

FINAL REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: FF-075

Product name(s): EUSKATEL PRO

Chemical active substance:

Prothioconazole, 200 g/L

Azoxystrobin 150 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(New Product Authorization)

Applicant: Rotam Agrochemical Europe Limited

Submission date: June 2021

MS Finalisation date: February 2022; 08/2022

FF-075 / EUSKATEL PRO
Part B – Section 7 - Core Assessment
Applicant version

Version history

When	What
1 June 2021	New product application in accordance with Article 33 of Regulation (EC) No. 1107/2009.
November 2021	Additional information added by applicant regarding triazole derivative metabolites (TDMs)
February 2022	Additional information added by applicant regarding triazole derivative metabolites (TDMs)
February 2022	zRMS evaluation
08/2022	Final version after commenting period

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

Prothioconazole

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.

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).

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

Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)

Proposed GAPs:

1-2 Applications (14 days interval), BBCH 30 69, 0.20 kg as/ha, PHI: 35 days

EU GAPs:

Wheat, rye, triticale

The intended GAP of prothioconazole in FF-075 is less critical than the EU-GAP:

3 x 0.2 kg a.s./ha, BBCH 69, PHI 35 d, int. 14-21 d

Barley, oat

The intended GAP of prothioconazole in FF-075 is the same than the EU-GAP:

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

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).

TDMs

Applicant refers to data presented in the EFSA Journal 2018;16(7):5376.

However, data gaps relevant for the risk assessment to cover the complete group of triazole derivate metabolites were found.

EFSA 2018: *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.*

Nevertheless, no chronic or acute intake concerns were identified.

A 'worst-case' consumer dietary intake assessment with regard to the TDMs for the complete group of triazole active substances that were assessed in the framework of these confirmatory data has been conducted and it was demonstrated that the risk for the consumers is unlikely. The overall consumer exposure assessment for the TDMs could, however, not be finalised in view of the identified data gaps for additional storage stability data for the TDMs in several crop commodities and missing data to finalise the livestock exposure assessment.

No critical areas of concern have been identified.

Therefore, supplementing the above-mentioned deficiencies can be considered as a post-registration requirement. Uses are accepted.

Oilseed Rape

Proposed GAPs:

1-2 Applications (14 days interval), BBCH 55 69, 0.16 kg as/ha, PHI: 35 days

EU-GAP:

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

Applicant refers to the unprotected EU data compliant with EU GAP.

Prothioconazole

Residues Seed (n = 8, E): 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).

PHI of 56 is proposed by z zRMS as in EU GAP.

TDMs

Data gap: Residue trials analysing for all TDMs supported by acceptable storage stability data for 1,2,4-T in rapeseeds - post-registration requirement

Livestock Feeding Studies:

The calculated dietary burdens were found to exceed the trigger value of 0.004 mg/kg bw/day. Further investigation of residues in livestock is required. 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 of FF-075

TDMs

Applicant refers to data presented in the 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.

The above mentioned data gap should be addressed as part of the next renewal of approval of the active substance prothioconazole, or for the triazole fungicides as a whole.

Industrial Processing and/or Household Preparation:

As the proposed uses are supported by EU agreed data previously considered for Annex I approval, no further investigation into the magnitude of residues in processed commodities is considered necessary. No data gaps were found.

The TDMs remained stable under the standard hydrolysis conditions simulating processing of pasteurisation, baking, brewing and boiling and sterilisation.

Residues in Representative Succeeding Crops:

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.

zRMS considers that the missing data can be provided when the product is reassessed.

The consumer risk assessment

Chronic and acute exposure calculations were performed using EFSA PRIMo revision 3.1 and calculated exposures were compared with the established toxicological reference values. The proposed uses of prothioconazole in the formulation FF-075 do not represent unacceptable acute and chronic risks for the consumer.

TDMs

Applicant refers to data presented in the EFSA Journal 2018;16(7):5376.

EFSA Journal 2018;16(7):5376:

The ‘worst-case’ consumer dietary intake assessment with regard to the TDMs for the complete group of triazole active substances that were assessed in the framework of these confirmatory data has been conducted by the RMS using the EFSA PRIMo rev.3 and by EFSA using the EFSA PRIMo rev.2A since PRIMo rev.3 is not applicable in the framework of confirmatory data assessed here.

The chronic and acute dietary intakes have been carried out using the highest input residue values for risk assessment (STMR values and the HR values), derived for each TDM for each crop groups and each product of animal origin. Since in most of the residue trials in primary and rotational crops, higher residue levels of the TDMs in the control samples were observed, these levels were also considered in the dietary intake calculation. Using the EFSA PRIMo rev.3, the IEDI accounted for 93% of the ADI (NL toddler) for 1,2,4-T, 6% of the ADI (NL toddler) for TA, 1% of the ADI (NL toddler) for TAA and 1% of the ADI (NL toddler) for TLA. No acute intake concern was identified as the calculated international estimated short-term intake (IESTI) accounted for up to 40% of the ARfD (cattle milk) for 1,2,4-T, 28% of the ARfD (oranges) for TA, 1% of the ARfD (oranges) for TAA and 7% of the ARfD (potatoes) for TLA. Using the EFSA PRIMo rev.2A, the IEDI accounted for 60% of the ADI (FR toddler) for 1,2,4-T, 5% of the ADI (WHO Cluster diet B) for TA, 1% of the ADI (WHO Cluster diet B) for TAA and < 1% of the ADI (FR toddler) for TLA. The acute intake was estimated to be 40% of the ARfD (milk) for 1,2,4-T, 28% of the ARfD (oranges) for TA, 1% of the ARfD (oranges) for TAA and 6.7% of the ARfD (potatoes) for TLA. Since the toxicological reference values for TLA were derived by bridging with the reference values of TA, a combined dietary risk assessment for TA and TLA was performed. No chronic or acute intake concerns were identified with up to 6% ADI (WHO Cluster diet B), and 34% and 8% ARfD (watermelons) respectively for children and adults.

SANCO/3923 /07 – final 10 December 2007, 26 January 2021: *A ‘worst-case’ consumer dietary intake assessment with regard to the TDMs for the group of triazole active substances that were assessed in the framework of the confirmatory data submitted for several triazole active substances was conducted by the RMS. This assessment concluded that an unacceptable risk for consumers is unlikely. The proposed uses of prothioconazole in the formulation FF-075 do not represent unacceptable acute and chronic risks for the consumer. Therefore, no changes to the existing provisions of the approval of prothioconazole are required.*

Other / special studies

Since the intended uses are performed during flowering in a honey-relevant crop (oilseed rape), information on potential residues of prothioconazole and azoxystrobin in honey is required in case of use on oilseed rape. No new data are submitted in the framework of this application. Study to investigate residues in honey resulting from the use of FF-075 has recently been initiated.

Therefore, currently use after BBCH 59 is not accepted. Data gap should be supplemented.

Azoxystrobin

Storage stability

In the framework of the peer review, storage stability of azoxystrobin was demonstrated for a period of 24 months at -18°C in:

dry/starch commodities (cereal grain, straw, carrot)

high water content (apple, peach, tomato, cucumber, lettuce, banana)

high acid content (grape, orange)

high oil content (soybean meal, oilseed rape, pecans, peanut, orange oil)

Azoxystrobin was shown to be stable in freezer storage at approximately -18°C in animal tissues, eggs and milk after storage for up to ten months.

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

Metabolism in plants and animals

All metabolism data are active substance data and were evaluated in the EU review of azoxystrobin.

Plant and animal residue definition for monitoring and risk assessment: azoxystrobin. No further evaluation is required.

Magnitude of residues in plants

Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)

Proposed GAPs:

1-2 Applications (14 days interval), BBCH 30-69, 0.15 kg as/ha, PHI: 35 days

Applicant refers to the unprotected EU data compliant with EU GAP.

Trials GAP: 2 x 0.25 kg as/ha (14 days interval), BBCH 31-59 and 31-69, PHI 35d (DAR 2009).

Proposed GAP is less critical than EU GAP. The number of trials is sufficient as to support the use of azoxystrobin in wheat and barley according to the proposed GAP in Central Zone. 35 days is proposed for PHI.

The residues arising from the proposed uses will not exceed the MRLs for wheat and barley (set at 1.5 for barley, oats and 0.5 mg/kg for wheat, durum, spelt, triticale, rye - Reg. (EU) 2021/1807, SANTE/11280/2021).

Oilseed Rape

Proposed GAPs:

1-2 Applications (14 days interval), BBCH 55-69, 0.12 kg as/ha, PHI: 35 days

This application relies upon the now-unprotected trials previously evaluated at EU level.

EU-GAP: : 2 x 0.25 kg a.s./ha (foliar), BBCH 55, PHI 21 d, int. not stated

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 Azoxystrobin established for oilseed Rape (0.5 mg/kg, Reg. (EU) 2021/1807, SANTE/11280/2021).

Livestock Feeding Studies:

The calculated dietary burdens were found to exceed the trigger value of 0.004 mg/kg bw/day (2017 Animal Model, OECD methodology). Further investigation of residues in livestock is required.

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

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints. No exceedances of the existing EU MRLs for azoxystrobin in animal commodities are anticipated as a result of the proposed uses of FF-075.

Industrial Processing and/or Household Preparation:

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints.

Residues in Representative Succeeding Crops:

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

Rotational crop field trials were evaluated in the framework of the EU peer review (EFSA, 2010).

Residues in rotational crops will have no impact on the MRLs in plants and livestock products, provided that azoxystrobin is applied in compliance with the EU cGAPs.

The consumer risk assessment

Chronic and acute exposure calculations were performed using EFSA PRIMo revision 3.1 and calculated exposures were compared with the established toxicological reference values. The proposed uses of azoxystrobin in the formulation FF-075 do not represent unacceptable chronic risks for the consumer.

Other / special studies

Since the intended uses are performed during flowering in a honey-relevant crop (oilseed rape), information on potential residues of prothioconazole and azoxystrobin in honey is required in case of use on oilseed rape. No new data are submitted in the framework of this application. Study to investigate residues in honey resulting from the use of FF-075 has recently been initiated.

Therefore, currently use after BBCH 59 is not accepted. Data gap should be supplemented.

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 FF-075 are presented in Table 7.1-1. They have been selected from the individual GAPs in the zone for oilseed rape, and cereals. 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. No exceedance of the current MRLs for prothioconazole or azoxystrobin as laid down in Reg. (EU) 396/2005 are expected.

The chronic and the short-term intakes of prothioconazole and azoxystrobin residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, the zRMS agrees with the authorization of the intended uses.

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

Data gaps

Data gaps should be listed in the summary to give an overview (especially for cMS).

Noticed data gaps are:

TDMs:

- Residue trials analysing for all TDMs supported by acceptable storage stability data for 1,2,4-T in cereal grain, straw and rapeseeds and for TLA in straw - post-registration requirement
- 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 - post-registration requirement.

This data gap should be addressed as part of the next renewal of approval of the active substance prothioconazole, or for the triazole fungicides as a whole.

- Rotational crops field residue trials supported by acceptable storage stability data on TDMs - post-registration requirement

zRMS considers that the missing data can be provided when the product is reassessed.

Other/special studies:

- Since the intended uses are performed during flowering (BBCH 55 69) in a honey-relevant crop (oilseed rape), information on potential residues of prothioconazole and azoxystrobin in honey is required in case of use on oilseed rape after BBCH 59 phase.

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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 situation **	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)	L product / ha a) max. rate per appl. b) max. total rate per crop/ season	kg as/ha a) max. rate per appl. b) max. total rate per crop/ season	Water L/ha min - max		
1	Oilseed Rape	CEU	FF-075	F	Aerial parts diseases	SC	200 (PT) 150 (AZ)	Foliar spray	BBCH 55-69 BBCH 55-59	1-2	14 days	a) 0.8 b) 1.6	a) (PT) 0.16 a) (AZ) 0.12 b) (PT) 0.32 b) (AZ) 0.24	100 - 400	35 56	A Acceptable to BBCH 59 phase PHI of 56 is proposed by zRMS
2	Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)	CEU	FF-075	F	Aerial parts diseases	SC	200 (PT) 150 (AZ)	Foliar spray	BBCH 30-69	1-2	14 days	a) 1.0 b) 2.0	a) (PT) 0.20 a) (AZ) 0.15 b) (PT) 0.40 b) (AZ) 0.30	100 - 400	35	A

* 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 FF-075 is composed of prothioconazole and azoxystrobin.

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

Reference value	Source	Year	Value	Study relied upon	Safety factor
Prothioconazole-desthio					
ADI	EFSA	2007	0.01 mg/kg bw/day	Rat - oncogenicity	100
ARfD	EFSA	2007	0.01 mg/kg bw	Rat - oncogenicity	100
1,2,4-triazole (1,2,4-T)					
ADI	EFSA	2018	0.023 mg/kg bw/day	Rat 12-month study	300
ARfD	EFSA	2018	0.1 mg/kg bw	Rabbit developmental study	300
Triazole alanine (TA)					
ADI	EFSA	2018	0.3 mg/kg bw/day	Rabbit developmental study	100
ARfD	EFSA	2018	0.3 mg/kg bw	Rabbit developmental study	100
Triazole acetic acid (TAA)					
ADI	EFSA	2018	1.0 mg/kg bw/day	Rat 2-generation and rabbit developmental studies	100
ARfD	EFSA	2018	1.0 mg/kg bw	Rat 2-generation and rabbit developmental studies	100
Triazole lactic acid (TLA)					
ADI	EFSA	2018	0.3 mg/kg bw/day	Bridging from TA	n/a
ARfD	EFSA	2018	0.3 mg/kg bw	Bridging from TA	n/a
Azoxystrobin					
ADI	EFSA	2010	0.2 mg/kg bw/day	2-year rat	100
ARfD	EFSA	2010	n/a	n/a	n/a

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	Oilseed rape	Yes	Yes (4 ^{8 trials¹})	Yes ² No PHI of 56 is proposed by zRMS	Yes	Yes	No	No
2	Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)	Yes	Yes (8 wheat, 8 barley)	Yes	Yes	Yes		No

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

1 The four ~~SEU~~ ~~NEU~~ trials considered acceptable to support the EU cGAP in the 2007 EFSA Conclusion are relied upon, with an additional 8 new ~~SEU~~ ~~NEU~~ trials in progress in support of the proposed GAP for FF-075 use on oilseed rape.

2 It is not clear whether the intended cGAP of prothioconazole in FF-075 is more or less critical than the EU cGAP; stages at last application are “BBCH 69” and “BBCH 53 onwards” respectively, with a slightly lower application rate and a shorter PHI in the intended cGAP for FF-075, though in both cases applications are likely to be made at similar timings. An additional 8 SEU trials are in progress in support of the proposed GAP for FF-075 use on oilseed rape.

As residues of prothioconazole-desthio 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, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.2 Summary for azoxystrobin

Table 7.1-4: Summary for azoxystrobin

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	Oilseed rape	Yes	Yes (4 ^{8 trials¹})	Yes ² No PHI of 56 is proposed by zRMS	Yes	Yes	No	No

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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?
2	Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)	Yes	Yes (8 wheat, 8 barley)	Yes	Yes	Yes		No

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

- The four SEU NEU trials considered acceptable to support the EU cGAP evaluated within the *EFSA Reasoned Opinion Modification of the existing MRLs for azoxystrobin in various oilseeds* (EFSA Journal 2011;9(6):2283) are relied upon, with an additional 8 new SEU NEU trials in progress in support of the proposed GAP for FF-075 use on oilseed rape.
- It is not clear whether the intended cGAP of azoxystrobin in FF-075 is more or less critical than the EU cGAP; stages at last application are “BBCH 69” and “BBCH 55” respectively, but with a significantly lower application rate and longer PHI for the intended cGAP for FF-075, likely to result in lower residues at crop harvest. An additional 8 SEU trials are in progress in support of the proposed GAP for FF-075 use on oilseed rape.

The effects of processing on the nature of azoxystrobin residues have been investigated. Data on effects of processing on the amount of residue have been submitted.
These data were considered for risk assessment.

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, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.3 Summary for FF-075

Table 7.1-5: Information on FF-075 (KCA 6.8)

Crop	PHI for FF-075 proposed by applicant	PHI/ Withholding period* sufficiently supported for		PHI for FF-075 proposed by zRMS	zRMS Comments (if different PHI proposed)
		Prothioconazole	Azoxystrobin		
Oilseed rape	35 days	Not relevant	Not relevant	35 days	PHI of 56 is proposed by zRMS
Wheat, durum, spelt, triticale, rye, oats, barley (spring and winter)	35 days	Not relevant	Not relevant	35 days	

NR: not relevant

* Purpose of withholding period to be specified

Assessment

7.2 Prothioconazole

Note on Triazole Derivative Metabolites (TDMs)

The updated Review Report for prothioconazole (SANCO/3923/07 - final; 26 January 2021) states that:

“[TDM] data gaps identified should be addressed either during renewal of approval of prothioconazole, during evaluation of plant protection products by Member States or during the evaluation of maximum residue levels under Regulation (EC) No 396/2005, as appropriate and taking into account procedures carried out under Regulation (EC) No 396/2005.”

and:

“In December 2019 the SCoPAFF took note of the reference values and residue definitions presented below and agreed that they should be used as part of the consumer risk assessment for triazole active substances and their TDMs for applications for approval or renewal of approval of active substances and authorisation of plant protection products. Since the agreed reference values are more scientifically robust than the values previously agreed (PRAPeR, 2007), they should be used for all ongoing and future applications. The residue definitions should apply to applications submitted from 1 July 2020 and if appropriate may also be applied sooner, including to ongoing applications, in particular if applicants already submitted residues data for the TDMs.”

The Triazole Derivative Metabolite Group (TDMG) data evaluated by the EU within 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) includes data generated for prothioconazole in support of representative uses which are comparable to the proposed uses of FF-075 (i.e. wheat, rye, barley, oats, triticale, rapeseed). It is noted that the confirmatory data was not considered sufficient to finalise the consumer risk assessment for prothioconazole (due to the lack of storage stability studies supporting analysis of TDMs in field trials); therefore further consideration of TDMs is not presented as part of this product submission, with the existing EU endpoints and conclusions relied upon to support the authorisation. However, the following new data (field trials) are being generated (in all cases, the field phase of trials is complete, with the analytical phase due to be completed in Q2/Q3 2021 as a result of delays associated with the synthesis of reference test items) including analysis of TDMs in crops resulting from the proposed uses of FF-075:

- 8 x NEU and 8 SEU trials on wheat (Study No. QG/20/005)
- 8 x NEU and 8 SEU trials on barley (Study No. QG/20/006)
- 8 x NEU and 8 SEU trials on oilseed rape (Study No. QG/20/005 - includes determination of residue in aerial parts)

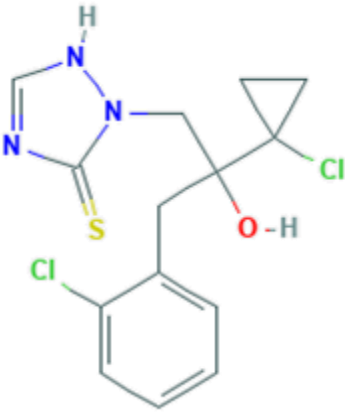
Details of these new (ongoing) studies have been added to Appendix 2 of this document, and may be updated once the analytical phases are completed and finalised study reports are available. In addition, consideration of TDMs with respect to the consumer risk assessment for FF-075 is presented in Appendix 4 of this document. The dietary risk assessment performed as part of the EU peer review (EFSA Journal 2018;16(7):5376) addresses the exposure to TDMs related to primary crops, processed commodities, rotational crops and food of animal origin, and is sufficient to conclude that no chronic health or acute effects are expected as a result of consumer exposure to the TDM residues associated with the proposed

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uses of FF-075, as the cGAPs for FF-075 are within the risk envelope considered in the EU Peer review. As these data are confirmatory data to the 2008 EU approval of prothioconazole, no additional data protected is afforded and so the EU-agreed conclusions may be relied upon for the consumer risk assessment of FF-075

General data on prothioconazole are summarized in the table below (last updated 2021/03/22).

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	 <p>Racemic mixture of the R- and S-enantiomer (50/50)</p>
Molecular formula	C ₁₄ H ₁₅ Cl ₂ N ₃ OS
Molar mass	344.26 g/mol
Chemical group	Triazolinthiones
Mode of action (if available)	Sterol biosynthesis inhibitor (demethylation inhibitor: FRAC code group 3)
Systemic	Yes
Company (ies)	Bayer CropScience AG (now: Bayer CropScience)
Rapporteur Member State (RMS)	UK Co-RMS: France
Approval status	Approved on 01/08/2008 COMMISSION DIRECTIVE 2008/44/EC ; Reg. (EU) No. 2019/707 ; Reg. (EU) No. 540/2011
Restriction	Only uses as fungicide may be authorised.
Review Report	SANCO/3923/07 - final 10 December 2007 26 January 2021
Current MRL regulation	Regulation (EC) 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
Current MRL applications on intended uses	n/a

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 are submitted in the framework of this application.

Out of protection EU-reviewed active substance data are available that demonstrate the storage stability of prothioconazole and prothioconazole-desthio for periods of 60-180 and 540 days (respectively) in wheat green matter (forage), grain and straw. The 2007 EFSA Conclusion (EFSA Scientific Report (2007) 106, 1-98) concluded that the available data are sufficient to cover the sample storage durations in the evaluated magnitude of residue trials on wheat, barley and oilseed rape:

2007 EFSA Conclusion

In rape, 12 valid trials were performed (8 for Northern region and 4 for Southern region). Residues in seeds were low, ranging from below the LOQ of 0.01 mg/kg to 0.02 mg/kg. The Highest Residue level (HR) found in rape straw was 0.20 mg/kg.

These results can be considered as reliable on the basis of storage stability studies demonstrating that residues of prothioconazole and its metabolite prothioconazole-desthio are stable in wheat matrices under deep-freeze conditions for periods of 60-180 and 540 days respectively.

2006 DAR Addendum

A freezer stability study showed that residues of JAU 6476 in wheat matrices declined slowly during storage below -18°C, but were acceptably stable for at least 60 days. However, the residue of interest is JAU 6476-desthio and this was shown to be stable in all wheat matrices for greater than 540 days. This indicates that all storage periods for samples from supervised trials were acceptable, prior to analysis.

In addition, a frozen storage stability study (Freitag, T.; 2007) is summarised in the dRAR (UK, 2018), conducted with prothioconazole-desthio in canola (seed, pod, straw), spinach (leaves), sugar beet (root, leaf with root collar), tomato (fruit), and field pea (field pea dried). The study was first evaluated in support of the 2009 Art. 10 modification of MRLs in head cabbage and Brussel sprouts (EFSA Scientific Report (2009) 261, 1-24) and was relied upon to support the Art. 10 modification of MRLs in oilseeds (EFSA Journal 2012;10(11):2952).

