrometry) equipped with a differential mobility separation device (DMS), acquiring 2 simultaneous MRM transitions (primary and confirmatory) for each analyte.

The analytical method was validated under GLP compliance according to SANTE/2020/12830 Rev.1 guideline.

Results of the validation parameters are summarised below. Details are included in dRR Part B5 (Analytical Methods).

Table A 10: Validation results summary for the determination of Prothioconazole and Prothioconazole-desthio

<table>
<tr><th>Parameter</th><th>Result</th><th>SANTE/2020/12830 rev.1 limit</th></tr>
<tr><td>Matrix effect</td><td>
<table>
<tr><th>Analyte</th><th>Matrix effect (%)</th></tr>
<tr><td>Prothioconazole</td><td>-2.1 (not significant)</td></tr>
<tr><td>Prothioconazole-desthio</td><td>-12.2 (not significant)</td></tr>
</table>
</td><td>< ±20%</td></tr>
<tr><td rowspan="2">Calibration (matrix-matched)</td><td>
<table>
<tr><th>Analyte</th><th>Range (µg/L)</th><th>Range</th></tr>
<tr><td>Prothioconazole</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Prothioconazole-desthio</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
</table>
</td><td>At least from 30% of LOQ to at least 20% above the highest level</td></tr>
<tr><td>The regressions residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.</td><td>Residuals randomly distributed</td></tr>
<tr><td>Recovery and precision (repeatability)</td><td>
<table>
<tr><th colspan="5">Prothioconazole</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (344.0/125.0)</td><td>90.3</td><td>4.3</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>89.4</td><td>6.3</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (344.0/125.0)</td><td>92.4</td><td>3.5</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>93.5</td><td>3.7</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (344.0/125.0)</td><td>91.3</td><td>3.9</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>91.5</td><td>5.4</td></tr>
</table>
<table>
<tr><th colspan="5">Prothioconazole-desthio</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (312.2/69.8)</td><td>100.4</td><td>2.1</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>100.6</td><td>2.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (312.2/69.8)</td><td>98.4</td><td>1.6</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>97.7</td><td>2.0</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (312.2/69.8)</td><td>99.4</td><td>2.1</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>99.2</td><td>2.6</td></tr>
</table>
n = number of replicates
</td><td><u>LOQ level</u>
<u>(0.01 mg/kg or 0.01 mg/L)</u>
recoveries 60 – 120%
RSD ≤ 30%

<u>10xLOQ level</u>
<u>(0.1 mg/kg or 0.1 mg/L)</u>
recoveries 70 – 120%
RSD ≤ 20%</td></tr>
<tr><td>Untreated sample</td><td>For each analyte: < 30% LOQ (< LOD, 2 replicates)</td><td>≤ 30% of LOQ</td></tr>
<tr><td>Limit of quantification (LOQ)</td><td>Verified at 0.01 mg/kg for each analyte:
recovery and repeatability data in compliance with the guideline</td><td>LOQ: lowest validated level with sufficient recovery and precision</td></tr>
<tr><td>Limit of detection (LOD)</td><td>Verified at 0.0020 mg/kg for each analyte (at the lowest calibration point of 20% of LOQ), with a signal/noise ratio higher than 3</td><td>LOD ≤ 30% of LOQ</td></tr>
<tr><td>Selectivity and specificity</td><td>Verified for each analyte: no interferences found untreated samples in amounts higher than 30% of the LOQ (< LOD)</td><td>Blank values not higher than 30% of LOQ</td></tr>
<tr><td>Confirmation</td><td>Confirmation of each analyte achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements</td><td>Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity</td></tr>
<tr><td>Stability of the analyte in the samples extract</td><td>Verified for 3 days at 5 ± 3°C in the dark, in detail:
<table>
<tr><th>Analyte</th><th>Storage conditions</th><th>% Residual analyte after storage</th></tr>
<tr><td>Prothioconazole</td><td rowspan="2">3 days at 5 ± 3°C</td><td>94.7</td></tr>
<tr><td>Prothioconazole-desthio</td><td>98.7</td></tr>
</table>
</td><td>70-120%</td></tr>
<tr><td>Stability of the analyte in the standard solution</td><td>Verified for 29 days at 5±3°C in the dark (stock solution in acetonitrile).
Variation of analytes after storage:
<table>
<tr><th>Analyte</th><th>Storage conditions</th><th>% difference after storage</th></tr>
<tr><td>Prothioconazole</td><td rowspan="2">29 days at 5 ± 3°C</td><td>-0.4</td></tr>
<tr><td>Prothioconazole-desthio</td><td>-0.1</td></tr>
</table>
</td><td>< 10%</td></tr>
</table>

Table A 11: Validation results summary for the determination of TDM

<table>
<tr><th>Parameter</th><th>Result</th><th>SANTE/2020/12830 rev.1 limit</th></tr>
<tr><td>Matrix effect</td><td>
<table>
<tr><th>Analyte</th><th>Matrix effect (%)</th></tr>
<tr><td>1,2,4-Triazole</td><td>-5.7 (not significant)</td></tr>
<tr><td>Triazole Alanine</td><td>-8.9 (not significant)</td></tr>
<tr><td>Triazole Acetic Acid</td><td>-1.1 (not significant)</td></tr>
<tr><td>Triazole Lactic Acid</td><td>-4.3 (not significant)</td></tr>
</table>
</td><td>< ±20%</td></tr>
<tr><td rowspan="2">Calibration (matrix-matched)</td><td>
<table>
<tr><th>Analyte</th><th>Range (µg/L)</th><th>Range</th></tr>
<tr><td>1,2,4-Triazole</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Alanine</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Acetic Acid</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Lactic Acid</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
</table>
</td><td>At least from 30% of LOQ to at least 20% above the highest level</td></tr>
<tr><td>The regressions residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.</td><td>Residuals randomly distributed</td></tr>
<tr><td>Recovery and precision (repeatability)</td><td>
<table>
<tr><th colspan="5">1,2,4-triazole</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (70.1/43.1)</td><td>86.9</td><td>7.8</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>90.1</td><td>5.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (70.1/43.1)</td><td>93.6</td><td>2.7</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>94.0</td><td>3.7</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (70.1/43.1)</td><td>90.3</td><td>6.7</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>92.0</td><td>4.9</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-alanine</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (157/70)</td><td>96.9</td><td>5.7</td></tr>
<tr><td>Confirmatory (157/88)</td><td>88.6</td><td>5.8</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (157/70)</td><td>93.1</td><td>6.6</td></tr>
<tr><td>Confirmatory (157/88)</td><td>87.3</td><td>5.9</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (157/70)</td><td>95.0</td><td>6.2</td></tr>
<tr><td>Confirmatory (157/88)</td><td>88.0</td><td>5.6</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-acetic acid</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (128/70)</td><td>102.1</td><td>3.7</td></tr>
<tr><td>Confirmatory (128/73)</td><td>103.9</td><td>8.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (128/70)</td><td>97.1</td><td>4.8</td></tr>
<tr><td>Confirmatory (128/73)</td><td>96.5</td><td>8.9</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (128/70)</td><td>99.6</td><td>4.8</td></tr>
<tr><td>Confirmatory (128/73)</td><td>100.2</td><td>9.1</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-lactic acid</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (158/70)</td><td>96.7</td><td>7.5</td></tr>
<tr><td>Confirmatory (158/43)</td><td>95.9</td><td>13.6</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (158/70)</td><td>96.0</td><td>7.4</td></tr>
<tr><td>Confirmatory (158/43)</td><td>99.0</td><td>6.2</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (158/70)</td><td>96.4</td><td>7.0</td></tr>
<tr><td>Confirmatory (158/43)</td><td>97.4</td><td>10.0</td></tr>
</table>
n = number of replicates
</td><td><u>LOQ level</u>
<u>(0.01 mg/kg or 0.01 mg/L)</u>
recoveries 60 – 120%
RSD ≤ 30%

