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| **REGISTRATION REPORT**  Part B  Section 7  Metabolism and Residues  Detailed summary of the risk assessment |
| Product code: -  Product name(s): **ULTRACENT 460 EC**  Chemical active substance(s):  Prothioconazole, 160 g/L Spiroxamine, 300 g/L |
| Central Zone  Zonal Rapporteur Member State: Poland |
| CORE ASSESSMENT  (authorization) |
| Applicant: XXXX  Submission date: August 2023  update December 2023, update January 2025  Evaluation date: October 2024  MS Finalisation date: February 2025 |

Version history

|  |  |
| --- | --- |
| When | What |
| August 2023 | First submission – application according to Article 33 in connection with Article 34 of Regulation (EC) No. 1107/2009 with reference to unprotected data of the product INPUT 460 EC authorized in Poland |
| December 2023 | The dossier was updated to include available information on the unprotected data of the reference product INPUT 460 EC (R-61/2011). |
| October 2024 | The refusal of the authorisation due to a lack of the required data and MRL inconsistency. |
| January 2025 | This part was updated after request of the authority |
| February 2025 | Final update of the evaluation of zRMS |

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# Metabolism and residue data (KCA section 6)

## Summary and zRMS Conclusion

**dRR B7 of the applicant was not rewritten by the evaluator. The opinion of the evaluator is stated as follows:**

The purpose of the submitted dossier was to authorise **ULTRACENT 460 EC** by referring to the unprotected data of Input authorized in Poland in 2011 (R-61/2011). However, the unprotected data of **INPUT** being a basis of the authorisation request was not provided (the data of 2007 provided is insufficient) i.e. the relevant registration report of INPUT 460 EC was not provided.

It should be noted in this context that according to the Article 34 applicants shall be exempted from supplying study reports where the Member State to which an application is made has study reports concerned.

The Input report was not provided but the applicant shows in the present B7 old residue data tables probably of INPUT 460 EC. The inconsistency of **spiroxamine** MRL for barley can be identified there.

Furthermore, ULTRACENT 460 EC contains **prothioconazole**. Therefore, the current authorisation cannot refer only to data from 2011. Currently, in such a case, it is also required to submit data allowing for the assessment of the risk from **triazoles** when using the product. The applicant did not meet this requirement (for the same reason, the reference product Input, to remain present on the market, probably in the past had to be renewed related to the assessment of the triazole data).

It should be also noted that in the context of the Article 34 and residues assessment, a physicochemical identity of the products is not a necessary condition for the possibility of mutual using the data, and - obviously - the physicochemical identity of the agents does not mean the possibility of automatic authorisation in the residue area. The authorisation basis is always an applicant’s legal access to the required data and finally the presentation of this data within the submitted dossier in a way that allows an assessment.

Finally concluding, since the relevant registration report of INPUT 460 EC was not provided, the inconsistency of spiroxamine MRL for the barley was already identified within INPUT 460 EC residue data and in the context of prothioconazole the triazoles data submission requirement was not met, **the authorization for ULTRACENT 460 EC cannot be granted.**

**Note**: to authorise the product the applicant should consider a reconstruction of the B7 (and B5) from scratch clearly providing all required data consistently with the current requirements (MRL consistency, animal dietary burden, triazoles and honey issues etc). The clear list of already evaluated unprotected studies applied for the assessment is also required.

**February 2025**: the applicant reconstructed the B7 clearly providing all required data consistently with the current requirements. The data available are now considered sufficient for risk assessment. An exceedance of the current MRLs is not expected to be exceeded. The chronic and the short-term intakes of the actives are unlikely to present a public health concern. The approval for the intended GAP of Ultracent 460 EC can be granted.