The storage stability of relevant analytes in animal matrices was not evaluated during the EU approval process. However, this was not established as a data gap during the EU approval process since sample storage durations in the evaluated feeding studies were less than 30 days.

Table 7.2-2: Summary of stability data achieved at $\leq -18^{\circ}\text{C}$ (unless stated otherwise)

Matrix	Characteristics of the matrix ¹	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Wheat grain	High starch content	Prothioconazole: 60-180 days Prothioconazole-desthio: 540 days	UK, 2007 EFSA, 2007
Wheat straw	No specific category	Prothioconazole: 60-180 days Prothioconazole-desthio: 540 days	UK, 2007 EFSA, 2007
Wheat green material	High water content	Prothioconazole: 60-180 days Prothioconazole-desthio: 540 days	UK, 2007 EFSA, 2007
Canola (seed)	High oil content	Prothioconazole-desthio: 734 days	dRAR (UK, 2018) EFSA, 2009 EFSA, 2012
Canola (pod)	No specific category		
Canola (straw)	No specific category		
Spinach (leaves)	High water content		
Sugar beet (root)	High starch content		
Sugar beet (leaf)	High water content		
Tomato (fruit)	High water content		
Field pea (dried)	High protein content		

¹ In accordance with OECD 506: Stability of Pesticide Residues in Stored Commodities

Conclusion on stability of residues during storage

The available unprotected data are considered sufficient to support the proposed uses of FF-075 on wheat, barley and other cereals uses (i.e. triticale, rye, oat) and oilseed rape when evaluating against existing EU-agreed endpoints. The unprotected storage stability data generated on wheat were accepted as supporting the magnitude of residue trials performed using oilseed rape that were evaluated for the Annex I inclusion of prothioconazole and are relied upon in support of the proposed uses of FF-075. In addition, the stability of prothioconazole-desthio in various matrices (including high oil crops) when stored under frozen conditions for up to 734 days has been demonstrated and is considered sufficient to support the proposed uses of FF-075.

zRMS comment:

Storage stability for TDMs (EFSA Journal 2018;16(7):5376):

Plant products (Category)	Commodity	Stability (Months)			
		1,2,4-Triazole	TA	TAA	TLA

High water content	Apples, tomatoes, mustard leaves, wheat forage, radishes tops/roots, turnips roots, sugar beet roots, cabbages, lettuces	6	53	53	48 ((lettuce only)
High starch content	Barley, wheat	12	26	26	48
High oil content	Oilseed rape (seed), soya beans	12 (soya bean only; not stable in rape seed)	26 (soya bean only; not stable in rape seed)	53	48
High protein content	Peas, dry; Navy beans	No data	15	25	48
High acid content	Oranges	No data	No data	No data	48
Others	Cereal straw	12	53	40	No data
Animal	Animal commodity	Stability (Month/Year)			
	Muscle	No data	No data	No data	No data
	Liver	No data	No data	No data	No data
	Kidney	No data	No data	No data	No data
	Milk	No data	No data	No data	No data
	Egg	No data	No data	No data	No data

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

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

Out of protection EU-reviewed active substance data (UK, 2004; EFSA, 2007) are available to demonstrate the storage stability of prothioconazole-desthio in sample extracts for cereal and canola matrices (no significant changes observed when stored at 4±3 °C for up to 4 weeks).¹ The 2007 EFSA Conclusion (EFSA

¹ Analytical determination of residues of JAU6476 and JAU6476-desthio in/on cereals and canola by HPLC-MS/MS (method modification 00598/M001); Heinemann, O.; Report No.: 00598/M001; Date:2000-08-28

Scientific Report (2007) 106, 1-98) concluded that the available data are sufficient to cover the sample storage durations in the evaluated magnitude of residue trials on wheat, barley and oilseed rape.

Conclusion on stability of residues in sample extracts

The available unprotected data are considered sufficient to support the proposed uses of FF-075 on cereals (wheat, barley, triticale, rye, oat) and oilseed rape when evaluating against existing EU-agreed endpoints.

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

The nature of residues in primary crops for prothioconazole was previously evaluated in the framework of the Annex I inclusion process and summarised in the context of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014).

Metabolism of prothioconazole has been investigated for foliar application on cereals (wheat), pulses and oilseeds (peanut) and root and tuber vegetables (sugar beet) using either [phenyl-UL-¹⁴C]-prothioconazole, [3,5-¹⁴C-triazole]-prothioconazole or [3,5-¹⁴C-triazole]-prothioconazole-desthio.

A summary of the available data is provided in Table 7.2-3.

No new data are submitted in the framework of this application. Rotam has access to all studies summarised in EFSA, 2014.

Table 7.2-3: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G ^[1]	Rate (kg a.s./ha)	No (Stage)	Sampling	Remarks	
EU data								
Pulses and oilseeds	Peanut	[phenyl-UL- ¹⁴ C]-prothioconazole	Foliar, G	0.30 ^[6]	3 (BBCH 66-75)	14 DALA	21 d int.	EFSA, 2014 EFSA, 2007 UK, 2007 UK, 2004
	Peanut	[3,5- ¹⁴ C-triazole]-prothioconazole	Foliar, G	0.297	3 (BBCH 66, 71, 75)	BBCH 89-91	21 d int. PHI 14 d	UK, 2018 (provisional) ^[2] EFSA, 2014
Cereals	Wheat	[phenyl-UL- ¹⁴ C]-prothioconazole	Foliar, G ^[7]	0.20	2 (BBCH 32, 65)	6, 26, 48 DALA	-	EFSA, 2014 EFSA, 2007 UK, 2007 UK, 2004

		[3,5- ¹⁴ C-triazole]-prothioconazole-desthio	Foliar, G ^[7]	0.25	2 (BBCH 31, 59)	0, 14, 48 DALA	27 d int.	EFSA, 2014 EFSA, 2007 UK, 2007 UK, 2004
		[3,5- ¹⁴ C-triazole]-prothioconazole	Foliar, F ^[3]	i) 0.178 ii) 0.292	2 (BBCH 32, 65)	NCH	-	UK, 2018 (provisional) ^[2] EFSA, 2014
Root and tuber vegetables	Sugar beet	[phenyl-UL- ¹⁴ C]-prothioconazole	Foliar, F ^[4]	0.288	4 (not stated)	7 DALA	14 d int.	UK, 2018 (provisional) ^[2] EFSA, 2014 EFSA, 2009 ^[8]
	Sugar beet	[3,5- ¹⁴ C-triazole]-prothioconazole	Foliar, G ^[5]	i) 0.260 ii) 0.291 iii) 0.285 iv) 0.321	4	7 DALA	14 d int.	UK, 2018 (provisional) ^[2] EFSA, 2014

^[1] Outdoor/field application (F) or glasshouse/protected/indoor application (G).

^[2] Unprotected studies evaluated in the dRAR as part of the on-going EU renewal of prothioconazole.

^[3] 1 day after application, the soil tub was moved to the outside of the greenhouse.

^[4] Sugar beets were grown in boxes in a greenhouse until seedlings were approximately 2 inches tall. The sugar plants were then planted outdoor and treated (Netherlands, 2007).

^[5] The sugar beet plants were moved to a fenced area outside of the greenhouse and remained there until harvest.

^[6] In the JMPR report, it is stated, that a 5x application was also tested in order to collect sufficient amounts of radioactivity to identify metabolites.

^[7] The plants were grown under environmental conditions (sunlight and temperatures). A glass roof protected the plants from rainfall. The soil was surface irrigated.

^[8] Also previously considered by NL in MRL application (EFSA, 2009)

Summary of plant metabolism studies reported in the EU

EFSA (2014):

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 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 (see also section 1.1).

It is noted that the above studies do not investigate the possible impact of plant metabolism on the isomer ratio of prothioconazole and further investigation on this matter would in principle be required. Since guidance on the consideration of isomer ratios in the consumer risk assessment is not yet available, EFSA recommends that this issue is reconsidered when such guidance is available.

EFSA also emphasises that the above residue definitions do not yet take into consideration triazole derivative metabolites (TDMs). Since these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommends that a separate risk assessment should be performed for TDMs as soon as the confirmatory data requested for triazole compounds in the framework of Regulation (EC) No 1107/2009 have been evaluated and a general methodology on the risk assessment of triazole compounds and their triazole derivative metabolites is available.

Conclusion on metabolism in primary crops

The proposed metabolic pathway of prothioconazole in plants based on available data is illustrated in the DAR (UK, 2004), DAR Addendum (UK, 2007) and the dRAR (UK, 2018).

It is noted that *Guidance of EFSA on risk assessments for active substances of plant protection products that have stereoisomers as components or impurities and for transformation products of active substances that may have stereoisomers* was published in 2019 (EFSA Journal 2019;17(8):5804). In 2020, as part of the 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), EFSA proposed that consideration of the possible impact of plant metabolism on the isomer ratio of prothioconazole is further considered in the framework of the renewal of the approval process of prothioconazole. Further consideration of the topic as part of this submission – that is based on existing endpoints – is therefore not applicable.

Additionally, the *Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data* submitted for a subset of triazole active substances was published in 2018 (EFSA Journal 2018;16(7):5376). However, a common risk assessment methodology is not yet finalised for all triazole containing compounds. Consideration of TDMs with respect to the consumer risk assessment for FF-075 is presented within Appendix 4 of this document. The dietary risk assessment performed as part of the EU peer review addresses the exposure to TDMs related to primary crops, processed commodities, rotational crops and food of animal origin, and is sufficient to provisionally conclude that no chronic health or acute effects are expected as a result of consumer exposure to the TDM residues associated with the proposed uses of FF-075.

In conclusion, the metabolism of prothioconazole can be considered sufficiently investigated in primary crops to support the proposed uses of FF-075 on cereals (wheat, barley, triticale, rye, oat) and oilseed rape in accordance with existing endpoints.

Available data

The confined rotational crop study in cereals, leafy vegetables and root crops was conducted with [phenyl-UL-¹⁴C]-prothioconazole. Rotam has access to this out-of-protection study principally relied on in EFSA, 2014.

A summary of the available data is provided in Table 7.2-4. Rotam has access to all studies summarised in EFSA, 2014.

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G ^[1]	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Swiss chard	[phenyl]-UL- ¹⁴ C)-prothioconazole	Bare soil application ^[3]	0.58	28, 146, 269	80, 188, 348	-	EFSA, 2014 EFSA, 2012 EFSA, 2010a EFSA, 2010b EFSA, 2009 EFSA, 2007 UK, 2007 UK, 2004
Root and tuber vegetables	Turnip					94, 201, 349 (roots, tops)	-	
Cereals	Wheat					73, 178, 327 (green mat.) 111, 231, 377 (hay) 145, 269, 412 (grain, straw)	-	
New unprotected data evaluated in dRAR (UK, 2018)								
Leafy vegetables	Swiss chard	[3,5- ¹⁴ C-triazole]-prothioconazole	Bare soil application, F ^[4]	0.204 (n = 4)	30, 125, 366	NCH	Total rate:	UK, 2018 (provisional) ^[2] Duah and Kraai, 2004, Report no.
Root and tuber vegetables	Turnip						0.816 kg a.s./ha 14 d int.	

Cereals	Wheat							200623
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^[1] Outdoor/field application (F) or glasshouse/protected/indoor application (G).

^[2] Unprotected study evaluated in the dRAR as part of the on-going EU renewal of prothioconazole.

^[3] Indoor/outdoor application not stated.

^[4] The trough was kept outdoors under natural weather conditions and was moved to a greenhouse one day before each application to minimize spray drift and contamination as well as when outdoor temperatures were not suitable for the growth of Swiss chard and turnips.

Summary of plant metabolism studies reported in the EU

UK (2007):

Although there are no significant soil residues of JAU 6476 at times of sowing following crops, residues of JAU 6476-desthio are predicted to be at most 42% 120 days after treatment (Section B.8.1.1.1 of the Draft Assessment Report). A study of uptake and metabolism in rotational crops showed that residues in all rotational crops declined between first and third rotations. Significant residues (>0.1 mg/kg) were found in wheat straw and hay and these were at similar or lower levels than those recorded for the directly treated crop, also with similar metabolic profiles. Therefore, residues in rotational crops will not lead to any additional exposure to JAU 6476-desthio above that from directly treated crops.

EFSA (2007):

In succeeding crops, the residue pattern is similar to that observed in primary crops. The residue definitions proposed for primary crops are evenly valid. Under the experimental conditions of the submitted confined rotational crop study, residues of prothioconazole-desthio were present in edible part of Swiss chard and turnip at the level of 0.01 mg/kg, when these plants were sowed 28 and 146 days after application of the highest possible annual dose of prothioconazole on bare soil. The total amount of all metabolites containing the prothioconazole-desthio common structural moiety was around 0.03 mg/kg for the same time intervals. Therefore, under practical conditions of use of prothioconazole according to the representative uses and considering that a fraction of the applied rate is intercepted by the cereal crop, no residue of any metabolite above 0.01 mg/kg is expected in rotational crops and no plant back restriction needs to be proposed. No information is available as far as the uptake of triazole derivative metabolites by rotational crops is concerned, given that no study was conducted with radiolabelling in the triazole ring.

EFSA (2014):

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.

[...]

No rotational crop studies with prothioconazole radiolabelled on the triazole ring were assessed in the framework of the peer review.

Summary of new plant metabolism studies

A new rotational crop study was submitted for the purposes of active substance renewal, using an additional radio-labelled position. The study involves three crops from three different groups of crops, in accordance with Reg. (EU) No. 283/2013. A summary of the study can be found in the dRAR (see below). The new study covers the critical GAP applied for (i.e. maximum total application rate of 0.400 kg a.s./ha per crop

per season). The results of the study do not affect the proposed residue definition for rotational crops – that is, no specific residue definition for rotational crops is required.

dRAR (UK, 2018; provisional), Volume B7, Section 7.6.1:

The major residues found in all rotational crop matrices were triazolyl alanine (TA), triazolyl hydroxy propionic acid (THP), and triazolyl acetic acid (TAA).

TA (M31) represented 44 - 51 % of the TRR (0.120 - 0.252 mg/kg) in wheat forage, 33 - 36 % (0.719 - 0.846 mg/kg) in wheat hay, 15 - 28 % (0.197 - 0.407 mg/kg) in wheat straw, 58 - 68 % (2.264 - 3.940 mg/kg) in wheat grain, 49 - 56 % (0.023 - 0.096 mg/kg) in Swiss chard, 74 - 92 % (0.077 - 0.377 mg/kg) in turnip tops, and 81 - 93 % (0.048 - 0.411 mg/kg) in turnip roots.

THP (M30) represented 32 - 35 % (0.087 - 0.184 mg/kg) of the TRR in wheat forage, 24 - 39 % (0.562 - 0.871 mg/kg) in wheat hay, 28 - 33 % (0.382 - 0.498 mg/kg) in wheat straw, <1 - 1 % (0.023 - 0.047 mg/kg) in wheat grain, 30 - 32 % (0.038 - 0.060 mg/kg) in Swiss chard, 7 % (0.035 mg/kg) in turnip tops at 125 DAT, and 1 - 5 % (0.003 - 0.005 mg/kg) in turnip roots at 30 DAT and 125 DAT.

TAA represented 1 - 6 % (0.006 - 0.034 mg/kg) of the TRR in wheat forage, 10 - 22 % (0.222 - 0.578 mg/kg) in wheat hay, 17 - 26 % (0.233 - 0.437 mg/kg) in wheat straw, 23 - 29 % (0.958 - 1.485 mg/kg) in wheat grain, 1 - <18 % (0.001 - <0.008 mg/kg) in Swiss chard, <7 % (0.009 mg/kg or less) in turnip tops, and <5 % (<0.005 mg/kg) in turnip roots.

The minor residues found in the rotational crops were prothioconazole-desthio (M04), <1 - 4 % of the TRR (0.001 - 0.020 mg/kg) in all matrices except wheat grain; prothioconazole-triazolyl-ethanol-glucoside (M46), <1 - 5 % of the TRR (0.001 - 0.063 mg/kg) in all matrices except wheat grain and Swiss chard; prothioconazole-triazolyl-ethanol (M45), <1 - 7 % of the TRR (0.002 - 0.030 mg/kg) in all matrices except wheat grain; and prothioconazole- α -hydroxy-desthio (M18), <1 - 2 % of the TRR (0.002 - 0.026 mg/kg) in all matrices except wheat grain and Swiss chard. No prothioconazole was detected in any matrix at any DAT interval.

An overall summary of the nature of residue in rotational crops was also provided in the dRAR (UK, 2018; provisional):

The major metabolites found in all crops were prothioconazole-desthio (M04), TA (M31), THP (M30) and TAA (M29). As no 1,2,4-triazole was detected in any matrix it is assumed that 1,2,4 triazole (M13) was rapidly transformed to the metabolites TA, THP and TAA.

In summary, the metabolic pattern in rotational crops is similar to that observed in primary crops and no specific residue definition for rotational crops is required. The proposed metabolic pathway of prothioconazole in rotational crops is shown in Figure B.7.6.1-1. Residues in rotational crops at harvest were similar to those observed in trials evaluated in the DAR and largely <0.01 mg/kg, therefore further investigation into the magnitude of residues in rotational crops is not required.

It is noted that the studies indicate a potential uptake of the TDMs in rotational crops. Noting that these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA has recommended that a separate risk assessment should be performed for TDMs in rotational crops as soon as the confirmatory data requested for triazole compounds in the framework of Regulation (EC) No 1107/2009 have been evaluated and a general methodology on the risk assessment of triazole compounds and their TDMs is available. It is advised that THP is also considered within any further TDM consideration.

Conclusion on metabolism in rotational crops

The metabolism of prothioconazole has been sufficiently investigated in rotational crops to support the

proposed uses of FF-075 on cereals (wheat, barley, triticale, rye, oat) and oilseed rape.

In the EFSA Conclusion (EFSA, 2007), the following open point was identified:

- No information is available as far as the uptake of triazole derivative metabolites by rotational crops is concerned, given that no study was conducted with radiolabelling in the triazole ring.

A new study is now available to address this point, that has been presented to support the renewal of prothioconazole at EU level, though for which no data protection has been claimed. The study was also assessed by the JMPR (FAO, 2008a, 2008b) and discussed in the 2014 Reasoned Opinion (EFSA, 2014). The study indicated a cleavage of the triazole linkage with the formation of the major metabolites found in all rotational crop matrices as triazole alanine, triazole lactic acid and triazole acetic acid. Both the parent prothioconazole and prothioconazole-desthio (M04) were identified as minor metabolites. No further information is necessary.

The proposed metabolic pathway of prothioconazole in rotational crops based on available data is illustrated in the DAR (UK, 2004) and the dRAR (UK, 2018). No plant back intervals are proposed, nor any risk mitigation measures.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

The effects of processing on the nature of prothioconazole was not investigated in the framework of the Annex I inclusion process.

(EFSA, 2007):

As residues in treated commodities at harvest are at or near the LOQ, and given the low degree of ADI exhaustion in consumer risk assessment, the effect of processing on the nature and level of residues were not investigated.

Supervised residue trials relied on here to support authorisation of FF-075 are from previously EU agreed studies. Therefore, the existing conclusion – that no processing studies are required as residues remain at or near the LOQ at harvest, remains unchanged.

Notwithstanding, consideration of the nature of residues in processed commodities has been made in the framework of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014) and also in the context of the on-going renewal program (UK, 2018; provisional).

A hydrolysis study² was conducted where the stability of [phenyl-UL-¹⁴C]-prothioconazole (ca. 4.6 mg/L in citrate buffers in drinking water) was tested under conditions 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).

An overview of this study is given in Table 7.2-5.

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

² The hydrolysis study (Gilges, 2001, MR-166/00) is not summarised in Vol. 3, section B.7 (Residues) of the 2018 UK dRAR, though is listed in Vol. 2 of the 2018 UK dRAR, where data protection is not claimed. A summary of the study was given in the 2008 FAO Evaluation Manual (FAO, 2008), that has been reproduced here.

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

Conditions (Duration, Temperature, pH)	Identified compound(s) (% of applied radioactivity)	Reference
EU data		
Pasteurisation (20 minutes, 90 °C, pH 4)	Prothioconazole (89.1%) Prothioconazole-desthio (M04) (2.8%) Sum of minor degradation products (5.7%) <i>Recovery: 97.7%</i>	UK, 2018 (provisional) ^[1] EFSA, 2014
Pasteurisation - control (20 minutes, 90 °C, pH 4)	Prothioconazole (94.3%) Prothioconazole-desthio (M04) (1.2%) Sum of minor degradation products (4.5%)	
Baking, boiling, brewing (60 minutes, 100 °C, pH 5)	Prothioconazole (86.2%) Prothioconazole-desthio (M04) (7.4%) Sum of minor degradation products (3.1%) <i>Recovery: 96.7%</i>	
Baking, boiling, brewing – control (60 minutes, 100 °C, pH 5)	Prothioconazole (93.0%) Prothioconazole-desthio (M04) (1.5%) Sum of minor degradation products (5.5%)	
Sterilisation (20 minutes, 120 °C, pH 6)	Prothioconazole (79.0%) Prothioconazole-desthio (M04) (10.6%) Sum of minor degradation products (4.8%) <i>Recovery: 94.4%</i>	
Sterilisation – control (20 minutes, 120 °C, pH 6)	Prothioconazole (90.9%) Prothioconazole-desthio (M04) (3.4%) Sum of minor degradation products (5.7%)	

^[1] Unprotected study evaluated in the dRAR as part of the on-going EU renewal of prothioconazole.

Conclusion on nature of residues in processed commodities

Parent compound prothioconazole is stable under processing by pasteurisation and baking/brewing/boiling. However, under sterilisation, prothioconazole slightly degrades (≤ 11 %) to prothioconazole-desthio (M04).

The components of the residue definition for risk assessment in primary crops – i.e. the sum of prothioconazole-desthio (M04) 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) – are structurally similar to the parent compound and can therefore also be assumed to also remain stable under hydrolysis (EFSA, 2014).

The residue definition for enforcement and risk assessment in processed commodities is the same as for primary crops.