<u>10xLOQ level</u>
<u>(0.1 mg/kg or 0.1 mg/L)</u>
recoveries 70 – 120%
RSD ≤ 20%</td></tr>
<tr><td>Untreated sample</td><td>For each analyte: < 30% LOQ (< LOD, 2 replicates)</td><td>≤ 30% of LOQ</td></tr>
<tr><td>Limit of quantification (LOQ)</td><td>Verified at 0.01 mg/kg for each analyte:
recovery and repeatability data in compliance with the guideline</td><td>LOQ: lowest validated level with sufficient recovery and precision</td></tr>
<tr><td>Limit of detection (LOD)</td><td>Verified at 0.0020 mg/kg for each analyte (at the lowest calibration point of 20% of LOQ), with a signal/noise ratio higher than 3</td><td>LOD ≤ 30% of LOQ</td></tr>
<tr><td>Selectivity and specificity</td><td>Verified for each analyte: no interferences found untreated samples in amounts higher than 30% of the LOQ (< LOD)</td><td>Blank values not higher than 30% of LOQ</td></tr>
</table>

<table>
<tr><td>Confirmation</td><td colspan="2">Confirmation of each analyte achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements</td><td>Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity</td></tr>
<tr><td>Stability of the analyte in the samples extract</td><td colspan="2">Not required since ILIS were used</td><td>Not required since ILIS were used</td></tr>
<tr><td>Stability of the analyte in the standard solution</td><td colspan="2">Verified for 29 days at 5±3°C in the dark (stock solution in water).
Variation of analytes after storage:
<table><tr><th>Analyte</th><th>Storage conditions</th><th>% difference after storage</th></tr><tr><td>1,2,4-Triazole</td><td rowspan="4">29 days at 5 ± 3°C</td><td>-0.1</td></tr><tr><td>Triazole Alanine</td><td>-0.5</td></tr><tr><td>Triazole Acetic Acid</td><td>6.2</td></tr><tr><td>Triazole Lactic Acid</td><td>7.6</td></tr></table></td><td>< 10%</td></tr>
</table>

Results and Discussion

Residues of difenoconazole in honey are presented in the tables below. Residues in honey in all treated and untreated samples were below the LOQ (0.01 mg/kg).

Table A 12: Samples analysis results - Prothioconazole and Prothioconazole-desthio

Trial no.	Plot ID	Specimen id Plot		Analytical phase sample code	Sample weight [g]	Final volume [mL]	Analysis date	Result [mg/kg]	
								Prothioconazole	Prothioconazole-desthio
22SGS46-01	U	22SGS46-01	1	CDS-22-839	5.05	20	22/09/2022	< LOD	< LOD
	T	22SGS46-01	2	CDS-22-840	5.11	20	22/09/2022	< LOD	< LOD
22SGS46-02	U	22SGS46-02	1	CDS-22-841	4.97	20	22/09/2022	< LOD	< LOD
	T	22SGS46-02	2	CDS-22-842	4.99	20	22/09/2022	< LOD	< LOD

U: untreated plot, T: treated plot
LOQ: limit of quantification (0.010 mg/kg)
LOD: limit of detection (0.002 mg/kg)

Table A 13: Samples analysis results - TDM

Trial no.	Plot ID	Specimen id Plot		Analytical phase sample code	Sample weight [g]	Final volume [mL]	Analysis date	Result (mg/kg)			
								1,2,4-triazole	Triazole-Alanine	Triazole-Acetic acid	Triazole-Lactic acid
22SGS46-01	U	22SGS46-01	1	CDS-22-839	5.09	20	22/09/2022	< LOD	< LOQ (0.00208)	< LOD	< LOD
	T	22SGS46-01	2	CDS-22-840	5.06	20	22/09/2022	< LOD	< LOQ (0.00648)	< LOD	< LOD
22SGS46-02	U	22SGS46-02	1	CDS-22-841	4.98	20	22/09/2022	< LOD	< LOQ (0.00768)	< LOD	< LOD
	T	22SGS46-02	2	CDS-22-842	4.93	20	22/09/2022	< LOD	< LOQ (0.00613)	< LOD	< LOD

U: untreated plot, T: treated plot
LOQ: limit of quantification (0.010 mg/kg)
LOD: limit of detection (0.002 mg/kg)

Conclusion

Study 22SGS46; LBN-0044-2022 for the analysis of residues of prothioconazole in honey sampled from flowering phacelia in tunnel trials has not previously been submitted.
Two residue trials were conducted on phacelia rape in Poland in 2022 where honey was sampled following the exposure of bees to treated crop. Prothioconazole was applied at a rate of 385.8 g a.s./ha at BBCH 65. Mature honey was sampled 18-21 days after application of prothioconazole. The health status of all colonies was good throughout all trials.

Residues of prothioconazole, prothioconazole-desthio and TDM in honey in all treated plots were below the LOQ (0.01 mg/kg).

Table A 14: Residue trial summary for Protiokonazol 300 EC in honey from bees foraging on phacelia (study no. 22SGS46)

Trial No./ Location/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or number and last date	Growth stage at last treatment	Date colony placed in tunnel	Portion analysed	Residues (mg/kg)						Remarks
			g a.s./ha	Water (l/ha)	g a.s./hl					Prothiocon azole	Prothiocon azole-desthio	1,2,4-triazole	Triazole-Alanine	Triazole-Acetic acid	Triazole-Lactic acid	
22SGS46-01/ Poland/ 2022	Phacelia/ Stala	1. 03/06/2022 2. no data 3. NAP	385.8	296.7	130.03	09/08/2022	BBCH 65	09/08/2022 before application	Honey	<LOD	<LOD	<LOD	< LOQ	<LOD	<LOD	HPLC-MS/MS LOQ - 0.01 mg/kg LOD - 0.002 mg/kg
22SGS46-02/ Poland/ 2022	Phacelia/ Stala	1. 01/06/2022 2. no data 3. NAP	385.8	294.4	131.04	12/08/2022	BBCH 65	12/08/2022 before applicztion	Honey	<LOD	<LOD	<LOD	< LOQ	<LOD	<LOD	HPLC-MS/MS LOQ - 0.01 mg/kg LOD - 0.002 mg/kg

LOD = Limit of detection
LOQ = Limit of quantification
NAP = not applicable

A 2.1.7.1.2 Study 2

Comments of zRMS:	Study is accepted

Reference: KCA 6.10/02a
KCA 6.10/02b

Report: Magnitude of the residue of prothioconazole, prothioconazole-desthio and triazole-derivative metabolites (TDMs) in honey after one application of PROTIOKONAZOL 300 EC on Phacelia crop under semi field conditions in two trials in Southern Europe - 2022; Company Report No.: 1147.2F.SAG22; LBN-0045-2022, Rovetto. I, 2022/2023 (Field and Analytical Report)

Guideline(s): Reg. (EC) no. 1107/2009; Reg. (EU) 283/2013 and 284/2013; 7029/VI/95 rev.5; OECD TG 509; SANTE/2020/12830 rev.1; SANTE/11956/2016 rev.9; SANTE/2019/12752; ENV/MC/CHEM(98)17; ENV/JM/MONO(99)22; ENV/JM/MONO(2002)9

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods

The objective of this study was to determine the magnitude of residues of prothioconazole, its metabolite prothioconazole-desthio and the triazole-derivative metabolites (TDMs): triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole lactic acid (TLA), triazole acetic acid (TAA) in honey after one application of PROTIOKONAZOL 300 EC.
For this purpose, two trials were conducted in Southern Europe (Italy) in 2022.

Table A 15: Test item data

Name	Protiokonazol 300 EC
Code	Protiokonazol 300 EC
Batch No.	01/PRO/2022
Active substance	prothioconazole
CAS	178928/70-6
Formulation	Emulsifiable concentrate (EC)
Density	1.031 g/cm^3
Content of a.s.	Nominal: 300 g/L Analysed: 306.3 g/L
Expiration date	March 2025

Table A 16: Test system

Crop	Phacelia (*Phacelia tanacetifolia*)
Variety, planting date	F03942, 28/07/2022 F03942, 30/07/2022
RACs harvested	Honey

Study Design and Methods

Table A 17: Test facilities

Field Phase	SAGEA Centro di Saggio s.r.l., Via San Sudario, 15, 12050 Castagnito d'Alba (CN), Italy
Analytical Phase	LabAnalysis s.r.l., GLP Studies Department, Via Europa 5, 27041 Casanova Lonati (PV), Italy

Field phase

Two trials were conducted in Italy (SEU) in 2022. Tunnels trials were set up to assess the inadvertent residues in honey arising from application of plant protection products. Insect-proof tunnels were used to maximize the exposure of the bee colonies to treated plants.