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	Pulses and oilseeds (peanut) Cereals (wheat) Root and tuber vegetables (sugar beet)
Rotational crops covered	Leafy vegetables (Swiss chard) Cereals (wheat) Root and tuber vegetables (turnip)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes EFSA, 2014: <i>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.</i> UK, 2018 (provisional): <i>the metabolic pattern in rotational crops is similar to that observed in primary crops and no specific residue definition for rotational crops is required.</i>
Processed commodities	Prothioconazole is stable under processing by pasteurisation and baking/brewing/boiling. Prothioconazole shows slight degradation (to prothioconazole-desthio (M04) under conditions simulating sterilisation.
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes EFSA, 2014: <i>it can be concluded that the relevant residue for enforcement and risk assessment in processed commodities is expected to be the same as for primary crops.</i>
Plant residue definition for monitoring	Reg. (EU) No. 2019/552, Amending Annexes II and III to Regulation (EC) No 396/2005: <i>Prothioconazole-desthio (sum of isomers)</i>
Plant residue definition for risk assessment	EFSA, 2014; EFSA, 2007; Review Report, 2021: 1) <i>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)</i> 2) <i>Triazole Alanine (TA) and Triazole Lactic Acid (TLA)</i> 3) <i>Triazole Acetic Acid (TAA)</i> 4) <i>1,2,4-Triazole (1,2,4-T)</i>
Conversion factor from enforcement to RA	EFSA, 2007: CF 2 (cereal grain and oilseeds) CF 3 (cereal and rapeseed straw) EFSA, 2014: CF 2 (cereal grain, pulses and oilseeds, leafy vegetables, root and tuber vegetables – tentative ^[1]) CF 3 (cereal straw)

^[1] Conversion factors have been proposed based on metabolism studies, but are regarded by EFSA as tentative, awaiting sufficient residue trials analysing residues in compliance with the proposed residue definition for risk assessment

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

Available data

The nature of residues in livestock for prothioconazole was previously evaluated in the framework of the Annex I inclusion process and summarised in the context of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014).

Metabolism of prothioconazole has been investigated in poultry and lactating ruminants using either [phenyl-UL-¹⁴C]-prothioconazole, [phenyl-UL-¹⁴C]-prothioconazole-desthio or [3,5-¹⁴C-triazole]-prothioconazole.

A summary of the available data is provided in Table 7.2-7.

No new data are submitted in the framework of this application. Rotam has access to all studies summarised in EFSA, 2014.

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	[phenyl-UL- ¹⁴ C]-prothioconazole	1	10 (250 mg a.s./kg feed)	3	Milk	Twice daily and immediately before sacrifice ^[1]	EFSA, 2014 UK, 2007 UK, 2004
						Urine and faeces	Daily and immediately before sacrifice ^[1]	
						Tissues	At sacrifice	
		[phenyl-UL- ¹⁴ C]-prothioconazole-desthio	1	10 (ca. 200 mg a.s./kg feed)	3	Milk	Twice daily and immediately before sacrifice ^[1]	EFSA, 2014 UK, 2007 UK, 2004
						Urine and faeces	Daily and immediately before sacrifice ^[1]	
						Tissues	At sacrifice	
		[3,5- ¹⁴ C-triazole]-prothioconazole	1	10	3	Milk	Twice daily	UK, 2018 (provisional) ^[2] EFSA, 2014
						Urine and faeces	Daily and at sacrifice	
						Tissues	At sacrifice	
Laying poultry	Hens	[phenyl-UL- ¹⁴ C]-prothioconazole	6	10	3	Eggs	Twice daily	EFSA, 2014 UK, 2007 UK, 2004
						Excreta	Regular intervals	
						Tissues	At sacrifice	
				[3,5- ¹⁴ C-	6	10	3	Eggs

		triazole]- prothioconazole				Excreta	Regular intervals	(provisional) [2]
						Tissues	At sacrifice [1]	EFSA, 2014
Pig	Not necessary – no significant difference in prothioconazole metabolism were observed in rat, laying hen and lactating ruminant following oral administration.							
Fish	Not applicable – standardised test methods and guidance for conducting fish metabolism studies are not yet available. [3]							

[1] Five hours after final dose.

[2] Unprotected study evaluated in the dRAR as part of the on-going EU renewal of prothioconazole.

[3] As stated in SANCO document 10181/2013-rev. 3 (12 December 2014), in cases where “test methods or guidance documents are not yet available for particular data requirements [...] waiving of these particular data requirement points is considered acceptable as long as no test methods or guidance documents are published in form of an update of the Commission Communications 2013/C 95/01 and 2013/C 95/02.” Further, in the November 2014 SCoPAFF (pesticide residues) the EU Commission stated: “The Commission emphasized that for the time being there are no agreed test guidelines and that hence the pertinent data requirements can be waived. This was also clarified in general at the meeting of them Committee’s section on Plant Protection Products - Legislation on 09/10 October 2014, and laid down in document SANCO/10181/2013 Rev 2.1. Such test guidelines must be published in the form of an update of the respective Commission Communications.”

Summary of animal metabolism studies reported in the EU

EFSA, 2014:

Lactating goats

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

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.

Overall assessment

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.

Based on the overall metabolic picture of prothioconazole and prothioconazole-desthio in animals, the residue definition for enforcement in animal products is proposed as prothioconazole-desthio (sum of isomers) for all livestock matrices. It is noted that although only the glucuronide conjugates of prothioconazole-desthio were detected in milk, the actual residue levels are expected at a trace level at the calculated dietary burden (< 0.01 mg/kg) and EFSA considers that analysing the conjugates of prothioconazole-desthio would have a negligible impact on the residue levels enforced in milk. In case the livestock dietary burden is further increased in the future due to additional uses on feed items, the residue definition for enforcement might have to be revised by including the glucuronide conjugates of prothioconazole-desthio for all livestock matrices.

For risk assessment, since all the metabolites are structurally related to prothioconazole-desthio and consist mainly in hydroxylated derivatives, EFSA assumes as a worst case that the toxicological end points allocated to prothioconazole-desthio should also be applied to these metabolites. The residue is therefore defined in all commodities of animal origin 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).

[...]

Since higher prothioconazole-desthio residue levels were found in fat compared to fat free muscle, EFSA concludes that the residue definition for enforcement in commodities of animal origin is fat soluble.

It is noted that the above studies do not investigate the possible impact of livestock metabolism on the isomer ratio of prothioconazole and the same considerations as for plant commodities apply.

EFSA emphasises that the above residue definitions do not yet take into consideration triazole derivative metabolites (TDMs). Since these metabolites may be generated by several pesticides belonging to the group of triazole fungicides, EFSA recommends that a separate risk assessment should be performed for TDMs as soon as the confirmatory data requested for triazole compounds in the framework of Regulation (EC) No 1107/2009 have been evaluated and a general methodology on the risk assessment of triazole compounds and their triazole derivative metabolites is available.

Conclusion on metabolism in livestock

The proposed metabolic pathway of prothioconazole in livestock based on available data is illustrated in the DAR (UK, 2004), DAR Addendum (UK, 2007) and the dRAR (UK, 2018) concluding that as there are no significant changes to the proposed metabolic pathway in ruminants, and no new rat metabolism studies have been assessed, the conclusions on the need for metabolism studies in pigs remain unchanged from the 2014 Article 12 MRL Review (EFSA Journal 2014;12(5):3689):

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.

Rotam has access to all studies summarised in EFSA, 2014.

It is noted that *Guidance of EFSA on risk assessments for active substances of plant protection products that have stereoisomers as components or impurities and for transformation products of active substances that may have stereoisomers* was published in 2019 (EFSA Journal 2019;17(8):5804). In 2020, as part of the 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), EFSA proposed that consideration of the possible impact of plant metabolism on the isomer ratio of prothioconazole is further considered in the framework of the renewal of the approval process of prothioconazole. Further consideration of the topic as part of this submission – that is based on existing endpoints – is therefore not applicable.

Additionally, the *Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data* submitted for a subset of triazole active substances was published in 2018 (EFSA Journal 2018;16(7):5376). However, a common risk assessment methodology is not yet finalised for all triazole containing compounds. Consideration of TDMs with respect to the consumer risk assessment for FF-075 is presented within Appendix 4 of this document. The dietary risk assessment performed as part of the EU peer review addresses the exposure to TDMs related to primary crops, processed commodities, rotational crops and food of animal origin, and is sufficient to provisionally conclude that no chronic health or acute effects are expected as a result of consumer exposure to the TDM residues associated with the proposed uses of FF-075.

In conclusion, the metabolism of prothioconazole can be considered sufficiently investigated in livestock to support the proposed uses of FF-075 on cereals (wheat, barley, triticale, rye, oat) and oilseed rape in accordance with existing endpoints.

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	Egg: Not applicable – a plateau concentration was not reached under the conditions of the metabolism studies.
	Milk: In the lactating goat metabolism study with [3,5- ¹⁴ C-triazole]-prothioconazole, the TRR recovered in milk samples reached a plateau at 32 to 48 hours after the first administration.
Animal residue definition for monitoring	Reg. (EU) No. 2019/552, Amending Annexes II and III to Regulation (EC) No 396/2005: Prothioconazole-desthio (sum of isomers)
Animal residue definition for risk assessment	EFSA, 2014; EFSA, 2007; Review Report, 2021: <ol style="list-style-type: none"> 1) 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) 2) Triazole Alanine (TA) and Triazole Lactic Acid (TLA) 3) Triazole Acetic Acid (TAA) 4) 1,2,4-Triazole (1,2,4-T)
Conversion factor	EFSA, 2007: CF 10 (milk, muscle) CF 2 (liver, kidney) CF 4 (fat) EFSA, 2014:

	CF 2 (liver) CF 9 (kidney) No conversion factor was set for milk, muscle and fat as the residue levels in these matrices are expected to be negligible (<0.01 mg/kg) at the calculated dietary burden.
Metabolism in rat and ruminant similar	Yes EFSA, 2014: <i>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.</i>
Fat soluble residue	Yes EFSA, 2014: <i>Since higher prothioconazole-desthio residue levels were found in fat compared to fat free muscle, EFSA concludes that the residue definition for enforcement in commodities of animal origin is fat soluble.</i>

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

Note: In support of the proposed uses on cereals and oilseed rape, the following trials are in progress (in all cases, the field phase is complete, with the analytical phase due to be completed in Q2/Q3 2021) with applications made at the proposed GAP:

- 8 x NEU and 8 SEU trials on wheat (Study No. QG/20/005)
- 8 x NEU and 8 SEU trials on barley (Study No. QG/20/006)
- 8 x NEU and 8 SEU trials on oilseed rape (Study No. QG/20/005 - includes determination of residue in aerial parts)

Details of these new (ongoing) studies have been added to Appendix 2 of this document, and may be updated once the analytical phases are completed and finalised study reports are available.

Residues will be determined according to the residue definition for risk assessment in plants: “*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 Annex I data summarised below provide an indication of the anticipated residues of prothioconazole in crops likely to result from applications made at the proposed GAPs for FF-075. Residues of prothioconazole in primary crops will be confirmed by the above trials, which are anticipated to be completed in Q2/Q3 2021.

Wheat (including triticale, spelt, durum)

Wheat is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires

eight trials per zone.

Residue trials conducted on wheat in the northern residue zone to support the EU critical GAP were previously evaluated in the framework of the Annex I inclusion process and in the context of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014). In the 2007 EFSA Conclusion, eleven trials (NEU) were considered acceptable to support the EU cGAP, i.e. **3 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.**

This application relies upon the trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition - prothioconazole-desthio (sum of isomers). The intended cGAP of prothioconazole in FF-075 on wheat (and triticale) is: **2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.** Therefore, the intended cGAP of prothioconazole in FF-075 is considered the same, or less critical than the EU-cGAP (identical application rate and growth stage at last application, with fewer maximum applications). The EU trials therefore can be used to support the registration of FF-075. No exceedance of the existing EU MRL for prothioconazole in wheat (0.1 mg/kg) is anticipated as a result of the proposed use.

Rye

According to the technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (SANTE/2019/12752), extrapolation to rye is permissible from wheat, either before or after formation of the edible part (defined as BBCH 51 for cereals).

The intended cGAP of prothioconazole in FF-075 on rye is identical to the cGAP for wheat, i.e.: **2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d,** therefore the EU data relied on to support the use of FF-075 on wheat can be extrapolated to cover the use on rye. No exceedance of the existing EU MRL for prothioconazole in rye (0.05 mg/kg) is anticipated as a result of the proposed use.

Barley

Barley is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires eight trials per zone.

Residue trials conducted on barley in the northern residue zone to support the EU critical GAP were previously evaluated in the framework of the Annex I inclusion process and in the context of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014). In the 2007 EFSA Conclusion, nine trials (NEU) were considered acceptable to support the EU cGAP, i.e.: **2 x 0.2 kg a.s./ha (foliar), BBCH 61, PHI 35 d, int. 14 d.**

This application relies upon the trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition – prothioconazole-desthio (sum of isomers). The intended cGAP of prothioconazole in FF-075 on barley is: **2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.** For uses on cereals, it is considered that the critical parameters in the GAP are the growth stage of the crop at last application and the application rate.

The intended cGAP of prothioconazole in FF-075 is therefore considered slightly more critical than the EU-cGAP (later growth stage at last application, BBCH 69 vs. BBCH 61). Though, it is expected that this difference will have no significant impact on the final residue value, given both growth stages are during flowering and there is an appreciable time from the last application at BBCH 69 to normal commercial harvest. In addition, SEU trials on barley evaluated in the DAR with two foliar applications at 0.2 kg a.s./ha and last applications at BBCH 69-71 resulted in residues in grain of <0.01 - 0.02 mg/kg. Consequently, it is not expected that the proposed cGAP for FF-075 would result in residues in barley of >0.02 mg/kg. The EU trials can therefore be used to support the registration of FF-075. No exceedance of the existing EU MRL for prothioconazole in barley (0.2 mg/kg) is anticipated as a result of the proposed use.

Oat

According to the technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (SANTE/2019/12752), extrapolation to oat is permissible from barley, either before or after formation of the edible part (defined as BBCH 51 for cereals).

The intended cGAP of prothioconazole in FF-075 on oat is the same as that for barley, i.e.: **2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d**, therefore the EU data relied on to support the use of FF-075 on barley can be extrapolated to cover the use on oat. No exceedance of the existing EU MRL for prothioconazole in oat (0.05 mg/kg) is anticipated as a result of the proposed use.

Oilseed rape

Oilseed rape is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires eight trials per zone.

Residue trials conducted on oilseed rape in the northern residue zone to support the EU critical GAP were previously evaluated in the framework of the Annex I inclusion process and in the context of the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014). In the 2007 EFSA Conclusion, eight trials (NEU) were considered acceptable to support the EU cGAP, i.e. **2 x 0.175 kg a.s./ha (foliar), BBCH 53 onwards, PHI 56 d, int. 14 d**.

This application relies upon the trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition – prothioconazole-desthio (sum of isomers). The intended cGAP of prothioconazole in FF-075 on oilseed rape is: **2 x 0.16 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d**. It is not clear whether the intended cGAP of prothioconazole in FF-075 is more or less critical than the EU-cGAP; stages at last application are “BBCH 69” and “BBCH 53 onwards” respectively, with a slightly lower application rate and a shorter PHI in the intended cGAP for FF-075, though in both cases applications are likely to be made at similar timings. The residues observed in the available trials (maximum of 0.02 mg/kg) indicate that exceedance of the current EU MRL for prothioconazole in oilseed rape (0.15 mg/kg) would not be anticipated as a result of the proposed use of FF-075. In addition, four of the NEU trials evaluated in the DAR included decline data for oilseed rape pods in which residues remained <LOQ at 41 or 42 day pre-harvest intervals.

Available data are summarised in Table 7.2-9 below.

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of FF-075 and conformity to existing MRL. Data not relevant to this assessment (i.e. SEU data) have been greyed out.

Commodity	Source	Residue zone (NEU, SEU, EU, non-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 (inc. durum, winter and spring wheat, spelt and triticale) → extrapolated to Rye	EFSA, 2007	NEU	cGAP on which EU a.s. assessment is based: 3 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 11, E): 11 x <0.01 Straw (n = 11, E): 0.08 ^[4] , 0.09, 0.11, 0.14, 0.15, 0.19, 0.20 ^[1] , 0.27, 0.31 ^[2] , 0.66, 0.72 ^[3]	N/A									
		SEU	cGAP on which EU a.s. assessment is based: 3 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 8, E): 8 x <0.01 Straw (n = 8, E): 0.25 ^[12] , 0.41, 0.42 ^[8] , 0.52 ^[6] , 0.53 ^[7] , 0.72 ^[5] , 0.77 ^[9] , 0.85										
	New trials	NEU	Trials in progress.										
		SEU											
	Overall supporting data for cGAP	NEU	cGAP: 2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 11, E): 11 x <0.01		0.01	0.01	0.01*	0.1 (wheat/ triticale) 0.05 (rye)	Yes				
			Straw (n = 11, E): 0.08, 0.09, 0.11, 0.14, 0.15, 0.19, 0.20, 0.27, 0.31, 0.66, 0.72		0.19	0.72	1.15	n/a	n/a				
			SEU	cGAP: 2 x 0.2 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 8 ^[15] , E): 8 x <0.01		0.01	0.01	0.01*	0.1 (wheat/ triticale) 0.05 (rye)	Yes			

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			Straw (n = 8 ^[15] , E): 0.25, 0.41, 0.42, 0.52, 0.53, 0.72, 0.77, 0.85	0.53	0.85	1.68	n/a	n/a
Barley → extrapolated to Oat	EFSA, 2007	NEU	cGAP on which EU a.s. assessment is based: 2 x 0.2 kg a.s./ha (foliar), BBCH 61, PHI 35 d, int. 14 d Grain (n = 9, E): 9 x <0.01 Straw (n = 9, E): 0.05, 0.08, 2 x 0.10, 2 x 0.13, 2 x 0.14, 0.30	N/A				
		SEU	cGAP on which EU a.s. assessment is based: 2 x 0.2 kg a.s./ha (foliar), BBCH 61, PHI 35 d, int. 14 d Grain (n = 8, E): 2 x <0.01, 2 x 0.01, 4 x 0.02 ^[10] Straw (n = 8, E): 0.16, 0.19, 0.38 ^[13] , 0.53 ^[11] , 0.75, 2 x 1.1, 1.2 ^[14]					
		New trials	NEU					
	SEU							
	Overall supporting data for cGAP	NEU	cGAP: 2 x 0.2 kg a.s./ha (foliar), BBCH 65, PHI 35 d, int. 14 d Grain (n = 9 ^[16] , E): 9 x <0.01	0.01	0.01	0.01*	0.2 (barley) 0.05 (oat)	Yes
			Straw (n = 9 ^[16] , E): 0.05, 0.08, 2 x 0.10, 2 x 0.13, 2 x 0.14, 0.30	0.13	0.30	0.41	n/a	n/a
		SEU	cGAP: 2 x 0.2 kg a.s./ha (foliar), BBCH 65, PHI 35 d, int. 14 d Grain (n = 8 ^[17] , E): 2 x <0.01, 2 x 0.01, 4 x 0.02	0.015	0.02	0.038	0.2 (barley) 0.05 (oat)	Yes
			Straw (n = 8 ^[17] , E): 0.16, 0.19, 0.38, 0.53, 0.75, 2 x 1.1, 1.2	0.64	1.20	2.38	n/a	n/a
Oilseed rape	EFSA, 2007	NEU	cGAP on which EU a.s. assessment is based: 2 x 0.175 kg a.s./ha (foliar), BBCH 53 onwards, PHI 56 d, int. 14 d Seed (n = 8, E): 5 x <0.01, 0.01, 2 x 0.02	N/A				
		SEU	cGAP on which EU a.s. assessment is based: 2 x 0.175 kg a.s./ha (foliar), BBCH 53 onwards, PHI 56 d, int. 14 d Seed (n = 4, E): 2 x <0.01, 2 x 0.01					
	New trials	NEU	Trials in progress.					

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		SEU						
Overall supporting data for cGAP	NEU	cGAP: 2 x 0.175 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Seed (n = 8, E): 5 x <0.01, 0.01, 2 x 0.02	0.01	0.02	0.031	0.15	Yes	
	SEU	cGAP: 2 x 0.175 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Seed (n = 4, E): 2 x <0.01, 2 x 0.01	0.01	0.01	Not possible (n = 2)	0.15	Yes ^[18]	

* Source of EU MRL: Reg. (EU) 2019/552, amending Annexes II and III to Regulation (EC) No 396/2005

E = prothioconazole-desthio (sum of isomers)

RA = 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)

^[1] 0.14 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.20 mg/kg was found at a later PHI of 51 d (accepted in EFSA, 2007 & EFSA, 2014).

^[2] 0.25 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.31 mg/kg was found at a later PHI of 50 d (accepted in EFSA, 2007 & EFSA, 2014).

^[3] 0.67 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.72 mg/kg was found at a later PHI of 46 d (accepted in EFSA, 2007 & EFSA, 2014).

^[4] 0.07 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.08 mg/kg was found at a later PHI of 46 d (accepted in EFSA, 2007 & EFSA, 2014).

^[5] 0.51 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.72 mg/kg was found at a later PHI of 40 d (accepted in EFSA, 2007 & EFSA, 2014).

^[6] 0.31 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.52 mg/kg was found at a later PHI of 42 d (accepted in EFSA, 2007 & EFSA, 2014).

^[7] 0.26 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.53 mg/kg was found at a later PHI of 57 d (accepted in EFSA, 2007 & EFSA, 2014).

^[8] 0.31 mg/kg was chosen as the critical residue (PHI 35 d) in the DAR Addendum (UK, 2007), however residue of 0.42 mg/kg was found at a later PHI of 49 d (accepted in EFSA, 2007 & EFSA, 2014).

^[9] 0.62 mg/kg was chosen as the critical residue (PHI 36 d) in the DAR Addendum (UK, 2007), however residue of 0.77 mg/kg was found at a later PHI of 42 d (accepted in EFSA, 2007 & EFSA, 2014).

^[10] 0.01 mg/kg was chosen as the critical residue (PHI 35 d) from one trial in EFSA 2014 and EFSA 2007, however a more critical residue of 0.02 mg/kg was found at a later PHI of 49 d.

^[11] 0.41 mg/kg was chosen as the critical residue (PHI 35 d) in EFSA 2014 and EFSA 2007, however a residue of 0.53 mg/kg was found at a later PHI of 42 d.

^[12] EFSA, 2014 and EFSA, 2007 accepted a critical residue of 0.22 mg/kg for this trial (PHI 42 d), however the correct critical residue is considered to be 0.25 mg/kg (at PHI 35 d).

^[13] EFSA, 2014 and EFSA, 2007 accepted a critical residue of 0.32 mg/kg for this trial (PHI 41 d), however the correct critical residue is considered to be 0.38 mg/kg (at PHI 35 d).

^[14] EFSA, 2014 and EFSA, 2007 accepted a critical residue of 0.42 mg/kg for this trial (PHI 48 d), however the correct critical residue is considered to be 1.2 mg/kg (at PHI 35 d).

^[15] Two trials with slightly earlier growth stages (last application at BBCH 68 & BBCH 67) are accepted in the data package to support the cGAP (BBCH 69). The impact on the final residue is expected to be negligible.

^[16] Nine trials with earlier growth stages at last application of BBCH 59-63 are accepted in the data package to support the cGAP (BBCH 69). The impact on the final residue is expected to be negligible, given sampling is in line with normal commercial harvest at a much later growth stage (BBCH 99).

^[17] Five trials with earlier growth stages at last application of BBCH 58 up to 69 are accepted in the data package to support the cGAP (BBCH 69). The impact on the final residue is expected to be negligible, given sampling is in line with normal commercial harvest at a much later growth stage (BBCH 99).

^[18] To be confirmed by the ongoing trials, which are anticipated to be completed in Q2/Q3 2021.

7.2.3.2 Conclusion on the magnitude of residues in plants

According to existing endpoints:

- Sufficient trials analysing for the single component of the enforcement residue definition (prothioconazole-desthio (M04)) are available to support the intended uses of FF-075 on wheat (including triticale, durum and spelt), rye, oat and barley in the northern residue zone.
- According to the available data, the intended uses of FF-075 are considered acceptable for outdoor uses.
- The data submitted show that no exceedance of the MRL will occur.
- The uses are considered acceptable.

Though, it is noted the proposed GAP for oilseed rape is not identical to the Annex I cGAP, the current EU MRL for oilseed (0.15 mg/kg) is an order of magnitude greater than the residues observed in the available trials (maximum of 0.02 mg/kg). MRLs in all commodities have been used as inputs for the consumer risk assessments resulting in a maximum chronic intake (TMDI) of 35 % (NL toddler) of the ADI for prothioconazole and a maximum acute intake (IESTI) of 29 % (wheat, children) of the ARfD. Therefore it can be reasonably expected that there will be no chronic or acute risk to health as a result of the proposed uses of FF-075 on crops including oilseed rape. Residues of prothioconazole in primary crops resulting from the proposed uses of FF-075 will be confirmed by the ongoing trials described above, which are anticipated to be completed in Q2/Q3 2021.

A comparison of the proposed GAPs for FF-075 to the relevant GAPs and residue trials considered as part of the EU *Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted* (EFSA Journal 2018;16(7):5376) is presented in Appendix 4. The FF-075 cGAPs are equivalent or less critical than the cGAPs evaluated as part of the EU TDM confirmatory data assessment; therefore, these data are relied upon without scaling for the consumer risk assessment. These confirmatory data were protected for 10 years from the inclusion of approval of prothioconazole in 2008; therefore, the data protection period has expired.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

The below dietary burden calculation (2017 Animal Model, OECD methodology) was performed by EFSA in the 2020 *Evaluation of confirmatory data following the Article 12 MRL review and modification of the existing MRLs for prothioconazole in celeriacs and rapeseeds* (EFSA Journal 2020;18(2):5999). As the proposed uses of FF-075 are supported by data evaluated as part of the Annex I inclusion for prothioconazole, the below animal dietary burden calculation, based on more critical GAPs, is considered to appropriate to support the proposed uses of FF-075. The only exception is for oilseed rape meal, for which the data considered in the MRL review is based on a cGAP of 2 x 120 g a.s./ha applications with a 14 day interval and PHI of 28 days; however, as the input value of 0.16 mg/kg (STMR (0.08) x PF (2)) indicates higher residues levels than the trials on oilseed rape considered in section 7.2.3 of this document (STMR of 0.01 mg/kg in oilseed rape trials performed in both Northern and Southern EU), no increase in the animal dietary burden can be anticipated as a result of the proposed uses of FF-075.

Table 7.2-10: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure (EFSA Journal 2020;18(2):5999) and the uses under consideration)

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)	0.16	STMR x PF(2) _(a)
Sunflower seed meal	0.04	STMR x CF (2) x PF (2) _(a) (EFSA, 2015a,b)	0.04	STMR x CF (2) x PF (2) _(a) (EFSA, 2015a,b) _(a)
Head cabbage	0.02	STMR x CF (EFSA, 2014)	0.12	HR x CF (EFSA, 2014)
Maize silage	0.01	STMR (EFSA, 2014)	0.01	HR (EFSA, 2014)
Maize grain	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2014)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2014)
Maize, milled by-products, hominy meal, gluten feed/meal, Distiller's grain _(b)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2014)	0.02	STMR (FAO, 2014) x CF (2) (EFSA, 2014)
Barley grain	0.07	STMR (FAO, 2009b) x CF (2) (EFSA, 2014)	0.07	STMR (FAO, 2009b) x CF (2) (EFSA, 2014)
Brewer's grain	0.23	STMR barley grain (FAO, 2009b) x CF (2) (EFSA, 2014) x PF (3.3) _(a)	0.23	STMR barley grain (FAO, 2009b) x CF (2) (EFSA, 2014) x PF (3.3) _(a)
Oat grain	0.02	STMR (FAO, 2009a) x CF (2) (EFSA, 2014)	0.02	STMR (FAO, 2009a) x CF (2) (EFSA, 2014)
Wheat grain	0.04	STMR (FAO, 2009b) x CF (2) (EFSA, 2014)	0.04	STMR (FAO, 2009b) x CF (2) (EFSA, 2014)
Wheat gluten meal _(b)	0.04	STMR wheat grain (FAO, 2009b) x CF (2) x PF (1.8) _(a)	0.04	STMR wheat grain (FAO, 2010) x CF (2) x PF (1.8) _(a)
Wheat milled by-products _(b)	0.28	STMR wheat grain (FAO, 2009b) x CF (2) x PF (7) _(a)	0.28	STMR wheat grain (FAO, 2010) x CF (2) x PF (7) _(a)
Rye grain	0.02	STMR (FAO, 2009a) x CF (2)	0.02	STMR (FAO, 2009a) x CF (2)
Barley straw	1.96	STMR (FAO, 2009b) x CF (3) (EFSA, 2014)	7.50	HR _(d) x CF (3) (EFSA, 2014)
Oat straw	1.26	STMR _(d) x CF (3) (EFSA, 2014)	7.50	HR _(d) x CF (3) (EFSA, 2014)
Wheat straw	2.69	STMR	5.52	HR _(d) (EFSA, 2014) x CF (2.3)
Rye straw	2.25	STMR _(d) x CF (3) (EFSA, 2014)	5.52	HR _(d) (EFSA, 2014) x CF (2.3)
Cotton seed	0.10	STMR (FAO, 2018) x CF (2)	0.10	STMR (FAO, 2018) x CF (2)
Cotton seed meal	0.14	STMR (FAO, 2018) x CF (2) x PF (1.3) _(a)	0.14	STMR (FAO, 2018) x CF (2) x PF (1.3) _(a)
Beans (dry)	0.02	STMR x CF (2) (EFSA, 2014)	0.02	STMR x CF (2) (EFSA, 2014)
Peas, lupins (dry)	0.10	STMR (FAO, 2009b) x CF (2)	0.10	STMR (FAO, 2009b) x CF (2)

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Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Lupin seed meal	0.11	STMR (FAO, 2009b) x CF (2) x PF (1.1) (a)	0.11	STMR (FAO, 2009b) x CF (2) x PF (1.1) (a)
Potatoes	0.01	STMR (EFSA, 2014)	0.01	HR (EFSA, 2014)
Potato process waste, Potato dried pulp (b)	0.01	STMR potato (EFSA, 2014) x PF (1)(c)	0.01	HR potato (EFSA, 2014) x PF (1)(c)
Turnips, swedes, carrot culls	0.08	STMR	0.10	HR
Peanut meal	0.04	STMR (FAO, 2009b) x CF (2) x PF (2)	0.04	STMR (FAO, 2009b) x CF (2) x PF (2)
Linseed meal	0.12	STMR x CF (2) x PF (2)(a) (EFSA, 2015a, b)	0.12	STMR x CF (2) x PF (2)(a) (EFSA, 2015a, b)
Soybean seed	0.10	STMR (FAO, 2014) x CF (2)	0.10	STMR (FAO, 2014) x CF (2)
Soybean seed meal	0.13	STMR (FAO, 2014) x CF (2) x PF (1.3) (a)	0.13	STMR (FAO, 2014) x CF (2) x PF (1.3) (a)
Soybean hulls (b)	1.30	STMR soybean (FAO, 2014) x CF (2) x PF (13)(a)	1.30	STMR soybean (FAO, 2014) x CF (2) x PF (13)(a)

STMR: supervised trials median residue; HR: highest residue; PF: processing factor; CF: conversion factor for enforcement to risk assessment residue definition.

[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.

[d] The STMR and HR values derived by the JMPR (FAO, 2009a,b) are lower than the values derived for cereals straws for the authorised EU uses reported in the MRL review.

The results of the calculations are reported in Table 7.2-11 (reproduced from EFSA, 2020). The calculated dietary burdens were found to exceed the trigger value of 0.004 mg/kg bw/day. Further investigation of residues in livestock is required.

Table 7.2-11: Results of the dietary burden calculation

Relevant groups	Dietary burden expressed in				Most critical diet (a)	Most critical commodity (b)		Trigger exceeded (Yes/No)	JMPR 2017 (FAO, 2018)
	mg/kg bw per day		mg/kg DM					0.10	Max burden
	Median	Maximum	Median	Maximum				mg/kg DM	mg/kg DM
Cattle (all diets)	0.036	0.109	1.15	3.10	Dairy cattle	Barley	Straw	Y	18.42 (AUT dairy cattle)
Cattle (dairy only)	0.036	0.109	0.84	2.85	Dairy cattle	Barley	Straw	Y	21.60 (AUT beef cattle)
Sheep (all diets)	0.075	0.236	1.77	5.55	Lamb	Barley	Straw	Y	Not calculated
Sheep (ewe only)	0.059	0.185	1.77	5.55	Ram/ewe	Barley	Straw	Y	Not calculated
Swine (all diets)	0.015	0.018	0.49	0.64	Swine (finishing)	Swede	Roots	Y	Not calculated

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Poultry (all diets)	0.035	0.059	0.52	0.86	Poultry layer	Wheat	Straw	Y	3.05 (EU poultry layer)
Poultry (layer only)	0.035	0.590	0.52	0.86	Poultry layer	Wheat	Straw	Y	Not calculated

(a): When several diets are relevant (e.g. cattle, sheep and poultry "all diets"), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day"

(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

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

Out of protection EU-reviewed active substance data are available that investigate the magnitude of residues in lactating dairy cows after oral administration of unlabelled prothioconazole-desthio at dose levels of 4, 25 and 100 mg/kg feed (equivalent to 0.16, 0.95 and 3.93 mg/kg bw/d) for 28 days. This dose level was equivalent to 1.3, 7.3 and 31 N based on the estimated animal intake calculation performed during the EU approval process, and 1.3, 8.1 and 32 N based on the estimated animal intake in table 7.2-11.

These data demonstrate that when considering the dietary burden intake for ruminants, measurable residues of prothioconazole-desthio equivalent may be expected in ruminant liver (0.04 mg/kg), and kidney (0.02 mg/kg), but no quantifiable residues of prothioconazole-desthio are expected in other tissues and milk (<LOQs of 0.01 and 0.004 mg/kg, respectively).

No swine feeding studies were evaluated during the EU approval process. Data were not required since metabolism in rat and ruminant are similar (EFSA, 2007).

Although the trigger is exceeded for poultry diets in the above dietary burden calculation (EFSA Journal 2020;18(2):5999), based on the intakes calculated in the DAR (UK, 2004) using the residues data relevant to the proposed applications of FF-075 (i.e. within the cGAPs considered for Annex I inclusion), residues of prothioconazole-desthio in poultry products were not anticipated to be relevant and therefore no poultry feeding study was required. Furthermore, the review of the existing MRLs for prothioconazole according to Article 12 of Reg. (EC) No. 396/2005 (EFSA, 2014) concluded that no residues above the LOQ are expected in poultry matrices and therefore that no feeding study is appropriate nor required:

...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.

The dRAR (UK, 2018) conclusion on fish feeding studies remains valid for FF-075:

At present there is no agreed guidance on how to conduct fish feeding metabolism studies in order to determine the residue definition for risk assessment and monitoring and there are no agreed guidance documents on how then to conduct a fish feeding study. It is also the case that there is no agreed EU diet for farmed fish. In the SCoPAFF (pesticide residues) the EU Commission stated the following in November 2014:

The Commission emphasised that for the time being there are no agreed test guidelines and that hence the pertinent data requirements can be waived. This was also clarified in general at the meeting of them Committee's section on Plant Protection Products - Legislation on 09/10 October 2014, and laid down in document SANCO/10181/2013 Rev 2.1. Such test guidelines must be published in the form of an update of the respective Commission Communications.

(NB - The above is taken from summary document of the meeting held on the 24-25 November 2014)

Hence at this time a further consideration of this annex point is not required.

Conclusion on feeding studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints. No exceedances of the existing EU MRLs for prothioconazole in animal commodities are anticipated as a result of the proposed uses of FF-075.

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 magnitude of residues in processed commodities were evaluated during the EU approval process. EFSA (2007) concluded that *“as residues in treated commodities at harvest are at or near the LOQ, and given the low degree of ADI exhaustion in consumer risk assessment, the effect of processing on the nature and level of residues were not investigated”*.

As the proposed uses are supported by EU agreed data previously considered for Annex I approval, no further investigation into the magnitude of residues in processed commodities is considered necessary.

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

7.2.5.2 Conclusion on processing studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints.

7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

Considering available data dealing with nature of residues (see 7.2.2.2), no study dealing with magnitude of residues in succeeding crops is needed (see below).

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

No magnitude of residue studies in rotational crops were evaluated during the EU approval process. Based on the residues observed in the confined rotational crop study, EFSA (2007) concluded that *“under practical conditions of use of prothioconazole according to the representative uses and considering that a fraction of the applied rate is intercepted by the cereal crop, no residue of any metabolite above 0.01 mg/kg is expected in rotational crops and no plant back restriction needs to be proposed.”*

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

Conclusion on rotational crops studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints.

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

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of FF-075. Residues are very low in all plant commodities investigated and cereals are not classed as having melliferous capacity according to the technical guidelines for determining the magnitude of pesticide residues in honey (SANTE/11956/2016 rev. 9).

Oilseed rape is classed as having melliferous capacity. However, based on the maximum residues observed in oilseed rape seed of 0.02 mg/kg (see section 7.2.3 above) and the low percentage of the ADI and ARfD accounted for by the 'worst case' chronic and acute intake estimates calculated using current EU MRL as inputs (see section 7.2.8 below), it is considered highly unlikely that any potential residues of prothioconazole-desthio in honey would result in an unacceptable risk to consumers. Studies investigating the magnitude of residues of prothioconazole in oilseed rape are in progress and are anticipated to be complete in Q3/Q4 2021 (see section 7.2.3.1). These include determination of residues in aerial parts of the oilseed rape crops grown in both the northern and southern EU zones. Furthermore, a study to investigate residues in honey resulting from the use of FF-075 has recently been initiated.

zRMS comment:

Since the intended uses are performed during flowering in a honey-relevant crop (oilseed rape), information on potential residues of prothioconazole and azoxystrobin in honey is required in case of use on oilseed rape. No new data are submitted in the framework of this application. Study to investigate residues in honey resulting from the use of FF-075 has recently been initiated. Therefore, currently use after BBCH 59 is not accepted. Data gap should be supplemented.

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

Chronic and acute exposure calculations were performed using EFSA PRIMo revision 3.1 and calculated exposures were compared with the established toxicological reference values. The toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2) and in the table below:

Table 7.2-12: Toxicological reference values for the dietary risk assessment

Reference value	Source	Year	Value	Study relied upon	Safety factor
Prothioconazole-desthio					
ADI	EFSA	2007	0.01 mg/kg bw/day	Rat - oncogenicity	100
ARfD	EFSA	2007	0.01 mg/kg bw	Rat - oncogenicity	100

7.2.8.1 Input values for the consumer risk assessment

Input values used for the consumer risk assessment are summarised in Table 7.2-13. Current EU MRLs were used as ‘worst-case’ scenario for the exposure calculations. Input values relevant to the plant commodities for the intended use of FF-075 are indicated in bold.

Table 7.2-13: 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 (sum of isomers)				
Wheat grain	0.2	MRL (0.1) x CF (2)	0.2	MRL (0.1) x CF (2)
Barley grain	0.4	MRL (0.2) x CF (2)	0.4	MRL (0.2) x CF (2)
Oat grain	0.1	MRL (0.05) x CF (2)	0.1	MRL (0.05) x CF (2)
Rye grain	0.1	MRL (0.05) x CF (2)	0.1	MRL (0.05) x CF (2)
Rapeseeds/canola seeds	0.3	MRL (0.15) x CF (2)	0.3	MRL (0.15) x CF (2)
All other crops/commodities	Current EU MRLs ^[1]	-	Current EU MRLs ^[1]	-

^[1] [Reg. \(EU\) 2019/552](#) - all commodities with an EU MRL have been included in the calculations.

7.2.8.2 Conclusion on consumer risk assessment

Results of the chronic and acute consumer risk assessments are summarised in Table 7.2-14. The detailed output reports are presented in Appendix 3.

Table 7.2-14: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo rev3.1	35 % (based on NL toddler)
IEDI (% ADI) according to EFSA PRIMo rev3.1	n/a
IESTI (% ARfD) according to EFSA PRIMo rev3.1*	Wheat: 29 % (children) Barley: 22 % (children) Rye: 6 % (children) Rapeseeds/canola seeds: 4 % (children) Oat: 1 % (children)
NTMDI (% ADI) **	n/a
NEDI (% ADI)**	n/a
NESTI (% ARfD) **	n/a

- * include raw and processed commodities if both values are required for PRIMo
- ** if national model is available

MRLs in all commodities were used as inputs for the chronic consumer risk assessments resulting in a maximum chronic intake (TMDI) of 35 % (NL toddler) of the ADI for prothioconazole.

Acute exposure assessments were conducted only for the commodities under consideration, again using current EU MRLs, and resulted in a maximum acute intake (IESTI) of 29 % (wheat, children) of the ARfD.

Based on the ‘worst-case’ TMDI and IESTI calculations performed with MRL inputs, no further refinement of the consumer risk assessment is considered necessary. The proposed uses of prothioconazole in the formulation FF-075 do not represent unacceptable acute and chronic risks for the consumer.

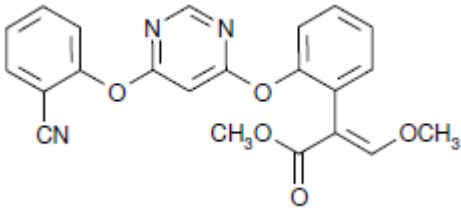
It is noted the *Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data* submitted for a subset of triazole active substances was published in 2018 (EFSA Journal 2018;16(7):5376). However, a common risk assessment methodology is not yet finalised for all triazole containing compounds, and the conclusions on the metabolism in primary crops reported in the DAR (UK, 2004), DAR Addendum (UK, 2007) and the dRAR (UK, 2018) do not take into consideration TDMs.

Consideration of TDMs with respect to the consumer risk assessment for FF-075 is presented in Appendix 4. The dietary risk assessment performed as part of the EU peer review (EFSA Journal 2018;16(7):5376) addresses the exposure to TDMs related to primary crops, processed commodities, rotational crops and food of animal origin, and is sufficient to conclude that no chronic health or acute effects are expected as a result of consumer exposure to the TDM residues associated with the proposed uses of FF-075, as the cGAPs for FF-075 are within the risk envelope considered in the EU Peer review.

7.3 Azoxystrobin

General data on azoxystrobin are summarized in the table below (last updated 2021/03/22)

Table 7.3-1: General information on prothioconazole

Active substance (ISO Common Name)	Azoxystrobin
IUPAC	Methyl (<i>E</i>)-2-{2 [6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate
Chemical structure	
Molecular formula	C ₂₂ H ₁₇ N ₃ O ₅
Molar mass	403.4 g/mol
Chemical group	Methoxyacrylates
Mode of action (if available)	Quinone Outside Inhibitor
Systemic	Yes
Company (ies)	Syngenta
Rapporteur Member State (RMS)	UK
Approval status	Approved on 01/01/2012 Reg. (EU) No 540/2011 Reg. (EU) No 703/2011 Reg. (EU) No 2019/291 Reg. (EU) 2018/155
Restriction	n/a
Review Report	SANCO/11027/2011 Rev 2 17 June 2011
Current MRL regulation	Regulation (EC) No 2019/552 Reg. (EU) 2021/1807 and SANTE/11280/2021
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal: Conclusion on the peer review	EFSA Journal 2010; 8(4):1542
EFSA Journal: Conclusion on Article 12	EFSA Journal 2013;11(12):3497
Current MRL applications on intended uses	n/a

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data

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

In the framework of the EU peer review, storage stability of azoxystrobin was demonstrated for a period of 24 months at -18 °C in commodities with high water content (banana, peach, tomato, cucumber, lettuce, carrot), high acid content (grape, apple, orange), high oil content (soybean meal, oilseed rape, pecans, peanut), dry commodities (cereal grain) as well as cereal straw (EFSA Journal 2010; 8(4):1542). Studies in animal matrices demonstrated storage stability of azoxystrobin in milk, muscle, fat, liver and kidney, eggs for up to 10 months when stored deep frozen (approximately -18 °C).

Table 7.3-2: 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			
Banana	High water content	24 months	UK, 2009 EFSA, 2010
Peach			
Tomato			
Cucumber			
Lettuce			
Carrot			
Oilseed rape	High oil content	24 months	UK, 2009 EFSA, 2010
Pecans			
Peanut			
Cereal grain	Dry/high starch content	24 months	UK, 2009 EFSA, 2010
Grape	High acid content	24 months	UK, 2009 EFSA, 2010
Apple			
Orange			
Straw	Other	24 months	UK, 2009 EFSA, 2010
Animal Products			
Ruminant	Muscle	10 months	UK, 2009 EFSA, 2010
	Fat		
	Liver		
	Kidney		
	Milk		

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G	Rate (kg as/ha)	No	Sampling (DAT)	Remarks	
EU data								

Crop group	Crop	Label position ^[1]	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	Lettuce	¹⁴ C-pyrimidinyl ¹⁴ C-cyanophenyl	G (bare soil)	2.2	30 200 365	At crop maturity	-	UK, 2009 EFSA, 2010
Root and	Radish	¹⁴ C-phenylacrylate						

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tuber vegetables								
Cereals	Wheat							

^[1] A study with each label was performed for each crop, separately.

Summary of plant metabolism studies reported in the EU

EFSA (2010):

Azoxystrobin follows a comparable pattern [to that in primary crops] in rotational crops but with a more extensive metabolism, with more metabolites being formed, most of them as glucose or amino acid conjugates. Based on these studies the residue for monitoring and risk assessment was defined as azoxystrobin only.

Conclusion on metabolism in rotational crops

The metabolism of azoxystrobin can be considered sufficiently investigated in rotational crops to support the proposed uses of FF-075 on cereals and oilseed rape in accordance with existing endpoints.

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data are submitted in the framework of this application. The nature of residues in processed commodities for azoxystrobin was previously evaluated in the framework of the Annex I inclusion process, and these data are now unprotected.