In each trial two insect-proof tunnels were set up for collection of honey specimens: one untreated tunnel U and one treated tunnel T. Two healthy and representative beehives were introduced respectively into the tunnel U and tunnel T the day before the application.

In the treated plot T, one application of the formulated product PROTIOKONAZOL 300 EC was carried out around crop full flowering (BBCH 65) at a rate of 1.3 L f.p./ha (390 g a.s./ha). The application occurred one day after introduction of the beehives in the tunnels.

Mature honey specimens were collected when honey was ripe, 13 days after the application and anyway before the end of the flowering.

The specimens were stored and shipped deep-frozen to the analytical facility (LabAnalysis s.r.l.) in Italy; specimens were received deep-frozen and in good conditions by the analytical laboratory.

Table A 18: Identification of the field trials

Trial no.	Study type	Country (region)	Trial site	Zip code
1147.F.SAG22/r	HS	Italy / Piedmont / Cuneo	Castagnito d'Alba	12050
1198.F.SAG22/r	HS	Italy / Piedmont / Cuneo	Baldissero d'Alba	12040

Table A 19: Application details

Trial	**1147.F.SAG22/r**		**1198.F.SAG22/r**	
Plot ID	**T (Subplot 1)**	**T (Subplot 2)**	**T (Subplot 1)**	**T (Subplot 2)**
Application number	A1	A1	A1	A1
Date	25 Oct 2022	25 Oct 2022	27 Oct 2022	27 Oct 2022
Application actual interval (days)	-	-	-	-
Test item (formulated product)	PROTIOKONAZOL 300 EC	PROTIOKONAZOL 300 EC	PROTIOKONAZOL 300 EC	PROTIOKONAZOL 300 EC
Crop growth stage (BBCH)	65	65	65	65
Target application volume	300 L/ha	300 L/ha	300 L/ha	300 L/ha
Target application rate (formulated product)	1300 mL/ha	1300 mL/ha	1300 mL/ha	1300 mL/ha
Target application rate of a.i. (from nominal content)	390 g/ha	390 g/ha	390 g/ha	390 g/ha
Deviation [%][a]	-0.67	+1.17	-1.07	+0.67
Actual application volume (water L/ha)	298.00 L/ha	303.50 L/ha	296.80 L/ha	302.00 L/ha
Actual application rate (formulated product)	1291.04 mL/ha	1314.87 mL/ha	1286.13 mL/ha	1308.67 mL/ha
Actual application rate (a.i. g/ha) (from actual content)[b]	395.45 g/ha	402.75 g/ha	393.94 g/ha	400.84 g/ha
Equipment type*	Boom sprayer + Compressed Air Pump	Boom sprayer + Compressed Air Pump	Boom sprayer + Compressed Air Pump	Boom sprayer + Compressed Air Pump
Equipment information	BT27/BT27A/BT	BT27/BT27A/BT	BT27/BT27A/BT	BT27/BT27A/BT

(codes)	27A-04/PP14/PP15/CR68	27A-04/PP14/PP15/CR68	27A-04/PP14/PP15/CR68	27A-04/PP14/PP15/CR68
Nozzle type	Flat fan (anti-drift)	Flat fan (anti-drift)	Flat fan (anti-drift)	Flat fan (anti-drift)
Nozzle size	TeeJet AI110015VS	TeeJet AI110015VS	TeeJet AI110015VS	TeeJet AI110015VS
Nozzle number/spacing (cm)	5 / 50	4 / 50	5 / 50	5 / 50
Application pressure (bar)	2.0	2.0	2.0	2.0
Spray width (m)	2.50	2.00	2.50	2.50
Distance from target (m)	0.50	0.50	0.50	0.50
Type of application	Foliar	Foliar	Foliar	Foliar
Transport temperature of the test item to the trial site (°C)	Min 16.2 – Max 18.9	Min 16.2 – Max 18.9	Min 15.1 – Max 18.4	Min 15.1 – Max 18.4
Air temp, shade (°C)	21.6	22.0	15.7	16.0
Soil temp, 10 cm (°C)	16.3	16.4	14.2	14.2
Relative humidity (%)	64	62	60	59
Wetness of foliage	Dry	Dry	Dry	Dry
Wetness of soil	Dry	Dry	Dry	Dry
Wind speed range (m/s)	0.0	0.0	0.0	0.0
Wind direction	-	-	-	-
Cloud cover (%)	0	0	30	30
Rainfall after application (within 6 hours)	No	No	No	No
Total crop height (m)	1.20	1.20	1.30	1.30

* Equipment calibration was performed on treatment date or the day before. Application rate was verified by calibration and confirmed by measuring the remaining volume after the application. Calibration records are archived with raw data.
a % deviation of the actual application rate versus the intended (target) application rate
b Based on the actual a.i. content stated in the certificate of analysis
BBCH: growth stage code for plants according to the BBCH Monograph

Table A 20: Sampling details

Sampling date	Actual timing	Days between application and harvest	Type of specimen	Weight [g] [net]*	Plot ID	Specimen ID
07 Nov 2022	As soon as mature honey** was available	13	Mature honey	41.5	U	1-U-1147.F.SAG22S
			Mature honey	46.0	U	2-U-1147.F.SAG22R
			Mature honey	47.5	T	3-T-1147.F.SAG22S
			Mature honey	47.0	T	4-T-1147.F.SAG22R
07 Nov 2022	As soon as mature honey** was available	11	Mature honey	43.5	U	5-U-1198.F.SAG22S
			Mature honey	40.0	U	6-U-1198.F.SAG22R
			Mature honey	48.0	T	7-T-1198.F.SAG22S
			Mature honey	48.0	T	8-T-1198.F.SAG22R

*Weight of the collected honey (weight of the container not included)
**Mature honey (= honey sampled from capped honey cells or honey with water content between 16% and 20%)

Honey was collected from the empty combs previously added just before the test item application event. The honey sample was taken at 3 different spots on 2 different combs per hive and combined as one pooled sample. Honey was collected on the combs by gently pushing a spoon into the walls of the storage cells, allowing the honey to flow onto the spoon, always ensuring that honey was collected without any

debris (no cell walls, no pollen, no wax). For each colony/sample a new tool or a cleaned tool was used.
The water content of the collected honey was measured by means of a refractometer, to ensure that it was mature (between 16-20%). Disposable gloves were worn for sampling. The untreated plot was sampled first. The sampling equipment (including gloves and bags) was dry and cleaned between each plot.
Specimens were stored deep frozen (temperature ≤ –18°C) within 12 hours from sampling, until the laboratory analysis.

Analytical phase
The objective of the analytical phase was to analyse honey specimens to determine the magnitude of residues of prothioconazole, its metabolite prothioconazole-desthio, and the triazole-derivative metabolites (TDMs) 1,2,4-triazole (1,2,4-T), triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA).
The analyses were carried out according to the following analytical methods validated under GLP compliance according to SANTE/12830/2020 rev.1:

- Analytical method AM1-LBN-0044-2022 "Determination of Prothioconazole and Prothioconazole-desthio in honey", validated under GLP compliance in the analytical phase LBN-0044-2022 (Test Site: LabAnalysis s.r.l., Principal Investigator: Longhi Diego) of the study 22SGS46 (Test Facility SGS Polska Sp. z o. o., Study Director Tomasz Peda);
- Analytical method AM2-LBN-0044-2022 "Determination of TDM in honey", validated under GLP compliance in the analytical phase LBN-0044-2022 (Test Site: LabAnalysis s.r.l., Principal Investigator: Longhi Diego) of the study 22SGS46 (Test Facility SGS Polska Sp. z o. o., Study Director Tomasz Peda).

The analytical method to quantify prothioconazole and its metabolite prothioconazole-desthio in honey (codified as AM1-LBN-0044-2022) was based in a dissolution of the sample in a mixture of acetonitrile/water 80:20 containing 5 g/L of L-cysteine hydrochloride. Then, the separation of the acetonitrile layer was achieved by the addition of sodium chloride. After centrifugation and filtration, the acetonitrile extract was analysed using a HPLC-MS/MS (high-performance liquid chromatography + triple-quadrupole mass spectrometry), acquiring 2 simultaneous MRM transitions (primary and confirmatory) for each analyte.