The effect of processing on the nature of azoxystrobin was investigated in the framework of the peer review. Studies were conducted 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 processing by pasteurisation, baking/brewing/boiling and sterilisation is not expected to have a significant impact on the composition of residues in matrices of plant origin (EFSA Journal 2010; 8(4):1542) The relevant residue for enforcement and risk assessment in processed commodities is therefore the same as for primary crops.

Conclusion on nature of residues in processed commodities

The residue definition for enforcement and risk assessment in processed commodities is the same as for primary crops, i.e. azoxystrobin only.

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

Table 7.3-5: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (wheat) Fruit crops (grapes) Oilseeds/Pulses (peanuts)

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Rotational crops covered	Wheat, radish, lettuce
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Azoxystrobin is stable under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Reg. (EU) No. 2019/552, Amending Annexes II and III to Regulation (EC) No 396/2005: <i>Azoxystrobin</i>
Plant residue definition for risk assessment	EFSA, 2010: <i>Azoxystrobin</i>
Conversion factor from enforcement to RA	None (UK, 2009; EFSA, 2010)

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

Available data

No new data are submitted in the framework of this application. The nature of residues in livestock for azoxystrobin was previously evaluated in the framework of the Annex I inclusion process, and these data are now unprotected.

Table 7.3-6: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg diet/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	¹⁴ C-pyrimidinyl- or ¹⁴ C-cyanophenyl- or ¹⁴ C-phenylacrylate	Not reported	23.2 - 32.7	7	Milk	Twice daily	UK, 2009 EFSA, 2010
						Urine and faeces	Daily	
						Tissues	After sacrifice	
		¹⁴ C-cyanophenyl-	1	25	7	Milk	Twice daily	UK, 2009 EFSA, 2010
						Urine and faeces	Daily	
						Tissues	After sacrifice	
Laying poultry	Hens	¹⁴ C-cyanophenyl- or ¹⁴ C-pyrimidinyl- or ¹⁴ C-phenylacrylate	Not reported	11	10	Eggs	Daily	UK, 2009 EFSA, 2010
						Excreta	Daily	
						Tissues	After sacrifice	

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			10	12.5	10	Eggs	n.r.	UK, 2009 EFSA, 2010
						Excreta	Daily	
						Tissues	After sacrifice	
Pig	Not necessary – no significant difference in azoxystrobin metabolism were observed in rat, laying hen and lactating ruminant following oral administration.							
Fish	Not applicable – standardised test methods and guidance for conducting fish metabolism studies are not yet available. ^[1]							

^[1] As stated in SANCO document 10181/2013-rev. 3 (12 December 2014), in cases where “test methods or guidance documents are not yet available for particular data requirements [...] waiving of these particular data requirement points is considered acceptable as long as no test methods or guidance documents are published in form of an update of the Commission Communications 2013/C 95/01 and 2013/C 95/02.” Further, in the November 2014 SCoPAFF (pesticide residues) the EU Commission stated: “The Commission emphasized that for the time being there are no agreed test guidelines and that hence the pertinent data requirements can be waived. This was also clarified in general at the meeting of the Committee’s section on Plant Protection Products - Legislation on 09/10 October 2014, and laid down in document SANCO/10181/2013 Rev 2.1. Such test guidelines must be published in the form of an update of the respective Commission Communications.”

Summary of animal metabolism studies reported in the EU

EFSA (2010):

Azoxystrobin was rapidly excreted in the metabolism studies performed on goats (2N dose) and poultry (8N dose). The transfer in tissues was limited, the TRRs in muscle, fat, milk and egg white being <0.02 mg/kg. Thus, characterisation of residues was only performed in goat liver and kidney, and in poultry liver and egg yolk, where the TRRs were in the range of 0.05 to 1.19 mg/kg. In these matrices, the metabolism was shown to be very extensive, more than 20 compounds being identified/characterised, each accounting mostly for less than 5% of the TRR. Some metabolites (M28, M20, L4...) were however observed in higher proportions in some matrices, depending on the ¹⁴C-label. The parent compound was less than 2% of the TRR, except in egg yolk (12% TRR for the cyanophenyl label). None of these compounds were considered as a sufficient marker for the residue in animal matrices, and the residue for monitoring and risk assessment was then defined by default as azoxystrobin only. However, the definition for risk assessment has to be considered provisional, pending additional information on the toxicological relevance of metabolites L1, L4 and L9.

It is noted that the residue definition for risk assessment remains provisional following the evaluation of confirmatory data following the Article 12 MRL review and modification of the existing maximum residue levels for azoxystrobin (EFSA Journal 2020;18(8):6231).

Conclusion on metabolism in livestock

The metabolism of azoxystrobin can be considered sufficiently investigated in livestock to support the proposed uses of FF-075 on cereals and oilseed rape in accordance with existing EU endpoints.

7.3.2.6 Conclusion on the nature of residues in commodities of animal origin

(KCA 6.7.1)

Table 7.3-7: 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	n/a (TRR <0.02 mg/kg)
Animal residue definition for monitoring	Reg. (EU) No. 2019/552, Amending Annexes II and III to Regulation (EC) No 396/2005: <i>Azoxystrobin</i>
Animal residue definition for risk assessment	EFSA, 2010: <i>Azoxystrobin (provisional)</i> ^[1]
Conversion factor	None (UK, 2009; EFSA, 2010)
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No

^[1] It is noted that the residue definition for risk assessment remains provisional following the evaluation of confirmatory data following the Article 12 MRL review and modification of the existing maximum residue levels for azoxystrobin (EFSA Journal 2020;18(8):6231).

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

Note: In support of the proposed uses on cereals and oilseed rape, the following trials are in progress (in all cases, the field phase is complete, with the analytical phase due to be completed in Q2/Q3 2021) with applications made at the proposed GAP:

- 8 x NEU and 8 SEU trials on oilseed rape (Study No. QG/20/005 - includes determination of residue in aerial parts)

Details of these new (ongoing) studies have been added to Appendix 2 of this document, and may be updated once the analytical phases are completed and finalised study reports are available.

Wheat (including triticale, spelt, durum)

Wheat is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires eight trials per zone.

Residue trials conducted on wheat in the northern residue zone to support the EU critical GAP were previously evaluated in the framework of the Annex I inclusion process. In the 2010 EFSA Conclusion, nine trials (NEU) were considered acceptable to support the EU cGAP, i.e. **2 x 0.25 kg a.s./ha (foliar)**,

BBCH 69, PHI 35 d, int. 14 d.

This application relies upon the trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition – azoxystrobin. The intended cGAP of azoxystrobin in FF-075 on wheat (including triticale, spelt, durum) is: **2 x 0.15 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.** Therefore, the intended cGAP of azoxystrobin in FF-075 is considered the same, or less critical than the EU cGAP, and the EU trials therefore can be used to support the registration of FF-075. No exceedance of the existing EU MRL for azoxystrobin in wheat (0.5 mg/kg) is anticipated as a result of the proposed use.

Rye

According to the technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (SANTE/2019/12752), extrapolation to rye is permissible from wheat, either before or after formation of the edible part (defined as BBCH 51 for cereals).

The intended cGAP of azoxystrobin in FF-075 on rye is identical to the cGAP for wheat, i.e.: **2 x 0.15 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d,** therefore the EU data relied on to support the use of FF-075 on wheat can be extrapolated to cover the use on rye. No exceedance of the existing EU MRL for azoxystrobin in rye (0.5 mg/kg) is anticipated as a result of the proposed use.

Barley

Barley is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires eight trials per zone.

Residue trials conducted on barley in the northern residue zone to support the EU critical GAP were previously evaluated in the framework of the Annex I inclusion process. In the 2010 EFSA Conclusion, eight trials (NEU) were considered acceptable to support the EU cGAP, i.e. **2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.**

This application relies upon the trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition – azoxystrobin. The intended cGAP of azoxystrobin in FF-075 on barley is: **2 x 0.15 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d.** Therefore, the intended cGAP of azoxystrobin in FF-075 is considered the same, or less critical than the EU cGAP, and the EU trials therefore can be used to support the registration of FF-075. No exceedance of the existing EU MRL for azoxystrobin in barley (1.5 mg/kg) is anticipated as a result of the proposed use.

Oat

According to the technical guidelines on data requirements for setting maximum residue levels, comparability of residue trials and extrapolation of residue data on products from plant and animal origin (SANTE/2019/12752), extrapolation to oat is permissible from barley, either before or after formation of

the edible part (defined as BBCH 51 for cereals).

The intended cGAP of azoxystrobin in FF-075 on oat is the same as that for barley, i.e. **2 x 0.15 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d**, therefore the EU data relied on to support the use of FF-075 on barley can be extrapolated to cover the use on oat. No exceedance of the existing EU MRL for azoxystrobin in oat (1.5 mg/kg) is anticipated as a result of the proposed use.

Oilseed rape

Oilseed rape is a major crop in the northern residue zone (SANTE/2019/12752) and therefore generally requires eight trials per zone.

Residue trials conducted on oilseed rape in the northern residue zone were previously evaluated at an EU level in accordance with Article 10 of Regulation (EC) No 396/2005 within the EFSA Reasoned Opinion *Modification of the existing MRLs for azoxystrobin in various oilseeds* (EFSA Journal 2011;9(6):2283). In the 2011 EFSA Reasoned Opinion, eight trials (NEU) were considered acceptable to support the EU cGAP, i.e. **2 x 0.25 kg a.s./ha (foliar), BBCH 55, PHI 21 d, int. not stated**.

This application relies upon the now-unprotected trials previously evaluated at EU level, for which storage stability durations were acceptable and where residues were measured according to the current enforcement residue definition – azoxystrobin. The intended cGAP of azoxystrobin in FF-075 on oilseed rape is: **2 x 0.12 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d**. It is not clear whether the intended cGAP of azoxystrobin in FF-075 is more or less critical than the evaluated EU cGAP; the growth stage at last application are “*BBCH 69*” and “*BBCH 55*” respectively, but with a significantly lower application rate and longer PHI for the intended cGAP for FF-075, likely to result in lower residues at crop harvest. The residues observed in the available trials (maximum of 0.24 mg/kg) indicate that exceedance of the current EU MRL for azoxystrobin in oilseed rape (0.5 mg/kg) would not be anticipated as a result of the proposed use of FF-075.

Available data are summarised in Table 7.3-8 below.

Table 7.3-8: Summary of EU reported and new data supporting the intended uses of FF-075 and conformity to existing MRL. Data not relevant to this assessment (i.e. SEU data) have been greyed out.

Commodity	Source	Residue zone (NEU, SEU, EU, non-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 (inc. durum, winter and spring wheat, spelt and triticale) → extrapolated to Rye	EFSA, 2010	NEU	cGAP on which EU a.s. assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 3 x <0.01, 0.01, 2 x 0.04, 0.07, 0.09, 0.23 Straw (n = 9): 0.34, 0.58, 0.65, 0.75, 0.82, 1.5, 2 x 1.6, 2.0	N/A					
		SEU	cGAP on which EU a.s. assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 3 x <0.01, 0.01, 0.02, 0.03, 2 x 0.04, 0.14 Straw (n = 9): 1.2, 1.6, 1.9, 2.0, 3.2, 2 x 3.5, 3.8, 6.2						
	New trials	NEU	None.						
		SEU							
	Overall supporting data for cGAP	NEU	cGAP: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 3 x <0.01, 0.01, 2 x 0.04, 0.07, 0.09, 0.23	0.04	0.23	0.342	0.5 (wheat) 0.5 (rye)	Yes	
			Straw (n = 9): 0.34, 0.58, 0.65, 0.75, 0.82, 1.5, 2 x 1.6, 2.0	0.82	2.0	3.426	n/a	n/a	
			SEU	cGAP: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 3 x <0.01, 0.01, 0.02, 0.03, 2 x 0.04, 0.14	0.02	0.14	0.201	0.5 (wheat) 0.5 (rye)	Yes
				Straw (n = 9): 1.2, 1.6, 1.9, 2.0, 3.2, 2 x 3.5, 3.8, 6.2	3.2	6.2	9.125	n/a	n/a
Barley → extrapolated	EFSA, 2010	NEU	cGAP on which EU a.s. assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d	N/A					

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Commodity	Source	Residue zone (NEU, SEU, EU, non-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		
to Oat			Grain (n = 8): <0.01, 0.01, 0.02, 2 x 0.04, 0.08, 0.20, 0.43 Straw (n = 8): 0.11, 0.39, 0.48, 0.91, 1.3, 1.5, 2.7, 5.1							
		SEU	cGAP on which EU a.s. assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 0.01, 0.03, 0.04, 0.08, 2 x 0.10, 0.11, 0.13, 0.28 Straw (n = 9): 0.65, 1.2, 1.3, 2x 2.3, 2.5, 2.9, 4.8, 5.5							
		NEU	None.							
	SEU									
	New trials	NEU	cGAP: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 8): <0.01, 0.01, 0.02, 2 x 0.04, 0.08, 0.20, 0.43 Straw (n = 8): 0.11, 0.39, 0.48, 0.91, 1.3, 1.5, 2.7, 5.1	0.04	0.43	0.687	1.5 (barley) 1.5 (oat)	Yes		
		SEU		1.1	5.1	8.145	n/a	n/a		
		Overall supporting data for cGAP		NEU	cGAP: 2 x 0.25 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Grain (n = 9): 0.01, 0.03, 0.04, 0.08, 2 x 0.10, 0.11, 0.13, 0.28 Straw (n = 9): 0.65, 1.2, 1.3, 2x 2.3, 2.5, 2.9, 4.8, 5.5	0.10	0.28	0.415	1.5 (barley) 1.5 (oat)	Yes
				SEU		2.3	5.5	9.084	n/a	n/a
Oilseed rape	EFSA, 2011	NEU	cGAP on which EU MRL assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 55, PHI 21 d, int. not stated Seed (n = 8): 2 x 0.01, 0.03, 0.04, 0.07, 0.10, 0.22, 0.24	N/A						
		SEU	cGAP on which EU MRL assessment is based: 2 x 0.25 kg a.s./ha (foliar), BBCH 55, PHI 21 d, int. not stated Seed (n = 4): <0.01, 0.01, 0.02, 0.05							

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Commodity	Source	Residue zone (NEU, SEU, EU, non-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
	New trials	NEU	Trials in progress.					
		SEU						
	Overall supporting data for cGAP	NEU	2 x 0.12 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Seed (n = 8): 2 x 0.01, 0.03, 0.04, 0.07, 0.10, 0.22, 0.24	0.06	0.24	0.457	0.5	Yes ^[1]
		SEU	2 x 0.12 kg a.s./ha (foliar), BBCH 69, PHI 35 d, int. 14 d Seed (n = 4): <0.01, 0.01, 0.02, 0.05	0.01	0.05	0.098	0.5	Yes ^[1]

* Source of EU MRL: ~~Reg. (EU) 2019/552~~ Reg. (EU) 2021/1807, amending Annexes II and III to Regulation (EC) No 396/2005

E and RA = azoxystrobin

^[1] To be confirmed by the ongoing trials, which are anticipated to be completed in Q2/Q3 2021.

7.3.3.2 Conclusion on the magnitude of residues in plants

According to existing endpoints:

- Sufficient trials analysing for the single component of the residue definition (azoxystrobin) are available to support the intended uses of FF-075 on wheat (including triticale, durum and spelt), rye, oat and barley in the northern residue zone.
- According to the available data, the intended uses of FF-075 are considered acceptable for outdoor uses.
- The data submitted show that no exceedance of the MRL will occur.
- The uses are considered acceptable.

Though, it is noted the proposed GAP for oilseed rape is not identical to the EU cGAP evaluated for the 2011 Article 10 MRL modification, the current EU MRL for oilseed (0.5 mg/kg) is higher than the residues observed in the available trials (maximum of 0.24 mg/kg), which were performed with a significantly higher application rate and a shorter PHI than the proposed cGAP for azoxystrobin in FF-075. MRLs in all commodities have been used as inputs for the consumer risk assessments resulting in a maximum chronic intake (TMDI) of 70 % (NL toddler) of the ADI for azoxystrobin. Therefore it can be reasonably expected that there will be no risk to health as a result of the proposed uses of FF-075 on crops including oilseed rape. Residues of azoxystrobin in oilseed rape resulting from the proposed uses of FF-075 will be confirmed by the ongoing trials described above, which are anticipated to be completed in Q2/Q3 2021.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

A dietary burden calculation was performed by EFSA in the 2013 *Review of the existing MRLs for azoxystrobin* (EFSA Journal 2013;11(12):3497) accounting for all registered uses of azoxystrobin. As the proposed uses of FF-075 are supported by data evaluated as part of the Annex I inclusion for azoxystrobin and in the Article 12 MRL review, the below input values for the animal dietary burden calculation are considered relevant for the proposed uses of FF-075.

Table 7.3-9: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: azoxystrobin				
Head cabbage	0.03	STMR	0.17	HR
Kale	1.04	STMR	3.50	HR
Sugar beet leaves	0.21	STMR	0.38	HR
Orange pomace	11.88	STMR x 2.5	11.88	STMR x 2.5
Other citrus fruit pomace	0.73	STMR x 2.5	0.73	STMR x 2.5

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Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Maize grain	0.01	STMR	0.01	STMR
Wheat, rye grain	0.08	STMR	0.08	STMR
Barley, oat grain	0.10	STMR	0.10	STMR
Wheat, rye bran	0.13	STMR x PF	0.13	STMR x PF
Wheat, rye straw	3.85	STMR	10.1	STMR
Barley, oat straw	2.30	STMR	5.50	STMR
Beans (dry)	0.01	STMR	0.01	STMR
Peas (dry)	0.01	STMR	0.01	STMR
Lupins (dry)	0.01	STMR	0.01	STMR
Potatoes	0.02	STMR	0.03	HR
Turnips	0.06	STMR	0.11	HR
Swedes	0.05	STMR	0.10	HR
Sugar beet roots	0.01	STMR	0.13	HR
Rape seed meal	0.11	STMR x 2	0.11	STMR x 2
Sunflower seed meal	0.02	STMR x 2	0.02	STMR x2
Soya bean	0.05	STMR	0.05	STMR
Soya bean meal	0.07	STMR x 1.3	0.07	STMR x 1.3

STMR: supervised trials median residue; HR: highest residue; PF: processing factor

The results of the calculations are reported in Table 7.3-10 (2017 Animal Model, OECD methodology). The calculated dietary burdens were found to exceed the trigger value of 0.004 mg/kg bw/day. Further investigation of residues in livestock is required.

Table 7.3-10: Results of the dietary burden calculation

Relevant groups	Dietary burden expressed in				Most critical diet (a)	Most critical commodity (b)		Trigger exceeded (Yes/No)
	mg/kg bw per day		mg/kg DM					0.004
	Median	Maximum	Median	Maximum				mg/kg bw
Cattle (all diets)	0.159	0.289	4.14	7.52	Dairy cattle	Kale	leaves	Yes
Cattle (dairy only)	0.159	0.289	4.14	7.52	Dairy cattle	Kale	leaves	Yes
Sheep (all diets)	0.110	0.237	3.18	6.12	Lamb	Rye	straw	Yes
Sheep (ewe only)	0.106	0.204	3.18	6.12	Ram/Ewe	Rye	straw	Yes
Swine (all diets)	0.067	0.109	2.89	4.73	Swine (breeding)	Kale	leaves	Yes
Poultry (all diets)	0.047	0.099	0.69	1.45	Poultry layer	Wheat	straw	Yes
Poultry (layer only)	0.047	0.099	0.69	1.45	Poultry layer	Wheat	straw	Yes

(a): When several diets are relevant (e.g. cattle, sheep and poultry "all diets"), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day"

(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

No new data are submitted in the framework of this application. The 2013 *Review of the existing MRLs for azoxystrobin* (EFSA Journal 2013;11(12):3497) considered the unprotected feeding studies previously evaluated in the framework of the Annex I inclusion process:

During the peer review under Directive 91/414/EEC, the magnitude of azoxystrobin residues in livestock was investigated in feeding studies with lactating cows and laying hens (United Kingdom, 2009a). Four groups of lactating cows, each consisting of three animals, were dosed for 30 consecutive days with azoxystrobin at levels of 5, 25, 75 and 250 mg/kg in the diet (equivalent to 0.18, 0.91, 2.73 and 9.09 mg/kg bw). Three groups of laying hens, each consisting of twelve animals were dosed for 28 consecutive days with azoxystrobin at levels of 6, 18, and 60 mg/kg in the diet (equivalent to 0.39, 1.2 and 3.9 mg/kg bw). The samples were analysed for parent azoxystrobin. Results of both livestock feeding studies are summarized in Table 3-8. In milk and eggs, a plateau level was never reached and no residues at or above 0.01 mg/kg was found in any of the samples.

The storage stability of azoxystrobin residues in animal products was evaluated under the peer review of Directive 91/414/EEC (United Kingdom, 2009a). Studies demonstrated storage stability of azoxystrobin in milk, muscle, fat, liver and kidney, eggs for up to 10 months when stored deep frozen. According to the RMS, all samples reported in the PROFile were stored in compliance with the above reported storage conditions.

Consequently, the available data are considered sufficient for deriving MRLs in ruminants, pigs and poultry. These MRLs were derived in compliance with the latest recommendations on this matter (FAO, 2009) and are summarized in Table 3-7. Significant residues in tissues of ruminants, pigs and poultry, eggs and milk, are not expected and MRLs for these commodities can be established at the LOQ. Considering that the residue definition for risk assessment is tentative, these MRLs are also considered tentative.

Conclusion on feeding studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints. No exceedances of the existing EU MRLs for azoxystrobin in animal commodities are anticipated as a result of the proposed uses of FF-075.

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

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

Studies investigating the magnitude of residues in processed commodities of grapes, wheat, barley and fresh beans with pods were reported in the framework of the EU peer review (EFSA, 2010), and transfer factors were proposed for beans, barley and wheat processed commodities.

Two additional studies, now unprotected, investigating the effects of processing on the magnitude of azoxystrobin residues in oilseed rape were subsequently evaluated at an EU level within the EFSA Reasoned Opinion *Modification of the existing MRLs for azoxystrobin in various oilseeds* (EFSA Journal 2011;9(6):2283). Azoxystrobin residues were measured in cleaned rape seed, press cake and refined oil. In one trial residues in the raw commodity were below the LOQ of 0.01 mg/kg and therefore the effect of processing on the magnitude of residues could not be clearly estimated. The second trial indicated a slight concentration of residues in refined oil (PF = 1.18) and reduction of residues in press cake (PF = 0.18). EFSA did not propose inclusion of the derived processing factors in Annex VI of Regulation (EC) No. 396/2005 as additional processing studies would be required to derive reliable processing factors for enforcement.