The applied analytical method (AM2-LBN-0044-2022) allowed the determination of the following TDM (triazole-derivative metabolites):
- 1,2,4-triazole (TRZ)
- Triazole-alanine (TA)
- Triazole-lactic acid (TLA)
- Triazole-acetic acid (TAA).

After addition of a proper amount of ILIS (isotope-labelled internal standards), the honey sample was dissolved in deionised water. After that, methanol with 1% formic acid was added. The mixture was then filtered and analyzed using a HPLC-MS/MS system (high-performance liquid chromatography + triple quadrupole mass spectrometry) equipped with a differential mobility separation device (DMS) acquiring 2 simultaneous MRM transitions (primary and confirmatory) for each analyte.
Results of the validation parameters are summarised below. Details are included in dRR Part B5.

Table A 21: Validation results summary for the determination of Prothioconazole and Prothioconazole-desthio

<table>
<tr><th>Parameter</th><th>Result</th><th>SANTE/2020/12830 rev.1 limit</th></tr>
<tr><td>Matrix effect</td><td>
<table>
<tr><th>Analyte</th><th>Matrix effect (%)</th></tr>
<tr><td>Prothioconazole</td><td>-2.1 (not significant)</td></tr>
<tr><td>Prothioconazole-desthio</td><td>-12.2 (not significant)</td></tr>
</table>
</td><td>< ±20%</td></tr>
<tr><td rowspan="2">Calibration (matrix-matched)</td><td>
<table>
<tr><th>Analyte</th><th>Range (µg/L)</th><th>Range</th></tr>
<tr><td>Prothioconazole</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Prothioconazole-desthio</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
</table>
</td><td>At least from 30% of LOQ to at least 20% above the highest level</td></tr>
<tr><td>The regressions residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.</td><td>Residuals randomly distributed</td></tr>
<tr><td>Recovery and precision (repeatability)</td><td>
<table>
<tr><th colspan="5">Prothioconazole</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (344.0/125.0)</td><td>90.3</td><td>4.3</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>89.4</td><td>6.3</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (344.0/125.0)</td><td>92.4</td><td>3.5</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>93.5</td><td>3.7</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (344.0/125.0)</td><td>91.3</td><td>3.9</td></tr>
<tr><td>Confirmatory (344.0/102.3)</td><td>91.5</td><td>5.4</td></tr>
</table>
<table>
<tr><th colspan="5">Prothioconazole-desthio</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (312.2/69.8)</td><td>100.4</td><td>2.1</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>100.6</td><td>2.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (312.2/69.8)</td><td>98.4</td><td>1.6</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>97.7</td><td>2.0</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (312.2/69.8)</td><td>99.4</td><td>2.1</td></tr>
<tr><td>Confirmatory (312.2/125.0)</td><td>99.2</td><td>2.6</td></tr>
</table>
n = number of replicates
</td><td><u>LOQ level</u>
<u>(0.01 mg/kg or 0.01 mg/L)</u>
recoveries 60 – 120%
RSD ≤ 30%

<u>10xLOQ level</u>
<u>(0.1 mg/kg or 0.1 mg/L)</u>
recoveries 70 – 120%
RSD ≤ 20%</td></tr>
<tr><td>Untreated sample</td><td>For each analyte: < 30% LOQ (< LOD, 2 replicates)</td><td>≤ 30% of LOQ</td></tr>
<tr><td>Limit of quantification (LOQ)</td><td>Verified at 0.01 mg/kg for each analyte:
recovery and repeatability data in compliance with the guideline</td><td>LOQ: lowest validated level with sufficient recovery and precision</td></tr>
<tr><td>Limit of detection (LOD)</td><td>Verified at 0.0020 mg/kg for each analyte (at the lowest calibration point of 20% of LOQ), with a signal/noise ratio higher than 3</td><td>LOD ≤ 30% of LOQ</td></tr>
<tr><td>Selectivity and specificity</td><td>Verified for each analyte: no interferences found untreated samples in amounts higher than 30% of the LOQ (< LOD)</td><td>Blank values not higher than 30% of LOQ</td></tr>
<tr><td>Confirmation</td><td>Confirmation of each analyte achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements</td><td>Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity</td></tr>
<tr><td>Stability of the analyte in the samples extract</td><td>Verified for 3 days at 5 ± 3°C in the dark, in detail:
<table>
<tr><th>Analyte</th><th>Storage conditions</th><th>% Residual analyte after storage</th></tr>
<tr><td>Prothioconazole</td><td rowspan="2">3 days at 5 ± 3°C</td><td>94.7</td></tr>
<tr><td>Prothioconazole-desthio</td><td>98.7</td></tr>
</table>
</td><td>70-120%</td></tr>
<tr><td>Stability of the analyte in the standard solution</td><td>Verified for 29 days at 5±3°C in the dark (stock solution in acetonitrile).
Variation of analytes after storage:
<table>
<tr><th>Analyte</th><th>Storage conditions</th><th>% difference after storage</th></tr>
<tr><td>Prothioconazole</td><td rowspan="2">29 days at 5 ± 3°C</td><td>-0.4</td></tr>
<tr><td>Prothioconazole-desthio</td><td>-0.1</td></tr>
</table>
</td><td>< 10%</td></tr>
</table>

Table A 22: Validation results summary for the determination of TDM

<table>
<tr><th>Parameter</th><th>Result</th><th>SANTE/2020/12830 rev.1 limit</th></tr>
<tr><td>Matrix effect</td><td>
<table>
<tr><th>Analyte</th><th>Matrix effect (%)</th></tr>
<tr><td>1,2,4-Triazole</td><td>-5.7 (not significant)</td></tr>
<tr><td>Triazole Alanine</td><td>-8.9 (not significant)</td></tr>
<tr><td>Triazole Acetic Acid</td><td>-1.1 (not significant)</td></tr>
<tr><td>Triazole Lactic Acid</td><td>-4.3 (not significant)</td></tr>
</table>
</td><td>< ±20%</td></tr>
<tr><td rowspan="2">Calibration (matrix-matched)</td><td>
<table>
<tr><th>Analyte</th><th>Range (µg/L)</th><th>Range</th></tr>
<tr><td>1,2,4-Triazole</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Alanine</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Acetic Acid</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
<tr><td>Triazole Lactic Acid</td><td>0.500 – 50.0</td><td>0.0020 mg/kg – 0.200 mg/kg (20% LOQ – 100% above 10xLOQ)</td></tr>
</table>
</td><td>At least from 30% of LOQ to at least 20% above the highest level</td></tr>
<tr><td>The regressions residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.</td><td>Residuals randomly distributed</td></tr>
<tr><td>Recovery and precision (repeatability)</td><td>
<table>
<tr><th colspan="5">1,2,4-triazole</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (70.1/43.1)</td><td>86.9</td><td>7.8</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>90.1</td><td>5.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (70.1/43.1)</td><td>93.6</td><td>2.7</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>94.0</td><td>3.7</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (70.1/43.1)</td><td>90.3</td><td>6.7</td></tr>
<tr><td>Confirmatory (70.1//70)</td><td>92.0</td><td>4.9</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-alanine</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (157/70)</td><td>96.9</td><td>5.7</td></tr>
<tr><td>Confirmatory (157/88)</td><td>88.6</td><td>5.8</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (157/70)</td><td>93.1</td><td>6.6</td></tr>
<tr><td>Confirmatory (157/88)</td><td>87.3</td><td>5.9</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (157/70)</td><td>95.0</td><td>6.2</td></tr>
<tr><td>Confirmatory (157/88)</td><td>88.0</td><td>5.6</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-acetic acid</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (128/70)</td><td>102.1</td><td>3.7</td></tr>
<tr><td>Confirmatory (128/73)</td><td>103.9</td><td>8.5</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (128/70)</td><td>97.1</td><td>4.8</td></tr>
<tr><td>Confirmatory (128/73)</td><td>96.5</td><td>8.9</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (128/70)</td><td>99.6</td><td>4.8</td></tr>
<tr><td>Confirmatory (128/73)</td><td>100.2</td><td>9.1</td></tr>
</table>
<table>
<tr><th colspan="5">Triazole-lactic acid</th></tr>
<tr><th>Level</th><th>Concentration</th><th>Transition</th><th>% Recovery</th><th>% RSD</th></tr>
<tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01 mg/kg</td><td>Primary (158/70)</td><td>96.7</td><td>7.5</td></tr>
<tr><td>Confirmatory (158/43)</td><td>95.9</td><td>13.6</td></tr>
<tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1 mg/kg</td><td>Primary (158/70)</td><td>96.0</td><td>7.4</td></tr>
<tr><td>Confirmatory (158/43)</td><td>99.0</td><td>6.2</td></tr>
<tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (158/70)</td><td>96.4</td><td>7.0</td></tr>
<tr><td>Confirmatory (158/43)</td><td>97.4</td><td>10.0</td></tr>
</table>
n = number of replicates
</td><td><u>LOQ level</u>
<u>(0.01 mg/kg or 0.01 mg/L)</u>
recoveries 60 – 120%
RSD ≤ 30%

<u>10xLOQ level</u>
<u>(0.1 mg/kg or 0.1 mg/L)</u>
recoveries 70 – 120%
RSD ≤ 20%</td></tr>
<tr><td>Untreated sample</td><td>For each analyte: < 30% LOQ (< LOD, 2 replicates)</td><td>≤ 30% of LOQ</td></tr>
<tr><td>Limit of quantification (LOQ)</td><td>Verified at 0.01 mg/kg for each analyte:
recovery and repeatability data in compliance with the guideline</td><td>LOQ: lowest validated level with sufficient recovery and precision</td></tr>
<tr><td>Limit of detection (LOD)</td><td>Verified at 0.0020 mg/kg for each analyte (at the lowest calibration point of 20% of LOQ), with a signal/noise ratio higher than 3</td><td>LOD ≤ 30% of LOQ</td></tr>
<tr><td>Selectivity and specificity</td><td>Verified for each analyte: no interferences found untreated samples in amounts higher than 30% of the LOQ (< LOD)</td><td>Blank values not higher than 30% of LOQ</td></tr>
</table>

<table>
<tr><td>Confirmation</td><td>Confirmation of each analyte achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements</td><td>Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity</td></tr>
<tr><td>Stability of the analyte in the samples extract</td><td>Not required since ILIS were used</td><td>Not required since ILIS were used</td></tr>
<tr><td>Stability of the analyte in the standard solution</td><td>Verified for 29 days at 5±3°C in the dark (stock solution in water).
Variation of analytes after storage:
<table>
<tr><th>Analyte</th><th>Storage conditions</th><th>% difference after storage</th></tr>
<tr><td>1,2,4-Triazole</td><td rowspan="4">29 days at 5 ± 3°C</td><td>-0.1</td></tr>
<tr><td>Triazole Alanine</td><td>-0.5</td></tr>
<tr><td>Triazole Acetic Acid</td><td>6.2</td></tr>
<tr><td>Triazole Lactic Acid</td><td>7.6</td></tr>
</table></td><td>< 10%</td></tr>
</table>

Results and Discussion

Residues of difenoconazole in honey are presented in the tables below. Residues in honey in all treated and untreated samples were below the LOQ (0.01 mg/kg).

Table A 23: Samples analysis results - Prothioconazole and Prothioconazole-desthio

Trial no.	Plot ID	Specimen id Plot	Analytical phase sample code	Sample weight [g]	Final volume [mL]	Analysis date	Result [mg/kg]	
							Prothioconazole	Prothioconazole-desthio
1147.F.SAG22/r	U	1-U-1147.F.SAG22S	CDS-22-1329	5.08	20	30/11/2022	< LOD	< LOD
	T	3-T-1147.F.SAG22S	CDS-22-1330	4.93	20	30/11/2022	< LOD	< LOD
1198.F.SAG22/r	U	5-U-1198.F.SAG22S	CDS-22-1331	5.08	20	30/11/2022	< LOD	< LOD
	T	7-T-1198.F.SAG22S	CDS-22-1332	5.03	20	30/11/2022	< LOD	< LOD

U: untreated plot, T: treated plot
LOQ: limit of quantification (0.010 mg/kg)
LOD: limit of detection (0.002 mg/kg)

Table A 24: Samples analysis results - TDM

Trial no.	Plot ID	Specimen id Plot	Analytical phase sample code	Sample weight [g]	Final volume [mL]	Analysis date	Result (mg/kg)			
							1,2,4-triazole	Triazole-Alanine	Triazole-Acetic acid	Triazole-Lactic acid
1147.F.SAG22/r	U	1-U-1147.F.SAG22S	CDS-22-1329	4.89	20	30/11/2022	< LOD	< LOD	< LOD	< LOQ (0.0020)
	T	3-T-1147.F.SAG22S	CDS-22-1330	4.96	20	30/11/2022	< LOD	< LOD	< LOD	< LOD
1198.F.SAG22/r	U	5-U-1198.F.SAG22S	CDS-22-1331	4.98	20	30/11/2022	< LOD	< LOD	< LOD	< LOQ (0.0022)
	T	7-T-1198.F.SAG22S	CDS-22-1332	4.95	20	30/11/2022	< LOD	< LOD	< LOD	< LOD

U: untreated plot, T: treated plot
LOQ: limit of quantification (0.010 mg/kg)
LOD: limit of detection (0.002 mg/kg)

Conclusion

Study 1147.2F.SAG22; LBN-0045-2022 for the analysis of residues of prothioconazole in honey sampled from flowering phacelia in tunnel trials has not previously been submitted.
Two residue trials were conducted on phacelia rape in Italy in 2022 where honey was sampled following the exposure of bees to treated crop. Prothioconazole was applied at a rate from 393.94 to 402.75 g a.s./ha at BBCH 65. Mature honey was sampled 18-21 days after application of prothioconazole. The health status of all colonies was good throughout all trials.

Residues of prothioconazole, prothioconazole-desthio and TDM in honey in all treated plots were below the LOD (0.002 mg/kg).

Table A 25: Residue trial summary for Protiokonazol 300 EC in honey from bees foraging on phacelia (study no. 1147.F.SAG22)

Trial No./ Location/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or number and last date	Growth stage at last treatment	Date colony placed in tunnel	Portion analysed	Residues (mg/kg)						Remarks
			g a.s./ha	Water (l/ha)	g a.s./hl					Prothiocon azole	Prothiocon azole-desthio	1,2,4-triazole	Triazole-Alanine	Triazole-Acetic acid	Triazole-Lactic acid	
1147.F.SAG22/r/ Italy/ 2022	Phacelia/ F03942	1. 28/07/2022 2. from 18/10/2022 to 10/11/2022 3. NAP	Subplot 1: 395.45 Subplot 2: 402.75	Subplot 1: 298 Subplot 2: 303.5	Subplot 1: 132.7 Subplot 2: 132.7	25/10/2022	BBCH 65	24/10/2022	Honey	<LOD	<LOD	<LOD	< LOQ	<LOD	<LOD	HPLC-MS/MS LOQ - 0.01 mg/kg LOD - 0.002 mg/kg
1198.F.SAG22/r/ Italy/ 2022	Phacelia/ F03942	1. 30/07/2022 2. from 18/10/2022 to 10/11/2022 3. NAP	Subplot 1: 393.94 Subplot 2: 400.84	Subplot 1: 296.8 Subplot 2: 302.0	Subplot 1: 132.7 Subplot 2: 132.7	27/10/2022	BBCH 65	26/10/2022	Honey	<LOD	<LOD	<LOD	< LOQ	<LOD	<LOD	HPLC-MS/MS LOQ - 0.01 mg/kg LOD - 0.002 mg/kg

LOD = Limit of detection
LOQ = Limit of quantification
NAP = not applicable

Appendix 3 Pesticide Residue Intake Model (PRIMo rev.3.1)

A 3.1 TMDI calculations - prothioconazole

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

prothioconazole (F)

LOQs (mg/kg) range from:	0,01	to:	0,05
Toxicological reference values			
ADI (mg/kg bw/day):	0,01	ARfD (mg/kg bw):	0,01
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2007	Year of evaluation:	2007