As the proposed uses are supported by EU-agreed data, no further investigation into the magnitude of residues in processed commodities is considered necessary. An overview of the available processing studies relevant to the proposed uses of FF-075 is presented in table 7.3-11:

Table 7.3-11: Overview of the available processing studies

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
EU data					
Risk assessment residue definition: Azoxystrobin					
Barley, brewing malt	4	0.19	1.0	Processing factor for malt, beer and pot are actually lower than the value reported as residues were below the LOQ (worst case assumption)	UK, 2009 EFSA, 2010
Barley, beer	4	0.23			
Barley, pot/pearl	4	0.25			
Barley, bran	4	3.25			
Wheat/rye, wholemeal flour	4	0.68			
Wheat/rye, wholemeal bread	4	0.51		None	

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
Wheat/rye, white flour	4	0.45			
Wheat/rye, bran	4	1.67			

* Median processing factor obtained by calculating the median of the individual processing factors of each processing study.

** Median conversion factor for enforcement to risk assessment obtained by calculating the median of the individual conversion factors of each processing study.

7.3.5.2 Conclusion on processing studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints.

Two new processing studies on rapeseeds were submitted in the framework of the MRL application (Greece, 2020). Processing factors (PFs) for the crops under assessment were derived (oilseed rape/meal: 0.175). Further specific studies investigating the magnitude of azoxystrobin residues in other processed commodities are not required, considering the low individual contribution of residues in the commodities under assessment to the total chronic consumer exposure. Results would not be expected to affect the outcome of the risk assessment (EFSA Journal 2022;20(1):7051).

No increased risk for consumers is expected.

7.3.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation. Data dealing with magnitude of residues in succeeding crops are available and are summarised hereafter.

7.3.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

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

Rotational crop field trials were evaluated in the framework of the EU peer review (EFSA, 2010). Azoxystrobin was applied on wheat, cucumber or lettuce at 2 x 0.896 kg a.s./ha, 7-8 x 0.224 kg a.s./ha and 6 x 0.373 kg a.s./ha respectively. After harvest of these crops, rotational crops (mustard, lettuce, radish, turnip, beetroot and wheat) were sown at one, two or three different plant-back intervals (29 to 60 days following application of the active substance) and magnitude of residues was investigated in the different commodities thereof. Considering that all trials were overdosed, a correction factor was applied to the highest residue found in each commodity. At harvest, azoxystrobin residues were expected to be below the LOQ (0.01 mg/kg) in all mature plant parts except in wheat forage and wheat straw. The highest residues were expected to be 0.05 mg/kg and 0.04 mg/kg, respectively. As these values are within the inputs for used in the dietary burden calculation (see section 7.3.4.1), no impact on the residue level in products of animal origin is anticipated.

The studies detailed above were considered sufficient by EFSA to demonstrate that residues in rotational crops will have no impact on the MRLs in plants and livestock products, provided that azoxystrobin is applied in compliance with the EU cGAPs.

Conclusion on rotational crops studies

The available unprotected data are considered sufficient to support the intended product uses of FF-075 on wheat (incl. triticale, durum, spelt), rye, barley, oat and rapeseed when evaluating against existing EU-agreed endpoints.

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

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of FF-075. Residues of azoxystrobin are low in all plant commodities investigated and cereals are not classed as having melliferous capacity according to the technical guidelines for determining the magnitude of pesticide residues in honey (SANTE/11956/2016 rev. 9).

Oilseed rape is classed as having melliferous capacity. However, based on the maximum residues observed in oilseed rape seed of 0.24 mg/kg (see section 7.3.3 above) and the low percentage of the ADI and ARfD accounted for by the ‘worst case’ chronic and acute intake estimates calculated using current EU MRL as inputs (see section 7.3.8 below), it is considered highly unlikely that any potential residues of azoxystrobin in honey would result in an unacceptable risk to consumers. Nevertheless, studies investigating the magnitude of residues of azoxystrobin in oilseed rape are in progress and are anticipated to be complete in Q3/Q4 2021 (see section 7.3.3.1). These include determination of residues in aerial parts of the oilseed rape crops grown in both the northern and southern EU zones.

zRMS comment:

Since the intended uses are performed during flowering in a honey-relevant crop (oilseed rape), information on potential residues of prothioconazole and azoxystrobin in honey is required in case of use on oilseed rape. No new data are submitted in the framework of this application. Study to investigate residues in honey resulting from the use of FF-075 has recently been initiated.

Therefore, currently use after BBCH 59 is not accepted. Data gap should be supplemented.

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

Chronic and acute exposure calculations were performed using EFSA PRIMo revision 3.1 and calculated exposures were compared with the established toxicological reference values. The toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2) and in the table below:

Table 7.3-12: Toxicological reference values for the dietary risk assessment

Reference value	Source	Year	Value	Study relied upon	Safety factor
Azoxystrobin					
ADI	EFSA	2010	0.2 mg/kg bw/day	2-year rat	100
ARfD	EFSA	2010	n/a	n/a	n/a

As an ARfD was not deemed necessary, acute risk assessment is not relevant.

7.3.8.1 Input values for the consumer risk assessment

Input values used for the consumer risk assessment are summarised in Table 7.3-13. Current EU MRLs were used as ‘worst-case’ scenario for the exposure calculations. Input values relevant to the plant commodities for the intended use of FF-075 are indicated in bold.

Table 7.3-13: 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: Azoxystrobin				
Wheat grain	0.5	MRL	n/a	-
Barley grain	1.5	MRL	n/a	-
Oat grain	1.5	MRL	n/a	-
Rye grain	0.5	MRL	n/a	-
Rapeseeds/canola seeds	0.5	MRL	n/a	-
All other crops/commodities	Current EU MRLs ^[1]	-	n/a	-

^[1] [Reg. \(EU\) 2019/552](#) Reg. (EU) 2021/1807- all commodities with an EU MRL have been included in the calculations.

7.3.8.2 Conclusion on consumer risk assessment

Results of the chronic consumer risk assessment are summarised in Table 7.3-14. The detailed output reports are presented in Appendix 3.

Table 7.3-14: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo rev3.1	70 % 82% (based on NL toddler)
IEDI (% ADI) according to EFSA PRIMo rev3.1	n/a
IESTI (% ARfD) according to EFSA PRIMo rev3.1	n/a
NTMDI (% ADI) *	n/a
NEDI (% ADI)*	n/a
NESTI (% ARfD) *	n/a

* if national model is available

MRLs in all commodities were used (Reg. (EU) 2021/1807) as inputs for the chronic consumer risk assessments resulting in a maximum chronic intake (TMDI) of ~~70 %~~ 82% (NL toddler) of the ADI for azoxystrobin.

Based on the ‘worst-case’ TMDI calculation performed with MRL inputs, no further refinement of the consumer risk assessment is considered necessary. The proposed uses of azoxystrobin in the formulation FF-075 do not represent unacceptable chronic risks for the consumer.

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.

7.4.1 Acute consumer risk assessment from combined exposure

The product is a mixture of two active substances, but for only one of them has an acute reference dose been allocated, therefore an acute consumer risk assessment from combined exposure is not 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, and currently no specific consideration is warranted in the scope of this evaluation.

However, a provisional consideration of the combined chronic exposure has been made using the following methodology (akin to the proposed methodology for combined acute exposure):

In the first step, dose addition residues of the individual active substances are 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 chronically toxic by performing deterministic TMDI calculations with the EU PRIMo model and dividing the individual exposure levels by the respective ADI. 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 HI calculations based on the critical consumer (NL toddler) are summarised in Table 7.4-1.

Table 7.4-1: Chronic dietary risk assessment from combined exposure

		% ADI		
		PTZ (HQ)	AZY (HQ)	Cumulative Risk (HI)
Commodities relevant to the intended uses of FF-075	Barley	0.7	0.1	0.8
	Wheat	7.9	1.0	8.9
	Rye	0.4	0.1	0.5
	Oat	0.2	0.2	0.4
	Oil seed rape	2.9	0.2	3.1
	Animal tissues	0.0	0.0	0.0

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	Milk	6.0	0.3	6.3
	Eggs	0.0	0.0	0.0
Total		18.1	1.9	20.0

The hazard index is <100 % for commodities relevant to the intended uses of FF-075 (20.0 % of the ADI). Therefore, the combined exposure to prothioconazole-desthio (PTZ) and azoxystrobin (AZY) resulting from the proposed uses of FF-075 is not expected to present an unacceptable risk to the consumer.


References

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- 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.
- United Kingdom, 2018. Draft (Renewal) Assessment report (**Initial RAR**) on the active substance Prothioconazole prepared by the rapporteur Member State United Kingdom according to the Commission Regulation (EC) No 1107/2009, February 2018.
- EFSA (European Food Safety Authority), 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance azoxystrobin. EFSA Journal 2010; 8(4):1542. doi:10.2903/j.efsa.2010.1542
- United Kingdom, 2009. Renewal Assessment Report (RAR) on the active substance azoxystrobin prepared by the rapporteur Member State United Kingdom in the framework of Council Directive 91/414/EEC, May 2009.
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EFSA (European Food Safety Authority), 2013. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for azoxystrobin according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2013;11(12):3497, 97 pp. doi:10.2903/j.efsa.2013.3497

EFSA (European Food Safety Authority), 2018. 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, 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



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
KCP XX	Author	YYYY	Title Company Report No Source GLP/non GLP/GEP/non GEP Published/Unpublished	Y/N	Owner

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

Prothioconazole

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
IIA 6.0/01	Heinemann, O.	2001a	18 months storage stability of residues of JAU 6476 and JAU 6476-Desthio during frozen storage in/on wheat matrices Bayer AG, Report No.: MR-282/00	N	Bayer
KCA 6.1/03	Freitag, T.	2007	Storage stability of prothioconazole-desthio in/on canola, spinach, sugar beet, tomato, and pea during freezer storage for 24 months MR-07/282	N	Bayer
IIA 4.1.2/23	Heinemann, O.	2000	Analytical determination of residues of JAU6476 and JAU6476-desthio in/on cereals and canola by HPLC-MS/MS (method modification 00598/M001) Bayer AG, Report No.: 00598/M001	N	Bayer
IIA 6.1.1/01	Haas, M.; Bornatsch, W.	2000	Metabolism of JAU6476 in spring wheat (after foliar application) Bayer AG, Report No.: MR-198/99	N	Bayer
IIA 6.1.1/03	Vogeler, K.; Sakamoto, H.; Brauner, A.	1993	Metabolism of SXX 0665 in summer wheat Bayer AG, Report No.: PF3906,	N	Bayer
IIA 6.1.1.1/01	Haas, M.	2001b	Extraction efficiency testing of the residue method (00647) for the determination of JAU 6476 residues in spring wheat using aged radioactive residues Bayer AG, Report No.: MR-084/01	N	Bayer
IIA 6.1.2/01	Haas, M.	2001d	Metabolism of [phenyl-UL- 14C]JAU6476 in peanuts Bayer AG, Report No.: MR-193/01	N	Bayer
IIA 6.2.1/02	Duah, F. K.; Lopez, R. T.	2004	The metabolism of [triazole-3,5-14 C] JAU 6476 in wheat Bayer AG, Report No.: 200733	N	Bayer
IIA	Haas, M.	2000	Metabolism of [triazole-UL-14C]JAU6476 in peanuts	N	Bayer

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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
6.2.1/06			Bayer AG, Report No.: MR-194/02		
IIA 6.2.1/07	Beedle, E. C.; Ying, S. L.	2004	The metabolism of [phenyl-UL-14C]JAU6476 in sugar beets Bayer AG, Repot No.: 200466	N	Bayer
IIA 6.2.1/08	Beedle, E. C.; Ying, S. L.	2004	The metabolism of [triazole-UL-14C]JAU6476 in sugar beets Bayer AG, Repot No.: 200467	N	Bayer
IIA 6.2.2.1 /01	xxxxxxx	2001a	[Phenyl-UL-14C]JAU6476 Absorption, distribution, excretion and metabolism in the lactating goat Bayer AG, Report No.: MR-092/01,	Y	Bayer
IIA 6.2.2.2 /01	xxxxxxx	2002a	[Phenyl-UL-14C]JAU6476-desthio Absorption, distribution, excretion, and metabolism in the lactating goat Bayer AG, Report No.: MR-091/01	Y	Bayer
IIA 6.2.3/02	xxxxxxx	2004	[Triazole-UL-14C]JAU 6476: Absorption, distribution, excretion, and metabolism in the lactating goat Bayer AG, Report No.: MR-448/02	Y	Bayer
IIA 6.2.2.2.1 /01	xxxxxxx	2002b	Validation of the residue analytical method for the determination of JAU6476-desthio, JAU6476-3-hydroxy-desthio and JAU6476-4- hydroxy-desthio residues in animal matrices using aged radioactive residues Bayer AG, Report No.: MR-091/01 Part 2	Y	Bayer
IIA 6.2.2.3 /01	xxxxxxx	2001b	[Phenyl-UL-14C]JAU6476 Absorption, distribution, excretion and metabolism in laying hens Bayer AG, Report No.: MR-309/01	Y	Bayer
IIA 6.2.2.3 /02	xxxxxxx	2001c	[Triazole-UL-14C]JAU6476: Absorption, distribution, excretion, and metabolism in laying hens Bayer AG, Report No.: MEF-005/03	Y	Bayer
IIA 6.3.2.1.2 /02	Heinemann, O.	2001i	Determination of residues of JAU 6476-desthio on spring wheat after spray application of JAU 6476 250 EC in Sweden, Germany, Northern France and Great Britain Bayer AG, Report No.: RA-2104/00, Report includes Trial Nos.: R 2000 0454/0 R 2000 0457/5 R 2000 0474/5	N	Bayer

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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
			R 2000 0475/3 R 2000 0476/1		
IIA 6.3.2.1.2 /04	Heinemann, O.	2001 l	Determination of residues of JAU 6476-desthio in/on wheat and triticale after spray application of JAU 6476 250 EC in Spain and France Bayer AG, Report No.: RA-2105/00, Report includes Trial Nos.: R 2000 0482/6 R 2000 0479/6 R 2000 0478/8 R 2000 0455/9	N	Bayer
IIA 6.3.2.1.3 /03	Heinemann, O.	2001j	Determination of residues of JAU 6476-desthio on spring barley after spray application of JAU 6476 250 EC in Sweden, Germany, Northern France and Great Britain Bayer AG, Report No.: RA-2101/00, Report includes Trial Nos.: R 2000 0452/4 R 2000 0456/7 R 2000 0462/1 R 2000 0464/8 R 2000 0465/6	N	Bayer
IIA 6.3.2.1.3 /05	Heinemann, O.; Elke, K.	2001b	Determination of residues of JAU 6476-desthio in/on winter barley after spray application of JAU 6476 250 EC in France, Italy and Portugal Bayer AG, Report No.: RA-2144/98, Report includes Trial Nos.: R 1998 1317/6 R 1998 1571/3 R 1998 1572/1	N	Bayer
IIA 6.3.2.1.3 /06	Heinemann, O.	2001 k	Determination of residues of JAU 6476-desthio in/on spring barley after spray application of JAU 6476 250 EC in Spain, Italy and Southern France Bayer AG, Report No.: RA-2103/00, Report includes Trial Nos.: R 2000 0473/7 R 2000 0472/9 R 2000 0470/2 R 2000 0453/2	N	Bayer

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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
IIA 6.3.2.2/01	Heinemann, O.	2002a	Determination of residues of JAU 6476-desthio on rape after spray application of JAU 6476 250 EC in Germany, Sweden, Northern France and Great Britain Bayer AG, Report No.: RA-2088/00, Report includes Trial Nos.: R 2000 0079/0 R 2000 0419/2 R 2000 0420/6 R 2000 0421/4	N	Bayer
IIA 6.3.2.2/02	Heinemann, O.	2001g	Determination of residues of JAU 6476-desthio on rape after spray application of JAU6476 250 EC in Southern France Bayer AG, Report No.: RA-2089/00, Report includes Trial Nos.: R 2000 0422/2 R 2000 0080/4	N	Bayer
IIA 6.3.2.2/03	Heinemann, O.	2002c	Determination of residues of JAU 6476-desthio on rape spray application of JAU 6476 250 EC in Germany, Northern France and Great Britain Bayer AG, Report No.: RA-2178/01, Report includes Trial Nos.: R 2001 0518/5 R 2001 0517/7 R 2001 0516/9 R 2001 0515/0	N	Bayer
IIA 6.3.2.2/04	Heinemann, O.	2002b	Determination of residues of JAU 6476-desthio on rape after spray application of JAU 6476 250 EC in southern France Bayer AG, Report No.: RA-2179/01, Report includes Trial Nos.: R 2001 0519/3 R 2001 0520/7	N	Bayer
IIA 6.4/01	xxxxxxxxx	2001	JAU 6476-desthio - Dairy cattle feeding study Bayer AG, Report No.: MR-535/00	Y	Bayer
IIA 6.5/01	Gilges, M.	2001	Hydrolysis of JAU 6476 under conditions of processing Bayer AG, Report No.: MR-166/00	N	Bayer
IIA 6.6/01	Haas, M.	2001c	Confined rotational crop study with JAU6476	N	Bayer

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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
			Bayer AG, Report No.: MR-159/00		
IIA 6.6/02	Duah, F. K.; Kraai, M. J.	2004	The accumulation of [triazole-3,5-14C] JAU6476 in confined rotational crops Bayer AG, Report No.: 200623	N	Bayer

Azoxystrobin

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
IIA 6.1	Allin, R.	1995	ICIA5504: Metabolism in Winter Wheat RJ1888B RIP96-00104	N	Syngenta
IIA 6.1	Earl, V.A. and Hadfield, S.T	1994	ICI5504: Metabolism in Vines RJ1676B RIP96-00105	N	Syngenta
IIA 6.1	Webb, J.	1995	ICI5504: Metabolism in Peanuts RJ1807B RIP96-00106	N	Syngenta
IIA 6.1	Wilkinson, M.J.	1994	ICI5504: Metabolism in Winter Wheat RJ1682B RIP96-00103	N	Syngenta
IIA 6.1.2	Burke, S.R.	1997	Azoxystrobin and R230310: Storage stability in various crops stored deep frozen for up to two years. Final Report. ZENECA Agrochemicals	N	Syngenta

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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
			Report RJ2352B		
IIA 6.1.2	Sapiets, A.	1997	Azoxystrobin: Storage stability of residues in eggs and tissues Study 95JH229 ZENECA Agrochemicals Report Series RJ2352B	N	Syngenta
IIA 6.2	xxxxxx	1994	The metabolism of 14C-Pyrimidinyl labelled ICIA5504 in the laying hen ISN331/942668 RIP96-00110	Y	Syngenta
IIA 6.2	xxxxxx	1995	The metabolism of 14C-Phenyl acrylate labelled ICIA5504 in the laying hen ISN333/950182 RIP96-00111	Y	Syngenta
IIA 6.2	xxxxxx	1995	The metabolism of 14C-Cyanophenyl labelled ICIA5504 in the laying hen ISN333/950918 RIP96-00109	Y	Syngenta
IIA 6.2	xxxxxx	1995	ICIA5504: Metabolism of orally administered multiple doses in the lactating goat RJ1805B RIP96-00107	Y	Syngenta
IIA 6.2	xxxxxx	1995	Further investigation of residues in liver following oral administration of multiple doses to the lactating goat RJ1957B RIP96-00108	Y	Syngenta
IIA 6.2.2/01	xxxxxx	1996	14A-ICIA5504: Metabolism of orally administered multiple doses in laying hens Report No. RJ2084B Syngenta File No. ICI5504/0738	Y	Syngenta
IIA	xxxxxx	1996	ICIA5504: Metabolism of orally administered multiple doses in the lactating goat	Y	Syngenta

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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
6.2.2/02			Report Number: RJ2083B Syngenta File No. ICI5504/0739		
IIA 6.3	Burke, S.R.	1995	ICIA5504 + R23031: Storage stability in various crops stored deep frozen for up to two years. Interim report 3 (Straw, Grapes and Wine) RJ1961B RIP96-00198	N	Syngenta
IIA 6.3	Burke, S.R.	1995	ICIA5504 + R23031: Storage stability in various crops stored deep frozen for up to two years. Interim report 1 (Cereals, Grapes and Wine) RJ1858B RIP96-00140	N	Syngenta
IIA 6.3	Sapiets, A.	1996	ICIA5504: Residue levels in wheat grain and milled process fractions from a trial carried out in Germany during 1995 JR2065B RIP96-00191	N	Syngenta
IIA 6.4	xxxxxx	1995	ICIA5504: Residue transfer study in dairy cows fed on a diet containing ICIA5504 RJ1878B RIP96-00141	Y	Syngenta
IIA 6.4.1/01	xxxxxx	1997	Azoxystrobin: Residue transfer in laying hens Report No. RJ2349B Syngenta File No. ICI5504/073	Y	Syngenta
IIA 6.5	Sapiets, A.	1997	ICIA5504: Residue levels in malting barley and process fractions from studies conducted in Germany during 1996 GLP Unpublished RJ2382B	N	Syngenta
IIA 6.5	Sapiets, A.	1998	ICIA5504: Residue levels in malting barley and brewing fractions from a trial conducted in the United	N	Syngenta

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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
			Kingdom during 1996 GLP Unpublished RJ2452B		
IIA 6.5	Sapiets, A.	1996	Processing study: milling/baking of wheat RJ2065B ICI5504/0718	N	Syngenta
IIA 6.5	Clarke, D.M.	1997	Processing study: milling/baking of wheat RJ2297B	N	Syngenta
IIA 6.5.1/01	Grout, S.J.	2002	14C-Phenylacrylate Azoxystrobin: Aqueous hydrolysis at 90, 100 & 120°C Report Number: RJ3296B Syngenta File No. ICI5504/1393	N	Syngenta
KIIA 6.3.5 / 02	Benazeraf L.	2004	Residue Study with Azoxystrobin (ICI5504) in or on Barley in UK Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0406 GLP, not published Syngenta File No ICI5504/2453	N	Syngenta
KIIA 6.3.5 / 04	Benazeraf L.	2004b	Residue Study with Azoxystrobin (ICI5504) in or on Barley in Switzerland Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0408 GLP, not published Syngenta File No ICI5504/2724	N	Syngenta
KIIA 6.3.5 / 05	Benazeraf L.	2004c	Residue Study with Azoxystrobin (ICI5504) in or on Barley in Switzerland Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0418 GLP, not published	N	Syngenta