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

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

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
	45%	NL toddler	4,50	14%	Maize/corn	8%	Wheat	6%	Milk: Cattle	11%	11%
	34%	GEMS/Food G10	3,40	13%	Soyabeans	8%	Wheat	2%	Barley	3%	11%
	34%	GEMS/Food G11	3,37	15%	Soyabeans	7%	Wheat	3%	Barley	3%	10%
	33%	GEMS/Food G06	3,34	14%	Wheat	5%	Soyabeans	3%	Maize/corn	3%	15%
	32%	GEMS/Food G15	3,22	9%	Wheat	7%	Soyabeans	3%	Barley	3%	13%
	32%	GEMS/Food G07	3,20	8%	Wheat	7%	Soyabeans	2%	Barley	3%	12%
	32%	GEMS/Food G08	3,16	8%	Wheat	8%	Soyabeans	4%	Barley	3%	13%
	23%	FR child 3 15 yr	2,26	9%	Wheat	4%	Lentils	2%	Milk: Cattle	5%	9%
	23%	IE adult	2,25	6%	Peas	5%	Wheat	3%	Lentils	3%	5%
	22%	NL child	2,19	8%	Wheat	2%	Milk: Cattle	1%	Sunflower seeds	6%	10%
	22%	ES child	2,19	9%	Wheat	5%	Lentils	2%	Peas	3%	9%
	21%	DK child	2,08	9%	Wheat	6%	Rye	1%	Carrots	3%	9%
	20%	RO general	2,02	10%	Wheat	3%	Sunflower seeds	2%	Maize/corn	3%	10%
	19%	UK infant	1,86	5%	Wheat	4%	Milk: Cattle	2%	Maize/corn	6%	5%
	18%	DE child	1,82	8%	Wheat	2%	Milk: Cattle	1%	Apples	6%	8%
	17%	FR toddler 2 3 yr	1,71	6%	Wheat	3%	Milk: Cattle	2%	Lentils	5%	6%
	16%	IT toddler	1,58	13%	Wheat	0,7%	Lentils	0,2%	Peas	1%	13%
	16%	UK toddler	1,55	8%	Wheat	2%	Milk: Cattle	0,8%	Beans	4%	8%
	15%	PT general	1,46	8%	Wheat	1%	Soyabeans	1%	Sunflower seeds	2%	8%
	13%	ES adult	1,33	5%	Wheat	2%	Lentils	2%	Barley	2%	7%
	13%	SE general	1,25	6%	Wheat	1%	Milk: Cattle	0,8%	Carrots	3%	6%
	12%	NL general	1,22	4%	Wheat	1%	Barley	0,8%	Milk: Cattle	3%	6%
	12%	DE general	1,17	4%	Wheat	2%	Barley	1%	Milk: Cattle	3%	6%
	11%	DE women 14-50 yr	1,08	4%	Wheat	1%	Milk: Cattle	0,8%	Barley	3%	5%
	10%	FR adult	1,03	4%	Wheat	1%	Lentils	0,4%	Milk: Cattle	2%	4%
	10%	IT adult	1,02	8%	Wheat	0,4%	Lentils	0,2%	Peas	0,8%	8%
	8%	FI 3 yr	0,83	2%	Wheat	0,9%	Potatoes	0,9%	Peas	2%	3%
	8%	UK vegetarian	0,79	4%	Wheat	0,8%	Lentils	0,6%	Peas	1%	4%
	7%	FI 6 yr	0,74	2%	Wheat	1%	Peas	0,8%	Potatoes	1%	2%
	7%	FR infant	0,73	2%	Milk: Cattle	2%	Wheat	1%	Carrots	3%	2%
	7%	FI adult	0,65	3%	Coffee beans	0,7%	Peas	0,7%	Rye	3%	0,7%
	6%	LT adult	0,64	2%	Wheat	1%	Rye	0,6%	Potatoes	1%	2%
	6%	UK adult	0,62	3%	Wheat	0,3%	Milk: Cattle	0,3%	Potatoes	1%	3%
	6%	DK adult	0,56	2%	Wheat	0,5%	Milk: Cattle	0,5%	Rye	1%	2%
	3%	IE child	0,34	2%	Wheat	0,4%	Milk: Cattle	0,2%	Carrots	0,7%	2%
	3%	PL general	0,28	0,7%	Potatoes	0,4%	Peas	0,3%	Head cabbages	1%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of prothioconazole (F) is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

A 3.2 IEDI calculations - prothioconazole

Not required. TMDI below 100%.

A 3.3 IESTI calculations - Raw commodities - prothioconazole

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the Eu

The calculation is based on the large portion of the most critical consumer group.

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
29%	Wheat	0,1 / 0,2	2,9
22%	Barley	0,2 / 0,4	2,2
4%	Rapeseeds/canola	0,15 / 0,3	0,41

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
19%	Barley	0,2 / 0,4	1,9
17%	Wheat	0,1 / 0,2	1,7
2%	Rapeseeds/canola seeds	0,15 / 0,3	0,16

A 3.4 IESTI calculations - Processed commodities - prothioconazole

Processed commodities

Results for children				**Results for adults**			
No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
24%	Wheat / milling (flour)	0,1 / 0,2	2,4	29%	Barley / beer	0,2 / 0,08	2,9
15%	Barley / cooked	0,2 / 0,4	1,5	9%	Wheat / bread/pizza	0,1 / 0,2	0,88
11%	Wheat / milling (wholemea	0,1 / 0,2	1,1	8%	Wheat / pasta	0,1 / 0,2	0,76
7%	Barley / milling (flour)	0,2 / 0,4	0,72	7%	Wheat / bread	0,1 / 0,2	0,70
2%	Rapeseeds / oils	0,15 / 0,6	0,18				
Expand/collapse list							

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of prothioconazole (F) is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

A 3.5 TMDI calculations - Triazole alanine (TA) and triazole lactic acid (TLA)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

TA and TLA

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0,3	ARfD (mg/kg bw):	0,3
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2018	Year of evaluation:	2018

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

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

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	11%	NL toddler	33,27	3%	Maize/corn	2%	Wheat	2%	Milk: Cattle		2%
	8%	GEMS/Food G10	23,03	2%	Soyabeans	2%	Wheat	0,5%	Rice		2%
	8%	GEMS/Food G06	22,86	3%	Wheat	0,9%	Soyabeans	0,7%	Rice		3%
	7%	GEMS/Food G11	21,42	3%	Soyabeans	2%	Wheat	0,5%	Potatoes		2%
	7%	GEMS/Food G08	20,84	2%	Wheat	1%	Soyabeans	0,5%	Potatoes		2%
	7%	GEMS/Food G07	19,99	2%	Wheat	1%	Soyabeans	0,5%	Potatoes		2%
	7%	GEMS/Food G15	19,73	2%	Wheat	1%	Soyabeans	0,5%	Potatoes		2%
	6%	DK child	18,88	2%	Rye	2%	Wheat	0,3%	Milk: Cattle		2%
	6%	NL child	17,49	2%	Wheat	0,7%	Milk: Cattle	0,5%	Potatoes		2%
	5%	DE child	15,61	2%	Wheat	0,5%	Milk: Cattle	0,5%	Oranges		2%
	5%	FR child 3 15 yr	15,51	2%	Wheat	0,6%	Milk: Cattle	0,4%	Oranges		2%
	5%	RO general	14,84	2%	Wheat	0,5%	Potatoes	0,5%	Sunflower seeds		2%
	4%	UK infant	13,17	1%	Wheat	1%	Milk: Cattle	0,4%	Potatoes		1%
	4%	ES child	12,88	2%	Wheat	0,3%	Milk: Cattle	0,3%	Olives for oil production		2%
	4%	IT toddler	12,74	3%	Wheat	0,6%	Other cereals	0,1%	Potatoes		3%
	4%	FR toddler 2 3 yr	12,44	1%	Wheat	0,8%	Milk: Cattle	0,3%	Rice		1%
	4%	PT general	12,35	2%	Wheat	0,7%	Potatoes	0,3%	Rice		2%
	4%	SE general	12,22	1%	Wheat	0,7%	Bovine: Muscle/meat	0,6%	Potatoes		1%
	4%	UK toddler	12,13	2%	Wheat	0,6%	Milk: Cattle	0,5%	Potatoes		2%
	4%	IE adult	11,42	1,0%	Wheat	0,5%	Sweet potatoes	0,3%	Potatoes		1,0%
	3%	NL general	9,43	0,8%	Wheat	0,3%	Potatoes	0,2%	Milk: Cattle		1%
	3%	DE general	8,56	0,8%	Wheat	0,3%	Milk: Cattle	0,2%	Rye		1%
	3%	DE women 14-50 yr	8,49	0,9%	Wheat	0,3%	Milk: Cattle	0,2%	Oranges		1%
	3%	IT adult	8,23	2%	Wheat	0,3%	Other cereals	0,1%	Tomatoes		2%
	3%	FI 3 yr	7,89	0,6%	Potatoes	0,5%	Wheat	0,3%	Rye		0,6%
	3%	ES adult	7,79	1%	Wheat	0,2%	Barley	0,2%	Olives for oil production		1%
	2%	FR adult	6,39	1,0%	Wheat	0,1%	Milk: Cattle	0,1%	Bovine: Muscle/meat		1,0%
	2%	LT adult	6,39	0,5%	Rye	0,5%	Wheat	0,4%	Potatoes		0,5%
	2%	FI 6 yr	6,30	0,5%	Potatoes	0,4%	Wheat	0,3%	Rye		0,5%
	2%	UK vegetarian	5,50	0,9%	Wheat	0,2%	Potatoes	0,2%	Rice		0,9%
	2%	FR infant	5,20	0,4%	Milk: Cattle	0,3%	Wheat	0,3%	Potatoes		0,3%
	2%	UK adult	4,93	0,7%	Wheat	0,2%	Potatoes	0,2%	Rice		0,7%
	2%	DK adult	4,76	0,5%	Wheat	0,2%	Rye	0,2%	Potatoes		0,5%
	1%	FI adult	3,34	0,3%	Rye	0,2%	Potatoes	0,1%	Wheat		0,1%
	0,9%	IE child	2,83	0,5%	Wheat	0,1%	Rice	0,1%	Milk: Cattle		0,5%
	0,8%	PL general	2,48	0,5%	Potatoes	0,1%	Tomatoes	0,0%	Apples		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of TA and TLA is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

A 3.6 IEDI calculations - Triazole alanine (TA) and triazole lactic acid (TLA)

Not required. TMDI below 100%.

A 3.7 IESTI calculations - Raw commodities - Triazole alanine (TA) and triazole lactic acid (TLA)

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the Eu

The calculation is based on the large portion of the most critical consumer group.

Show results of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
6%	Wheat	0,64 / 1,29	19
2%	Barley	0,64 / 1,29	7,2
1%	Rapeseeds/canola	1,1 / 2,21	3,0

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Wheat	0,64 / 1,29	11
2%	Barley	0,64 / 1,29	6,2
0,4%	Rapeseeds/canola seeds	1,1 / 2,21	1,2

A 3.8 IESTI calculations - Processed commodities - Triazole alanine (TA) and triazole lactic acid (TLA)

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
5%	Wheat / milling (flour)	0,64 / 1,29	16
2%	Wheat / milling (wholemea	0,64 / 1,29	7,1
2%	Barley / cooked	0,64 / 1,29	4,7
0,8%	Barley / milling (flour)	0,64 / 1,29	2,3
0,4%	Rapeseeds / oils	1,1 / 4,42	1,3

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
3%	Barley / beer	0,64 / 0,26	9,3
2%	Wheat / bread/pizza	0,64 / 1,29	5,6
2%	Wheat / pasta	0,64 / 1,29	4,9
1%	Wheat / bread	0,64 / 1,29	4,5

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of TA and TLA is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

A 3.9 TMDI calculations - Triazole acetic acid (TAA)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

TAA

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	1	ARfD (mg/kg bw):	1
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2018	Year of evaluation:	2018

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

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

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	2%	NL toddler	24,44	1%	Maize/corn	0,6%	Wheat	0,2%	Milk: Cattle		0,7%
	2%	DK child	17,76	0,9%	Rye	0,7%	Wheat	0,1%	Oat		0,7%
	2%	GEMS/Food G06	17,37	1%	Wheat	0,2%	Rice	0,2%	Maize/corn		1%
	1%	IT toddler	13,47	1%	Wheat	0,2%	Other cereals	0,0%	Rice		1%
	1%	GEMS/Food G10	12,32	0,6%	Wheat	0,2%	Rice	0,1%	Maize/corn		0,7%
	1%	GEMS/Food G15	11,87	0,7%	Wheat	0,1%	Barley	0,1%	Maize/corn		0,8%
	1%	GEMS/Food G08	11,72	0,6%	Wheat	0,1%	Barley	0,1%	Rye		0,8%
	1%	RO general	11,09	0,8%	Wheat	0,2%	Maize/corn	0,0%	Milk: Cattle		0,8%
	1%	DE child	10,91	0,7%	Wheat	0,1%	Rye	0,1%	Milk: Cattle		0,7%
	1%	FR child 3 15 yr	10,73	0,7%	Wheat	0,1%	Milk: Cattle	0,1%	Rice		0,7%
	1%	GEMS/Food G07	10,64	0,7%	Wheat	0,1%	Barley	0,1%	Rice		0,8%
	1%	NL child	10,22	0,6%	Wheat	0,1%	Milk: Cattle	0,0%	Maize/corn		0,7%
	1,0%	GEMS/Food G11	9,71	0,6%	Wheat	0,1%	Barley	0,1%	Soyabeans		0,7%
	0,9%	ES child	9,43	0,7%	Wheat	0,1%	Rice	0,0%	Milk: Cattle		0,7%
	0,9%	UK infant	9,29	0,4%	Wheat	0,2%	Maize/corn	0,2%	Milk: Cattle		0,4%
	0,9%	PT general	9,09	0,6%	Wheat	0,1%	Rice	0,1%	Maize/corn		0,6%
	0,9%	UK toddler	8,79	0,6%	Wheat	0,1%	Rice	0,1%	Milk: Cattle		0,6%
	0,8%	IT adult	8,17	0,7%	Wheat	0,1%	Other cereals	0,0%	Rice		0,7%
	0,8%	FR toddler 2 3 yr	8,03	0,5%	Wheat	0,1%	Milk: Cattle	0,1%	Rice		0,5%
	0,7%	SE general	7,26	0,5%	Wheat	0,1%	Rice	0,0%	Milk: Cattle		0,5%
	0,6%	IE adult	6,24	0,4%	Wheat	0,0%	Buckwheat and other pseudo-cereals	0,0%	Rice		0,4%
	0,6%	DE general	6,13	0,3%	Wheat	0,1%	Rye	0,1%	Barley		0,4%
	0,6%	DE women 14-50 yr	5,93	0,3%	Wheat	0,1%	Rye	0,0%	Milk: Cattle		0,4%
	0,6%	ES adult	5,65	0,4%	Wheat	0,1%	Barley	0,0%	Rice		0,4%
	0,5%	FI 3 yr	5,26	0,2%	Wheat	0,1%	Rye	0,1%	Oat		0,2%
	0,5%	NL general	5,18	0,3%	Wheat	0,0%	Barley	0,0%	Milk: Cattle		0,4%
	0,5%	LT adult	4,70	0,2%	Rye	0,2%	Wheat	0,0%	Rice		0,2%
	0,5%	FR adult	4,56	0,4%	Wheat	0,0%	Rice	0,0%	Milk: Cattle		0,4%
	0,4%	UK vegetarian	4,42	0,3%	Wheat	0,1%	Rice	0,0%	Milk: Cattle		0,3%
	0,4%	FI 6 yr	4,11	0,2%	Wheat	0,1%	Rye	0,1%	Rice		0,2%
	0,4%	UK adult	3,73	0,3%	Wheat	0,1%	Rice	0,0%	Milk: Cattle		0,3%
	0,3%	DK adult	3,25	0,2%	Wheat	0,1%	Rye	0,0%	Milk: Cattle		0,2%
	0,3%	IE child	2,56	0,2%	Wheat	0,0%	Rice	0,0%	Milk: Cattle		0,2%
	0,2%	FR infant	2,41	0,1%	Wheat	0,1%	Milk: Cattle	0,0%	Rice		0,1%
	0,2%	FI adult	2,26	0,1%	Rye	0,1%	Wheat	0,0%	Oat		0,1%
	0,0%	PL general	0,23	0,0%	Potatoes	0,0%	Apples	0,0%	Table grapes		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of TAA is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

A 3.10 IEDI calculations - Triazole acetic acid (TAA)

Not required. TMDI below 100%.