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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
			Syngenta File No ICI5504/2722		
KIIA 6.3.5 / 06	Benazeraf L.	2005b	Azoxystrobin (ICI5504): Residue Study in or on Winter Barley in the United Kingdom Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0403 GLP, not published Syngenta File No ICI5504/3004	N	Syngenta
KIIA 6.3.5 / 07 & KIIA 6.5.3 / 03	Simon P.	2006	Azoxystrobin - Residue study in or on barley and processed barley products in Germany 2004 (Test product A12705B) Syngenta Crop Protection AG, Basel, Switzerland Syngenta Agro GmbH, Maintal, Germany, gba210004 GLP, not published Syngenta File No ICI5504/3546	N	Syngenta
KIIA 6.3.5 / 08	Sole C.	2004	Residue study with Azoxystrobin (ICI5504) in or on Barley in Italy Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0301 GLP, not published Syngenta File No ICI5504/2659	N	Syngenta
KIIA 6.3.5 / 09	Sole C.	2004a	Residue study with Azoxystrobin (ICI5504) in or on Barley in Italy Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0302 GLP, not published Syngenta File No ICI5504/2660	N	Syngenta
KIIA 6.3.5 / 10	Sole C.	2004b	Residue study with Azoxystrobin (ICI5504) in or on Barley in France (South) Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0303 GLP, not published Syngenta File No ICI5504/2661	N	Syngenta

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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
KIIA 6.3.5 / 11	Sole C.	2004c	Residue Study with Azoxystrobin (ICI5504) in or on Barley in France (South) Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0304 GLP, not published Syngenta File No ICI5504/2455	N	Syngenta
KIIA 6.3.5 / 12	Sole C.	2004d	Residue Study with Azoxystrobin (ICI5504) in or on Barley in Spain Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0305 GLP, not published Syngenta File No ICI5504/2454	N	Syngenta
KIIA 6.3.5 / 13	Benazeraf L.	2005c	Azoxystrobin (ICI5504): Residue Study in or on Winter Barley in Southern France Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0304 GLP, not published Syngenta File No ICI5504/3000	N	Syngenta
KIIA 6.3.5 / 14	Benazeraf L.	2005d	Azoxystrobin (ICI5504): Residue Study in or on Winter Barley in Spain Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0305 GLP, not published Syngenta File No ICI5504/3001	N	Syngenta
KIIA 6.3.6 / 01	Sole C.	2004e	Residue Study with Azoxystrobin (ICI5504) in or on Winter Wheat in the UK Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0401 GLP, not published Syngenta File No ICI5504/2726	N	Syngenta
KIIA 6.3.6 /	Sole C.	2004f	Residue Study with Azoxystrobin (ICI5504) in or on Winter Wheat in the UK Syngenta Crop Protection AG, Basel, Switzerland	N	Syngenta

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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
02			ADME - Bioanalyses, Vergeze, France, 03-0402 GLP, not published Syngenta File No ICI5504/2725		
KIIA 6.3.6 / 03	Sole C.	2004g	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in France (North) Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0403 GLP, not published Syngenta File No ICI5504/2449	N	Syngenta
KIIA 6.3.6 / 04	Sole C.	2004h	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in Switzerland Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0404 GLP, not published Syngenta File No ICI5504/2448	N	Syngenta
KIIA 6.3.6 / 05	Sole C.	2004i	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in Switzerland Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0414 GLP, not published Syngenta File No ICI5504/2723	N	Syngenta
KIIA 6.3.6 / 06	Benazeraf L.	2005e	Azoxystrobin (ICI5504): Residue Study in or on Winter Wheat in United Kingdom Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0308 GLP, not published Syngenta File No ICI5504/3003	N	Syngenta
KIIA 6.3.6 / 07	Simon P.	2006a	Azoxystrobin: Residue study in or on wheat and processed wheat products in Germany 2004 (Test product: A12705B) Syngenta Agro GmbH, Maintal, Germany, gwh220004 GLP, not published	N	Syngenta

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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
			Syngenta File No ICI5504/3323		
KIIA 6.3.6 / 08	Benazeraf L.	2004d	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0306 GLP, not published Syngenta File No ICI5504/2632	N	Syngenta
KIIA 6.3.6 / 09	Benazeraf L.	2004e	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in Italy Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0307 GLP, not published Syngenta File No ICI5504/2633	N	Syngenta
KIIA 6.3.6 / 10	Benazeraf L.	2004f	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in France (South) Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0308 GLP, not published Syngenta File No ICI5504/2634	N	Syngenta
KIIA 6.3.6 / 11	Benazeraf L.	2004g	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in France (South) Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0309 GLP, not published Syngenta File No ICI5504/2728	N	Syngenta
KIIA 6.3.6 / 12	Benazeraf L.	2004h	Residue Study with Azoxystrobin (ICI5504) in or on Wheat in Spain Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 03-0310 GLP, not published Syngenta File No ICI5504/2727	N	Syngenta

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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
KIIA 6.3.6 / 13	Benazeraf L.	2005f	Azoxystrobin (ICI5504): Residue Study in or on Winter Wheat in Southern France Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0302 GLP, not published Syngenta File No ICI5504/3035	N	Syngenta
KIIA 6.3.6 / 14	Benazeraf L.	2005g	Azoxystrobin (ICI5504): Residue Study in or on Winter Wheat in Spain Syngenta Crop Protection AG, Basel, Switzerland ADME - Bioanalyses, Vergeze, France, 04-0303 GLP, not published Syngenta File No ICI5504/3041	N	Syngenta
IIA 6.5.3/04	Heillaut, C.	2008	Azoxystrobin (ICI5504): Residue Study on Wheat and Processed Wheat Products from Switzerland in 2006 Report No. T000676-06-REG. ADME Bioanalyses, France Syngenta File No. ICI5504/3940	N	Syngenta

The following tables are to be completed by MS.

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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
KCP XX	Author	YYYY	Title Company Report No Source GLP/non GLP/GEP/non GEP Published/Unpublished	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
KCP XX	Author	YYYY	Title Company Report No Source GLP/non GLP/GEP/non GEP Published/Unpublished	Y/N	Owner

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Prothioconazole

New data are currently being generated and will be fully summarised here when available.

A 2.1.1 Magnitude of residues in plants

A 2.1.1.1 Wheat

Table A 1: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2007)	3	0.2 kg as/ha	14 days	BBCH 69	35
cGAP EU (Art. 12, EFSA, 2014)	3	0.2 kg as/ha	14 days	BBCH 69	35
Intended cGAP 2*	2	0.2 kg as/ha	14 days	BBCH 69	35

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

A 2.1.1.1.1 Study 1

Comments of zRMS:	Study is ongoing. Study is not evaluated.
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Reference: TBC

Report Magnitude of Residues of Prothioconazole-desthio and Hydroxy-prothioconazole-desthio Metabolites Following Two Applications of a 250 g/L EC Formulation to Wheat in Northern and Southern Europe, 2020 Chambers, J.
Study No. QG/20/005

Guideline(s): General recommendations for the design, preparation and realization of residue trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
SANCO/3029/99 rev.4 (11/07/00): Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414
SANCO/825/00 rev.8.1 (16/11/10): Guidance document on pesticide residue analytical methods

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Deviations: TBC
GLP: Yes
Acceptability: TBC

A 2.1.1.2 Barley

Table A 2: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2007)	2	0.2 kg as/ha	14 days	BBCH 61	35
cGAP EU (Art. 12, EFSA, 2014)	2	0.2 kg as/ha	14 days	BBCH 69	35
Intended cGAP 2*	2	0.2 kg as/ha	14 days	BBCH 69	35

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

A 2.1.1.2.1 Study 1

Comments of zRMS:	Study is ongoing. Study is not evaluated
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Reference: TBC

Report: Magnitude of Residues of Prothioconazole-desthio and Hydroxy-prothioconazole-desthio Metabolites Following Two Applications of a 250 g/L EC Formulation to Wheat in Northern and Southern Europe, 2020 Chambers, J.
Study No. QG/20/006

Guideline(s): General recommendations for the design, preparation and realization of residue trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
SANCO/3029/99 rev.4 (11/07/00): Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414
SANCO/825/00 rev.8.1 (16/11/10): Guidance document on pesticide residue analytical methods

Deviations: TBC

GLP: Yes

Acceptability: TBC

A 2.1.1.3 Oilseed Rape

Table A 3: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2007)	2	0.175 kg as/ha	14 days	n/a	56
cGAP EU (Art. 12, EFSA, 2014)	2	0.12 kg as/ha	14 days	BBCH 69	28
Intended cGAP 1*	2	0.16 kg as/ha	14 days	BBCH 69	35

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

A 2.1.1.3.1 Study 1

Comments of zRMS:	Study is ongoing. Study is not evaluated
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Reference: TBC

Report: Magnitude of Residues of Prothioconazole-desthio and Hydroxy-prothioconazole-desthio metabolites Following Two Applications of a Prothioconazole 200 g/L + Azoxystrobin 150 g/L SC Coformulation to Oilseed Rape in Northern and Southern Europe, 2020
Chambers, J.
Study No. QG/20/007

Guideline(s): General recommendations for the design, preparation and realization of residue trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
SANCO/3029/99 rev.4 (11/07/00): Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414
SANCO/825/00 rev.8.1 (16/11/10): Guidance document on pesticide residue analytical methods

Deviations: TBC

GLP: Yes

Acceptability: TBC

A 2.2 Azoxystrobin

New data are currently being generated and will be fully summarised here when available.

A 2.2.1.1 Oilseed Rape

Table A 4: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2009)	2	0.25 kg as/ha	n/a	BBCH 55	21
cGAP EU (Art. 12, EFSA, 2013)	2	0.25 kg as/ha	n/a	n/a	21
Intended cGAP 1*	2	0.12 kg as/ha	14 days	BBCH 69	35

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

A 2.2.1.1.1 Study 1

Comments of zRMS: Study is ongoing. Study is not evaluated

Reference: TBC

Report: Magnitude of Residues of Prothioconazole-desthio and Hydroxy-prothioconazole-desthio metabolites Following Two Applications of a Prothioconazole 200 g/L + Azoxystrobin 150 g/L SC Coformulation to Oilseed Rape in Northern and Southern Europe, 2020
Chambers, J.
Study No. QG/20/007

Guideline(s): General recommendations for the design, preparation and realization of residue trials (SANCO 7029/VI/95 rev.5, 22 July 1997).
OECD Guideline for the Testing of Chemicals on Crop Field Trial (TG 509 published on 7 September 2009).
SANCO/3029/99 rev.4 (11/07/00): Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414
SANCO/825/00 rev.8.1 (16/11/10): Guidance document on pesticide residue analytical methods

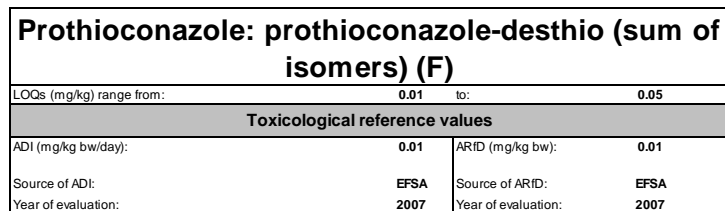
Deviations: TBC

GLP: Yes

Acceptability: TBC

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations



Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

			No of diets exceeding the ADI : ---								Exposure resulting from	
	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	MRLs set at the LOQ (in % of ADI)	commodities under assessment (in % of ADI)	
TMD/IN/ED/IED (calculation based on average food consumption)	35%	NL toddler	3.53	8%	Wheat	7%	Maize/corn	6%	Milk: Cattle	11%	12%	
	26%	GEMS/Food G06	2.60	14%	Wheat	2%	Soyabeans	1%	Maize/corn	3%	15%	
	25%	GEMS/Food G15	2.52	9%	Wheat	3%	Soyabeans	3%	Barley	3%	13%	
	25%	GEMS/Food G08	2.50	8%	Wheat	4%	Soyabeans	4%	Barley	3%	13%	
	25%	GEMS/Food G07	2.47	8%	Wheat	4%	Soyabeans	2%	Barley	3%	13%	
	25%	GEMS/Food G10	2.47	8%	Wheat	7%	Soyabeans	2%	Barley	3%	11%	
	25%	GEMS/Food G11	2.47	7%	Soyabeans	7%	Wheat	3%	Barley	3%	10%	
	20%	DK child	2.02	9%	Wheat	6%	Rye	1%	Carrots	3%	15%	
	20%	NL child	1.96	8%	Wheat	2%	Milk: Cattle	1%	Rapeseeds/canola seeds	6%	10%	
	19%	FR child 3 15 yr	1.93	9%	Wheat	2%	Lentils	2%	Lentils	5%	9%	
	18%	RO general	1.79	10%	Wheat	1%	Sunflower seeds	1%	Head cabbages	3%	10%	
	18%	DE child	1.75	8%	Wheat	2%	Milk: Cattle	1%	Apples	6%	9%	
	17%	ES child	1.73	9%	Wheat	2%	Lentils	1%	Milk: Cattle	3%	9%	
	16%	IE adult	1.64	5%	Wheat	3%	Peas	1%	Lentils	3%	5%	
	16%	UK infant	1.59	5%	Wheat	4%	Milk: Cattle	1%	Carrots	6%	5%	
	15%	IT toddler	1.52	13%	Wheat	0.4%	Lentils	0.2%	Carrots	1%	13%	
	15%	FR toddler 2 3 yr	1.52	6%	Wheat	3%	Milk: Cattle	1.0%	Lentils	5%	6%	
	14%	UK toddler	1.43	8%	Wheat	2%	Milk: Cattle	0.7%	Potatoes	4%	8%	
	13%	PT general	1.28	8%	Wheat	1%	Potatoes	0.7%	Carrots	2%	8%	
	13%	SE general	1.25	6%	Wheat	1%	Milk: Cattle	0.8%	Carrots	3%	7%	
	11%	DE general	1.12	4%	Wheat	2%	Barley	1%	Milk: Cattle	3%	7%	
	11%	ES adult	1.11	5%	Wheat	2%	Barley	1%	Lentils	2%	7%	
	11%	NL general	1.09	4%	Wheat	1%	Barley	0.8%	Milk: Cattle	3%	6%	
	10%	DE women 14-50 yr	1.03	4%	Wheat	1%	Milk: Cattle	0.8%	Barley	3%	6%	
	10%	IT adult	0.98	8%	Wheat	0.2%	Lentils	0.1%	Carrots	0.8%	8%	
	9%	FR adult	0.89	4%	Wheat	0.7%	Lentils	0.4%	Milk: Cattle	2%	4%	
	8%	FI 3 yr	0.78	2%	Wheat	0.9%	Potatoes	0.8%	Carrots	2%	4%	
	7%	UK vegetarian	0.70	4%	Wheat	0.4%	Lentils	0.3%	Milk: Cattle	1%	4%	
	7%	FR infant	0.67	2%	Milk: Cattle	2%	Wheat	1%	Carrots	3%	2%	
	7%	FI 6 yr	0.66	2%	Wheat	0.8%	Potatoes	0.7%	Peas	1%	3%	
	6%	LT adult	0.61	2%	Wheat	1%	Rye	0.6%	Potatoes	1%	4%	
	6%	FI adult	0.61	3%	Coffee beans	0.7%	Rye	0.6%	Wheat	3%	2%	
6%	UK adult	0.57	3%	Wheat	0.3%	Milk: Cattle	0.3%	Potatoes	1%	3%		
5%	DK adult	0.53	2%	Wheat	0.5%	Milk: Cattle	0.5%	Rye	1%	3%		
3%	IE child	0.34	2%	Wheat	0.4%	Milk: Cattle	0.2%	Carrots	0.7%	2%		
3%	PL general	0.26	0.7%	Potatoes	0.3%	Head cabbages	0.3%	Carrots	1%			

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Prothioconazole: prothioconazole-desethio (sum of isomers) (F) is unlikely to present a public health concern.

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European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

<h2 style="text-align: center;">Azoxystrobin</h2>			
LOQs (mg/kg) range from:		0.01	to: 0.05
Toxicological reference values			
ADI (mg/kg bw/day):	0.2	ARID (mg/kg bw):	not necessary
Source of ADI:	EFSA	Source of ARID:	EFSA
Year of evaluation:	2010	Year of evaluation:	2010

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 : ---								Exposure resulting from	
	Calculated exposure (% of ADI)		Exposure (µg/kg bw per day)	Highiest 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	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)		
TMD/(MED)/(EDI) calculation (based on average food consumption)	70%	NL toddler	139.77	17%	Oranges	15%	Potatoes	5%	Spinaches	0.4%	2%		
	69%	DE child	138.19	30%	Oranges	9%	Potatoes	3%	Mandarins	0.2%	1%		
	48%	FR child 3 15 yr	95.53	26%	Oranges	5%	Potatoes	1%	Tomatoes	0.2%	1%		
	48%	NL child	95.09	12%	Potatoes	11%	Oranges	5%	Mandarins	0.2%	1%		
	47%	IE adult	93.17	8%	Potatoes	8%	Oranges	5%	Grapefruits	0.0%	0.8%		
	46%	GEMS/Food G07	92.28	13%	Potatoes	10%	Oranges	2%	Wine grapes	0.1%	2%		
	46%	GEMS/Food G06	92.23	7%	Oranges	7%	Potatoes	5%	Tomatoes	0.0%	2%		
	45%	GEMS/Food G10	90.54	10%	Potatoes	8%	Oranges	3%	Rice	0.0%	2%		
	44%	GEMS/Food G11	87.59	14%	Potatoes	5%	Oranges	3%	Lemons	0.1%	2%		
	43%	SE general	86.86	15%	Potatoes	6%	Oranges	3%	Mandarins	0.1%	0.9%		
	41%	GEMS/Food G08	82.93	14%	Potatoes	3%	Oranges	3%	Onions	0.1%	2%		
	40%	UK toddler	80.58	15%	Oranges	12%	Potatoes	2%	Mandarins	0.1%	1%		
	39%	GEMS/Food G15	78.47	12%	Potatoes	5%	Oranges	3%	Onions	0.1%	2%		
	39%	PT general	77.61	19%	Potatoes	5%	Oranges	4%	Wine grapes	0.0%	1%		
	37%	FR toddler 2 3 yr	74.41	11%	Oranges	7%	Potatoes	6%	Mandarins	0.2%	0.8%		
	TMD/(MED)/(EDI) calculation (based on average food consumption)	37%	ES child	73.45	16%	Oranges	6%	Potatoes	3%	Lettuces	0.1%	1%	
		35%	RO general	69.81	13%	Potatoes	4%	Onions	4%	Head cabbages	0.1%	1%	
34%		FI 3 yr	67.05	17%	Potatoes	3%	Mandarins	2%	Onions	0.0%	1.0%		
33%		DE women 14-50 yr	65.33	14%	Oranges	4%	Potatoes	2%	Lemons	0.1%	0.9%		
32%		UK infant	64.49	11%	Potatoes	10%	Oranges	2%	Rice	0.2%	0.8%		
30%		DE general	59.38	12%	Oranges	4%	Potatoes	2%	Lemons	0.1%	1%		
30%		NL general	59.32	9%	Potatoes	8%	Oranges	1%	Mandarins	0.1%	0.8%		
27%		FI 6 yr	54.14	14%	Potatoes	2%	Mandarins	1%	Onions	0.0%	0.7%		
27%		ES adult	53.22	10%	Oranges	4%	Lettuces	3%	Potatoes	0.0%	1.0%		
23%		DK child	45.69	9%	Potatoes	1%	Rye	1%	Oranges	0.1%	3%		
22%		IT toddler	44.98	4%	Oranges	3%	Potatoes	2%	Lettuces	0.0%	2%		
22%		UK vegetarian	44.32	6%	Oranges	5%	Potatoes	1%	Wine grapes	0.0%	0.6%		
20%		IT adult	40.81	3%	Lettuces	3%	Oranges	2%	Potatoes	0.0%	1%		
20%		FR infant	39.91	7%	Potatoes	2%	Spinaches	2%	Oranges	0.1%	0.2%		
20%		PL general	39.56	12%	Potatoes	2%	Onions	1%	Tomatoes	0.0%			
20%		FR adult	39.42	4%	Oranges	3%	Wine grapes	3%	Potatoes	0.0%	0.6%		
18%		UK adult	35.81	5%	Potatoes	4%	Oranges	2%	Wine grapes	0.0%	0.5%		
16%		LT adult	32.82	11%	Potatoes	1.0%	Head cabbages	0.9%	Tomatoes	0.0%	0.6%		
15%		FI adult	29.68	4%	Potatoes	3%	Oranges	1%	Lettuces	0.0%	0.4%		
14%		DK adult	27.38	4%	Potatoes	1%	Wine grapes	1%	Oranges	0.0%	0.4%		
6%	IE child	11.34	2%	Potatoes	0.7%	Rice	0.6%	Oranges	0.0%	0.3%			


Conclusion:	
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The estimated long-term dietary intake (TMDI/NEDI/EDI) was below the ADI.

The long-term intake of residues of Azoxystrobin is unlikely to present a public health concern.

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zRMS comment: TMDI (input: Reg. (EU) 2021/1807)

 <p>EFSA PRIMO revision 3.1; 2021/01/06</p>		Azoxystrobin		Input values							
		LOQs (mg/kg) range from: to:		<div>Details - chronic risk assessment</div> <div>Supplementary results - chronic risk assessment</div>							
		Toxicological reference values									
		ADI (mg/kg bw/day):	0,2	ARID (mg/kg bw):	insert valid entry	<div>Details - acute risk assessment/children</div> <div>Details - acute risk assessment/adults</div>					
Source of ADI:		Source of ARID:									
Year of evaluation:		Year of evaluation:									
Comments:											
Normal mode											
Chronic risk assessment: JMPR methodology (IED/TMDI)											
No of diets exceeding the ADI : ---											
TMDI/NEDI 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)	commodities not under assessment (in % of ADI)
	82%	NL toddler	164,94	17%	Oranges	15%	Potatoes	13%	Sugar beet roots		
	69%	DE child	138,19	30%	Oranges	9%	Potatoes	3%	Mandarins		
	68%	NL child	135,62	21%	Sugar beet roots	12%	Potatoes	11%	Oranges		
	57%	FR child 3 15 yr	113,13	26%	Oranges	9%	Sugar beet roots	5%	Potatoes		
	50%	GEMS/Food G06	99,35	7%	Oranges	7%	Potatoes	5%	Tomatoes		
	48%	UK toddler	95,95	15%	Oranges	12%	Potatoes	8%	Sugar beet roots		
	47%	IE adult	93,10	8%	Potatoes	8%	Oranges	5%	Grapefruits		
	46%	GEMS/Food G07	92,29	13%	Potatoes	10%	Oranges	2%	Wine grapes		
	45%	GEMS/Food G10	90,54	10%	Potatoes	8%	Oranges	3%	Rice		
	44%	FR toddler 2 3 yr	88,06	11%	Oranges	7%	Sugar beet roots	7%	Potatoes		
	44%	GEMS/Food G11	87,59	14%	Potatoes	5%	Oranges	3%	Lemons		
	44%	DE women 14-50 yr	87,35	14%	Oranges	11%	Sugar beet roots	4%	Potatoes		
	43%	SE general	86,86	15%	Potatoes	6%	Oranges	3%	Mandarins		
	41%	GEMS/Food G08	82,93	14%	Potatoes	3%	Oranges	3%	Onions		
	40%	DE general	79,64	12%	Oranges	11%	Sugar beet roots	4%	Potatoes		
	39%	GEMS/Food G15	78,47	12%	Potatoes	5%	Oranges	3%	Onions		
	39%	PT general	77,61	19%	Potatoes	5%	Oranges	4%	Wine grapes		
	38%	RO general	76,13	13%	Potatoes	4%	Onions	4%	Head cabbages		
	37%	ES child	74,30	16%	Oranges	6%	Potatoes	3%	Lettuces		
	37%	NL general	73,09	9%	Potatoes	8%	Oranges	7%	Sugar beet roots		
	36%	UK infant	71,27	11%	Potatoes	10%	Oranges	4%	Sugar beet roots		
	34%	FI 3 yr	67,05	17%	Potatoes	3%	Mandarins	2%	Onions		
	27%	FI 6 yr	54,14	14%	Potatoes	2%	Mandarins	1%	Onions		
	27%	ES adult	53,86	10%	Oranges	4%	Oranges	3%	Potatoes		
	23%	UK vegetarian	46,85	6%	Oranges	5%	Potatoes	1%	Sugar beet roots		
	23%	FR infant	46,40	7%	Potatoes	3%	Sugar beet roots	2%	Spinaches		
	23%	DK child	45,69	9%	Potatoes	1%	Rye	1%	Oranges		
	22%	IT toddler	44,98	4%	Oranges	3%	Potatoes	2%	Lettuces		
	22%	FR adult	43,28	4%	Oranges	3%	Wine grapes	3%	Potatoes		
	20%	IT adult	40,81	3%	Lettuces	3%	Oranges	2%	Potatoes		
	20%	PL general	39,56	12%	Potatoes	2%	Onions	1%	Tomatoes		
19%	UK adult	38,49	5%	Potatoes	4%	Oranges	2%	Wine grapes			
16%	LT adult	32,82	11%	Potatoes	1,0%	Head cabbages	0,9%	Tomatoes			
15%	FI adult	29,68	4%	Potatoes	3%	Oranges	1%	Lettuces			
14%	DK adult	27,38	4%	Potatoes	1%	Wine grapes	1%	Oranges			
6%	IE child	11,34	2%	Potatoes	0,7%	Rice	0,6%	Oranges			
Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Azoxystrobin 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 IESTI calculations (Prothioconazole)

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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 ARID. 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 of IESTI calculation only for crops with GAPs under assessment																																								
Unprocessed commodities	Results for children No. of commodities for which ARID/ADI is exceeded (IESTI):										Results for adults No. of commodities for which ARID/ADI is exceeded (IESTI):										Results for children No. of commodities for which ARID/ADI is exceeded (IESTI new):										Results for adults No. of commodities for which ARID/ADI is exceeded (IESTI new):									
	---										---										---										---									
	IESTI										IESTI										IESTI new										IESTI new									
	Highest % of ARID/ADI		Commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/ADI		Commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/ADI		Commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/ADI		Commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)			
	29%	Wheat		0.1 / 0.2		2.9					19%	Barley		0.2 / 0.4		1.9					29%	Wheat		0.1 / 0.2		2.9					19%	Barley		0.2 / 0.4		1.9				
	22%	Barley		0.2 / 0.4		2.2					17%	Wheat		0.1 / 0.2		1.7					22%	Barley		0.2 / 0.4		2.2					17%	Wheat		0.1 / 0.2		1.7				
	6%	Rye		0.05 / 0.1		0.63					5%	Rye		0.05 / 0.1		0.49					6%	Rye		0.05 / 0.1		0.63					5%	Rye		0.05 / 0.1		0.49				
	4%	Rapeseeds/canola		0.15 / 0.3		0.41					2%	Rapeseeds/canola seeds		0.15 / 0.3		0.16					4%	Rapeseeds/canola		0.15 / 0.3		0.41					2%	Rapeseeds/canola seeds		0.15 / 0.3		0.16				
	1%	Oat		0.05 / 0.1		0.11					0.6%	Oat		0.05 / 0.1		0.06					1%	Oat		0.05 / 0.1		0.11					0.6%	Oat		0.05 / 0.1		0.06				
	Expand/collapse list																																							
Total number of commodities exceeding the ARID/ADI in children and adult diets (IESTI calculation)																				Total number of commodities found exceeding the ARID/ADI in children and adult diets (IESTI new calculation)																				
Processed commodities	Results for children No. of processed commodities for which ARID/ADI is exceeded (IESTI):										Results for adults No. of processed commodities for which ARID/ADI is exceeded (IESTI):										Results for children No. of processed commodities for which ARID/ADI is exceeded (IESTI new):										Results for adults No. of processed commodities for which ARID/ADI is exceeded (IESTI new):									
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	IESTI										IESTI										IESTI new										IESTI new									
	Highest % of ARID/ADI		Processed commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/ADI		Processed commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/ADI		Processed commodities		MRL / input for RA (mg/kg)		Exposure (µg/kg bw)				Highest % of ARID/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					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					15%	Barley / cooked		0.2 / 0.4		1.5					9%	Wheat / bread/pizza		0.1 / 0.2		0.88				
	11%	Wheat / milling (wholemeal)		0.1 / 0.2		1.1					8%	Wheat / pasta		0.1 / 0.2		0.76					11%	Wheat / milling		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					7%	Barley / milling (flour)		0.2 / 0.4		0.72					7%	Wheat / bread (wholemeal)		0.1 / 0.2		0.70				
	4%	Rye / boiled		0.05 / 0.1		0.36					2%	Oat / boiled		0.05 / 0.1		0.15					4%	Rye / boiled		0.05 / 0.1		0.36					2%	Oat / boiled		0.05 / 0.1		0.15				
	4%	Oat / boiled		0.05 / 0.1		0.36					#NUM!	#NUM!		#NUM!		#NUM!					4%	Oat / boiled		0.05 / 0.1		0.36					#NUM!	#NUM!		#NUM!		#NUM!				
	4%	Rye / milling (wholemeal)-t		0.05 / 0.1		0.35					#NUM!	#NUM!		#NUM!		#NUM!					4%	Rye / milling (wholemeal)-t		0.05 / 0.1		0.35					#NUM!	#NUM!		#NUM!		#NUM!				
	3%	Oat / milling (flakes)		0.05 / 0.1		0.30					#NUM!	#NUM!		#NUM!		#NUM!					3%	Oat / milling (flakes)		0.05 / 0.1		0.30					#NUM!	#NUM!		#NUM!		#NUM!				
	2%	Rapeseeds / oils		0.15 / 0.6		0.18					#NUM!	#NUM!		#NUM!		#NUM!					2%	Rapeseeds / oils		0.15 / 0.6		0.18					#NUM!	#NUM!		#NUM!		#NUM!				
	#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!					
	#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!					
	#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!					
	#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!					
#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!						
#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!					#NUM!	#NUM!		#NUM!		#NUM!				#NUM!	#NUM!		#NUM!		#NUM!						
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: prothioconazole-desethio (sum of isomers) (F) is unlikely to present a public health risk. For processed commodities, no exceedance of the ARID/ADI was identified.																																								

Appendix 4 Consideration of triazole derivative metabolites (TDMs) for FF-075

GAP comparison and residue trials summary from EU-evaluated TDM dataset

Table A 4-1 below provides a comparison of the prothioconazole cGAPs for FF-075 and the cGAPs considered as part of the EU *Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted* (EFSA Journal 2018;16(7):5376). For each of the proposed uses, the prothioconazole cGAP for FF-075 is equivalent or less critical than the cGAP evaluated as part of the EU confirmatory data assessment, and so the residues trials data relied upon for the EU risk assessment are relied upon without scaling for the consumer risk assessment of FF-075.

Table A 4-1: Summary of EU reported TDM GAPs and residue trials data supporting the intended uses of FF-075.

Commodity	Source	Residue zone	cGAP STMRs and HRs reported in EFSA Journal 2018;16(7):5376																																															
Wheat, rye, triticale	EFSA, 2018	NEU + SEU	cGAP on which EU TDM assessment is based: 3 x 187.5 g a.s./ha (foliar), BBCH 69-71, PHI = NCH, minimum interval 5-14 d																																															
			Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)				T	TA	TAA	TLA	T	TA	TAA	TLA	grain	8	0.010	0.434	0.189	NA	0.010	1.069	0.517	NA	plant	8	0.050	0.100	0.065	NA	0.050	0.524	0.434	NA	straw	8	0.050	0.050	0.058	NA	0.050	0.079	0.307	NA
					Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)																																							
			T	TA			TAA	TLA	T	TA	TAA	TLA																																						
			grain	8	0.010	0.434	0.189	NA	0.010	1.069	0.517	NA																																						
plant	8	0.050	0.100	0.065	NA	0.050	0.524	0.434	NA																																									
straw	8	0.050	0.050	0.058	NA	0.050	0.079	0.307	NA																																									
NA: not analysed																																																		
<u>Note:</u> The STMRs were calculated based on the highest residue levels from each trial.																																																		
30 g as/ha seed treatment + 3 x 200 g a.s./ha (foliar), BBCH 69, PHI = NCH, minimum interval 7 days																																																		

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			<table><tr><th rowspan="2">Commodity</th><th rowspan="2">No of Trials</th><th colspan="4">STMR (mg/kg)</th><th colspan="4">HR (mg/kg)</th></tr><tr><th>T</th><th>TA</th><th>TAA</th><th>TLA</th><th>T</th><th>TA</th><th>TAA</th><th>TLA</th></tr><tr><td>Plant</td><td>4</td><td>0.010</td><td>0.100</td><td>0.049</td><td>0.050</td><td>0.010</td><td>0.166</td><td>0.104</td><td>0.067</td></tr><tr><td>Grain</td><td>4</td><td>0.010</td><td>0.621</td><td>0.231</td><td>0.010</td><td>0.010</td><td>0.952</td><td>0.377</td><td>0.010</td></tr><tr><td>Straw</td><td>4</td><td>0.010</td><td>0.029</td><td>0.047</td><td>0.116</td><td>0.010</td><td>0.057</td><td>0.048</td><td>0.232</td></tr></table> <p><u>Note:</u> The STMRs were calculated based on the highest residue levels from each trial.</p>	Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)				T	TA	TAA	TLA	T	TA	TAA	TLA	Plant	4	0.010	0.100	0.049	0.050	0.010	0.166	0.104	0.067	Grain	4	0.010	0.621	0.231	0.010	0.010	0.952	0.377	0.010	Straw	4	0.010	0.029	0.047	0.116	0.010	0.057	0.048	0.232
Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)																																													
		T	TA	TAA	TLA	T	TA	TAA	TLA																																										
Plant	4	0.010	0.100	0.049	0.050	0.010	0.166	0.104	0.067																																										
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Straw	4	0.010	0.029	0.047	0.116	0.010	0.057	0.048	0.232																																										
	FF-075 cGAP	NEU	<p>cGAP: 2 x 200 g a.s./ha (foliar), BBCH 69, PHI = 35 days, minimum interval 14 d</p> <p>The cGAP for FF-075 on wheat, rye and triticale is equivalent or less critical than the cGAPs evaluated as part of the EU TDM confirmatory data assessment; therefore, these data are relied upon without scaling for the consumer risk assessment.</p>																																																
Barley, oat	EFSA, 2018	NEU + SEU	<p>cGAP on which EU TDM assessment is based: 2 x 150 g a.s./ha (foliar), BBCH 61, PHI = NCH, minimum interval 9 d</p> <table><tr><th rowspan="2">Commodity</th><th rowspan="2">No of Trials</th><th colspan="4">STMR (mg/kg)</th><th colspan="4">HR (mg/kg)</th></tr><tr><th>T</th><th>TA</th><th>TAA</th><th>TLA</th><th>T</th><th>TA</th><th>TAA</th><th>TLA</th></tr><tr><td>grain</td><td>12*</td><td>0.010</td><td>0.208</td><td>0.107</td><td>0.010</td><td>0.011</td><td>0.440</td><td>0.320</td><td>0.010</td></tr><tr><td>plant</td><td>8</td><td>0.050</td><td>0.061</td><td>0.050</td><td>NA</td><td>0.050</td><td>0.158</td><td>0.099</td><td>NA</td></tr><tr><td>straw</td><td>8</td><td>0.050</td><td>0.050</td><td>0.057</td><td>NA</td><td>0.050</td><td>0.050</td><td>0.136</td><td>NA</td></tr></table> <p>NA : not analysed * 4 trials for TLA</p> <p><u>Note:</u> For the calculation of the STMRs and HRs the residue values measured in the control samples were taken into account whenever they exceeded the values measured in the corresponding treated samples. The STMRs were calculated based on the highest residue levels from each trial.</p> <p>27 g as/ha seed treatment + 2 x 200 g a.s./ha (foliar), BBCH 61-62, PHI = NCH, minimum interval 7 d</p>	Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)				T	TA	TAA	TLA	T	TA	TAA	TLA	grain	12*	0.010	0.208	0.107	0.010	0.011	0.440	0.320	0.010	plant	8	0.050	0.061	0.050	NA	0.050	0.158	0.099	NA	straw	8	0.050	0.050	0.057	NA	0.050	0.050	0.136	NA
Commodity	No of Trials	STMR (mg/kg)				HR (mg/kg)																																													
		T	TA	TAA	TLA	T	TA	TAA	TLA																																										
grain	12*	0.010	0.208	0.107	0.010	0.011	0.440	0.320	0.010																																										
plant	8	0.050	0.061	0.050	NA	0.050	0.158	0.099	NA																																										
straw	8	0.050	0.050	0.057	NA	0.050	0.050	0.136	NA																																										

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			<table><tr><th rowspan="2">Commodity</th><th rowspan="2">No of Trials</th><th colspan="4">STM_R (mg/kg)</th><th colspan="4">HR (mg/kg)</th></tr><tr><th>T</th><th>TA</th><th>TAA</th><th>TLA</th><th>T</th><th>TA</th><th>TAA</th><th>TLA</th></tr><tr><td>Plant</td><td>4</td><td>0.010</td><td>0.039</td><td>0.010</td><td>0.029</td><td>0.010</td><td>0.075</td><td>0.010</td><td>0.064</td></tr><tr><td>Grain</td><td>4</td><td>0.010</td><td>0.186</td><td>0.039</td><td>0.010</td><td>0.010</td><td>0.382</td><td>0.500</td><td>0.010</td></tr><tr><td>Straw</td><td>4</td><td>0.010</td><td>0.016</td><td>0.012</td><td>0.112</td><td>0.014</td><td>0.018</td><td>0.013</td><td>0.157</td></tr></table> <p>Note: For the calculation of the STM_Rs and HRs the residue values measured in the control samples were taken into account whenever they exceeded the values measured in the corresponding treated samples. The STM_Rs were calculated based on the highest residue levels from each trial.</p>	Commodity	No of Trials	STM _R (mg/kg)				HR (mg/kg)				T	TA	TAA	TLA	T	TA	TAA	TLA	Plant	4	0.010	0.039	0.010	0.029	0.010	0.075	0.010	0.064	Grain	4	0.010	0.186	0.039	0.010	0.010	0.382	0.500	0.010	Straw	4	0.010	0.016	0.012	0.112	0.014	0.018	0.013	0.157
Commodity	No of Trials	STM _R (mg/kg)				HR (mg/kg)																																													
		T	TA	TAA	TLA	T	TA	TAA	TLA																																										
Plant	4	0.010	0.039	0.010	0.029	0.010	0.075	0.010	0.064																																										
Grain	4	0.010	0.186	0.039	0.010	0.010	0.382	0.500	0.010																																										
Straw	4	0.010	0.016	0.012	0.112	0.014	0.018	0.013	0.157																																										
	FF-075 cGAP	NEU	<p>cGAP: 2 x 200 g a.s./ha (foliar), BBCH 69, PHI = 35 days, minimum interval 14 d</p> <p>The cGAP for FF-075 on barley and oat is equivalent to the cGAPs evaluated as part of the EU TDM confirmatory data assessment (application rate slightly above 25 % compared to the foliar-only trials at 150 g a.s./ha, but trials using seed treatment followed by foliar application at 200 g a.s./ha were also used in the EU assessment; applications both performed at flowering); therefore, these data are relied upon without scaling for the consumer risk assessment.</p>																																																
Oilseed rape	EFSA, 2018	NEU + SEU	<p>cGAP on which EU TDM assessment is based: 2 x 150 g a.s./ha (foliar), BBCH 80-85, PHI 22-56 d, minimum interval 13 d</p> <table><tr><th rowspan="2">Commodity</th><th rowspan="2">No of Trials</th><th colspan="4">STM_R (mg/kg)</th><th colspan="4">HR (mg/kg)</th></tr><tr><th>T</th><th>TA</th><th>TAA</th><th>TLA</th><th>T</th><th>TA</th><th>TAA</th><th>TLA</th></tr><tr><td>plant</td><td>14</td><td>0.01</td><td>0.055</td><td>0.01</td><td>0.01</td><td>0.01</td><td>0.270</td><td>0.03</td><td>0.02</td></tr><tr><td>pod</td><td>8</td><td>0.01</td><td>0.130</td><td>0.01</td><td>0.01</td><td>0.01</td><td>0.7</td><td>0.02</td><td>0.06</td></tr><tr><td>seed</td><td>14</td><td>0.01</td><td>0.28</td><td>0.01</td><td>0.01</td><td>0.01</td><td>2.17</td><td>0.062</td><td>0.05</td></tr></table> <p>Note: For the calculation of the STM_Rs and HRs the residue values measured in the control samples were taken into account whenever they exceeded the values measured in the corresponding treated samples. The STM_Rs were calculated based on the highest residue levels from each trial.</p> <p>NB: additional EU TDM trials are available, with application rates of 125 g a.s./ha though are not considered relevant to the Rotam FF-075 cGAP and so are not summarised here.</p>	Commodity	No of Trials	STM _R (mg/kg)				HR (mg/kg)				T	TA	TAA	TLA	T	TA	TAA	TLA	plant	14	0.01	0.055	0.01	0.01	0.01	0.270	0.03	0.02	pod	8	0.01	0.130	0.01	0.01	0.01	0.7	0.02	0.06	seed	14	0.01	0.28	0.01	0.01	0.01	2.17	0.062	0.05
	Commodity	No of Trials	STM _R (mg/kg)				HR (mg/kg)																																												
T			TA	TAA	TLA	T	TA	TAA	TLA																																										
plant	14	0.01	0.055	0.01	0.01	0.01	0.270	0.03	0.02																																										
pod	8	0.01	0.130	0.01	0.01	0.01	0.7	0.02	0.06																																										
seed	14	0.01	0.28	0.01	0.01	0.01	2.17	0.062	0.05																																										
	FF-075 cGAP	NEU	<p>cGAP: 2 x 160 g a.s./ha (foliar), BBCH 69, PHI = 35 days, minimum interval 14 d</p> <p>The cGAP for FF-075 on oilseed rape is equivalent to the cGAP evaluated as part of the EU TDM confirmatory data assessment (application rate within 25 % compared to the trials at 150 g a.s./ha); therefore, these data are relied upon without scaling for the consumer risk assessment.</p>																																																

EU agreed toxicological reference values and residue definitions for TDMs

The December 2019 EU SCoPAFF (Legislation section) took note of the following toxicological reference values and residue definitions that must be used for the dietary exposure assessment for triazole active substances and their TDMs (also included in the 2021 Updated Review Report for prothioconazole - SANCO/3923/07 - final; 26 January 2021):

Table A 4-2: Summary of TDM toxicological reference values

Metabolite	Toxicological reference value	
	ADI (mg/kg bw/day)	ARfD (mg/kg bw)
1,2,4-triazole (1,2,4-T)	0.023	0.1
Triazole alanine (TA)	0.3	0.3
Triazole acetic acid (TAA)	1.0	1.0
Triazole lactic acid (TLA)	0.3	0.3

Table A 4-3: Summary of TDM residue definitions (applicable to plants and animal commodities)

Residue definition for enforcement	1) Triazole parent compound only
Residue definition for risk assessment	1) Triazole parent compound and any other relevant metabolite exclusively linked to the parent compound 2) TA and TLA, since these compounds share the same toxicity 3) TAA 4) 1,2,4-T

An estimation of the potential and actual exposure through diet and other sources was performed as part of the EU Peer review of the pesticide risk assessment for the triazole derivative metabolites in light of confirmatory data submitted (EFSA Journal 2018;16(7):5376; specifically within *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*), where it was provisionally concluded that no chronic health or acute effects are expected as a result of the exposure to the triazole derivative metabolites when accounting for the EU cGAPs detailed in table A 4-1 above:

Chronic and acute risk assessments using the UK models and EFSA PRIMo 3 have been undertaken for all four TDM.

The EU MS NEDIs are below the ADI.

The UK NEDIs for TA, TAA and TLA are all below the ADI. For T, the NEDIs are below the ADI for all consumer groups except for infants. For Infants the NEDI was 145 % of the ADI. It is noted that this exceedance is on the basis that the 97.5th percentile consumption data has been used for milk. If the mean consumption data are used, which is the approach in the EFSA model, the exceedance of the ADI does not occur for UK infants. In addition, it should be noted that the UK did not support the ADI of 0.023 mg/kg bw/day for 1,2,4-T. The UK supported an ADI of 0.05 mg/kg bw/day. Based on these considerations no health effects are expected for UK infants from the consumption of commodities containing 1,2,4-T residues.

For each TDM the UK and EU MS NESTIs are below the ARfD.

TA and TLA can be assigned to a common assessment group. Therefore a combined risk assessment for these TDM was undertaken.

The combined UK and EU MS NEDIs are less than the ADI of 0.3 mg/kg bw/day.

The combined UK and EU MS NESTIs are less than the ARfD of 0.3 mg/kg bw/day.

No chronic health effects are expected as a result of the combined exposure to TA and TLA. No chronic health effects are expected from the dietary exposure to T and TAA.

No acute health effects are expected as a result of the combined exposure to TA and TLA. No acute health effects are expected from the dietary exposure to T and TAA.

The conclusions on the consumer risk assessments are provisional owing for the need to consider the following issues:

- The lack of feeding studies for T and TLA*
- The storage intervals of the trials used to derive the HR (used in the acute risk assessments and maximum dietary burden calculations) not all being supported*
- The need to assess the storage intervals of the trials used to derive the STMRS used in the chronic risk assessments and in the medium livestock dietary burden calculations*

The dietary risk assessment performed as part of the EU Peer Review addresses the exposure to TDMs related to primary crops, processed commodities, rotational crops and food of animal origin, and is sufficient to provisionally conclude that no chronic health or acute effects are expected as a result of consumer exposure to the TDM residues associated with the proposed uses of FF-075, as the cGAPs are within those considered in the EU Peer Review. Furthermore, as the dietary risk assessment performed as part of the EU Peer Review accounts for the TDM residues expected as a result of the use of several triazole fungicides, the actual TDM residues expected as a result of the proposed uses of prothioconazole in FF-075 only will be significantly lower.