A 3.11 IESTI calculations - Raw commodities - Triazole acetic acid (TAA)

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the Eu

The calculation is based on the large portion of the most critical consumer group.

Show results of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI): ---				**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI): ---			
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Wheat	0,79 / 1,58	23	1%	Wheat	0,79 / 1,58	13
0,9%	Barley	0,79 / 1,58	8,9	0,8%	Barley	0,79 / 1,58	7,6
0,03%	Rapeseeds/canola	0,12 / 0,24	0,33	0,01%	Rapeseeds/canola seeds	0,12 / 0,24	0,13
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

A 3.12 IESTI calculations - Processed commodities - Triazole acetic acid (TAA)

Processed commodities

Results for children				**Results for adults**			
No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
2%	Wheat / milling (flour)	0,79 / 1,58	19	1%	Barley / beer	0,79 / 0,32	11
0,9%	Wheat / milling (wholemea	0,79 / 1,58	8,8	0,7%	Wheat / bread/pizza	0,79 / 1,58	6,9
0,6%	Barley / cooked	0,79 / 1,58	5,7	0,6%	Wheat / pasta	0,79 / 1,58	6,0
0,3%	Barley / milling (flour)	0,79 / 1,58	2,9	0,6%	Wheat / bread	0,79 / 1,58	5,5
0,0%	Rapeseeds / oils	0,12 / 0,48	0,14				
Expand/collapse list							

Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity.

A short term intake of residues of TAA is unlikely to present a public health risk.

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

A 3.13 TMDI calculations - 1,2,4-triazole

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

1,2,4-triazole

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	0,023	ARfD (mg/kg bw):	0,1
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2018	Year of evaluation:	2018

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

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

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	91%	NL toddler	20,85	78%	Milk: Cattle	3%	Maize/corn	2%	Wheat		2%
	56%	UK infant	12,85	50%	Milk: Cattle	1%	Bovine: Muscle/meat	1%	Wheat		1%
	45%	FR toddler 2 3 yr	10,26	38%	Milk: Cattle	1%	Bovine: Muscle/meat	1%	Wheat		1%
	40%	NL child	9,24	32%	Milk: Cattle	2%	Sugar beet roots	2%	Wheat		2%
	38%	FR child 3 15 yr	8,74	30%	Milk: Cattle	2%	Wheat	2%	Bovine: Muscle/meat		2%
	33%	UK toddler	7,55	27%	Milk: Cattle	2%	Wheat	2%	Bovine: Muscle/meat		2%
	32%	DE child	7,33	26%	Milk: Cattle	2%	Wheat	0,9%	Oranges		2%
	25%	DK child	5,78	16%	Milk: Cattle	2%	Rye	2%	Wheat		2%
	25%	SE general	5,64	16%	Milk: Cattle	5%	Bovine: Muscle/meat	1%	Wheat		1%
	24%	FR infant	5,50	22%	Milk: Cattle	0,4%	Bovine: Muscle/meat	0,3%	Wheat		0,3%
	23%	ES child	5,29	16%	Milk: Cattle	2%	Wheat	2%	Bovine: Muscle/meat		2%
	21%	DE women 14-50 yr	4,79	16%	Milk: Cattle	1,0%	Sugar beet roots	0,9%	Wheat		1%
	21%	DE general	4,78	16%	Milk: Cattle	0,9%	Sugar beet roots	0,8%	Wheat		1%
	21%	RO general	4,74	15%	Milk: Cattle	2%	Wheat	0,7%	Swine: Muscle/meat		2%
	17%	GEMS/Food G11	3,86	10%	Milk: Cattle	2%	Wheat	0,8%	Bovine: Muscle/meat		2%
	16%	GEMS/Food G15	3,73	9%	Milk: Cattle	2%	Wheat	0,8%	Swine: Muscle/meat		2%
	16%	GEMS/Food G07	3,61	8%	Milk: Cattle	2%	Wheat	1%	Bovine: Muscle/meat		2%
	15%	NL general	3,56	11%	Milk: Cattle	0,9%	Bovine: Muscle/meat	0,8%	Wheat		1%
	14%	GEMS/Food G10	3,32	7%	Milk: Cattle	2%	Wheat	1%	Bovine: Muscle/meat		2%
	14%	GEMS/Food G08	3,29	7%	Milk: Cattle	2%	Wheat	1%	Swine: Muscle/meat		2%
	11%	GEMS/Food G06	2,61	3%	Milk: Cattle	3%	Wheat	0,7%	Rice		3%
	10%	IE adult	2,40	6%	Milk: Cattle	1,0%	Wheat	0,5%	Bovine: Muscle/meat		1%
	10%	ES adult	2,40	6%	Milk: Cattle	1%	Wheat	0,9%	Bovine: Muscle/meat		1%
	10%	DK adult	2,20	7%	Milk: Cattle	0,6%	Bovine: Muscle/meat	0,5%	Swine: Muscle/meat		0,5%
	9%	FR adult	2,13	6%	Milk: Cattle	1,0%	Wheat	0,7%	Bovine: Muscle/meat		1,0%
	8%	LT adult	1,79	5%	Milk: Cattle	0,5%	Swine: Muscle/meat	0,5%	Rye		0,5%
	6%	UK adult	1,48	4%	Milk: Cattle	0,8%	Bovine: Muscle/meat	0,7%	Wheat		0,7%
	6%	UK vegetarian	1,44	4%	Milk: Cattle	0,9%	Wheat	0,2%	Oranges		0,9%
	6%	IE child	1,33	5%	Milk: Cattle	0,5%	Wheat	0,1%	Rice		0,5%
	4%	IT toddler	0,98	3%	Wheat	0,7%	Other cereals	0,1%	Bananas		3%
	3%	PT general	0,78	2%	Wheat	0,3%	Rice	0,2%	Potatoes		2%
	3%	IT adult	0,62	2%	Wheat	0,3%	Other cereals	0,1%	Oranges		2%
	2%	FI 3 yr	0,54	0,5%	Wheat	0,3%	Bananas	0,3%	Rye		0,6%
	2%	FI 6 yr	0,41	0,4%	Wheat	0,3%	Rye	0,2%	Rice		0,5%
	1%	FI adult	0,23	0,3%	Rye	0,1%	Wheat	0,1%	Oranges		0,1%
	0,5%	PL general	0,13	0,1%	Potatoes	0,1%	Apples	0,1%	Head cabbages		

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of 1,2,4-triazole is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

A 3.14 IEDI calculations - 1,2,4-triazole

Not required. TMDI below 100%.

A 3.15 IESTI calculations - Raw commodities - 1,2,4-triazole

Acute risk assessment /children	Acute risk assessment / adults / general population
Details - acute risk assessment /children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the Eu

The calculation is based on the large portion of the most critical consumer group.

Show results of IESTI calculation only for crops with GAPs under assessment

Unprocessed commodities

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI): ---				**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI): ---			
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Wheat	0,05 / 0,1	1,4	0,8%	Wheat	0,05 / 0,1	0,84
0,6%	Barley	0,05 / 0,1	0,56	0,5%	Barley	0,05 / 0,1	0,48
0,07%	Rapeseeds/canola	0,05 / 0,05	0,07	0,03%	Rapeseeds/canola seeds	0,05 / 0,05	0,03
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

A 3.16 IESTI calculations - Processed commodities - 1,2,4-triazole

Processed commodities

Results for children

No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
1%	Wheat / milling (flour)	0,05 / 0,1	1,2
0,6%	Wheat / milling (wholemea	0,05 / 0,1	0,55
0,4%	Barley / cooked	0,05 / 0,1	0,36
0,2%	Barley / milling (flour)	0,05 / 0,1	0,18
0,0%	Rapeseeds / oils	0,05 / 0,1	0,03

Expand/collapse list

Results for adults

No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
0,7%	Barley / beer	0,05 / 0,02	0,72
0,4%	Wheat / bread/pizza	0,05 / 0,1	0,44
0,4%	Wheat / pasta	0,05 / 0,1	0,38
0,3%	Wheat / bread	0,05 / 0,1	0,35

Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity.

A short term intake of residues of 1,2,4-triazole is unlikely to present a public health risk.

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

Appendix 4 Additional information provided by the applicant

Not relevant.