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) | kg as/hL  min max | water L/ha  min max | kg as/ha  min max |
| 1 | Wheat  (winter) | CEU | ULTRACENT 460 EC | F | Eyespot (PSDCHE), Fusarium sp. (FUSASP), powdery mildew (ERYSGR) | EC | 16~~2~~0 g/L prothioconazole, 300 ~~225~~ g/L spiroxamine | spraying | BBCH 30-31 | 1 | - | - | 200-400 | 0.12 kg/ha prothioconazole, 0.225 kg/ha sprioxamine | 35 | The denial of the authorisation due to a lack of the required data. |
| 2 | Wheat  (winter) | CEU | ULTRACENT 460 EC | F | Eyespot (PSDCHE), Fusarium sp. (FUSASP), powdery mildew (ERYSGR) | EC | 160 g/L prothioconazole, 300 g/L spiroxamine | spraying | BBCH 31-37 | 1 | - | - | 200-400 | 0.16 kg/ha prothioconazole, 0.3 kg/ha sprioxamine | 35 |
| **3** | **Wheat**  **(winter and spring)** | **CEU** | **ULTRACENT 460 EC** | **F** | **Rust species (PUCCSP),**  **Brown rust (PUCCRE)**  **Powdery mildew (ERYSGR)**  **Septoria leaf spot(SEPTTR)**  **Glume blotch (LEPTNO)**  **Tan spot(PYRNTR)** | **EC** | **160 g/L prothioconazole, 300 g/L spiroxamine** | **spraying** | **BBCH 30-59** | **1** | **-** | **-** | **200-400** | **0.16 kg/ha prothioconazole, 0.3 kg/ha sprioxamine** | **35** |
| 4 | Barley  (winter and spring) | CEU | ULTRACENT 460 EC | F | Eyespot (PSDCHE)  Brown rust (PUCCHD)  Powdery mildew (ERYSGR)  Rhynchosporium (RHYNSE)  Net blotch (PYRNTE)  Fusarium stem blight(FUSASP*)* | EC | 160 g/L prothioconazole, 300 g/L spiroxamine | spraying | BBCH 30-51 | 1 | - | - | 200-400 | 0.16 kg/ha prothioconazole, 0.3 kg/ha sprioxamine | 35 |

\* 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 |

### Summary of the evaluation

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

The residues of prothioconazole and spiroxamine, when applied as recommended in the directions for use do not pose a risk to the consumer.

No further residue studies are required. The studies submitted are sufficient for the assessment.

Residues of prothioconazole and spiroxamine do not pose a risk to the consumer after application according to the recommendations in the label - instructions for use.

Waiting period: 35 days

Prevention period for animals: not applicable

It is further stated that:

- There is the same metabolism of prothioconazole and spiroxamine in different plant species in the main crop as well as in succeeding crops;

- The product poses no risk to succeeding crops;

- There is similar metabolism of prothioconazole and spiroxamine in animals and plants;

- The field trials presented are performed in accordance with the GAP;

- The dynamics of the disappearance of the parent substances and the metabolites tested are very fast;

- No residues of toxicologically relevant metabolites of prothioconazole and spiroxamine are found in plant material;

- No increase in the levels of prothioconazole and spiroxamine residues was found in processed products;

- Consumer exposure to dietary intake residues will not increase due to consumption of foodstuffs of animal origin, taking into account data the uptake of prothioconazole and spiroxamine residues by animals through the feed.

However, a more detailed presentation of unprotected data will be presented in the following.

The preparation ULTRACENT 460 EC is composed of Prothioconazole and Spiroxamine.

Table 7.1‑2: Toxicological reference values for the dietary risk assessment of prothioconazole and spiroxamine

| Reference value | Source | Year | Value | Study relied upon | Safety factor |
| --- | --- | --- | --- | --- | --- |
| **Prothioconazole** - Parend compound | | | | | |
| ADI | EFSA | 2007 | 0.05 mg/kg bw/d | rat carcinogenicity study | 100 |
| ARfD | EFSA | 2007 | 0.2 mg/kg bw | rat developmental study | 100 |
| Prothioconazole-desthio – metabolite | | | | | |
| ADI | EFSA | 2007 | 0.01 mg/kg bw/d | rat carcinogenicity study | 100 |
| ARfD | EFSA | 2007 | 0.01 mg/kg bw | rat developmental study | 100 |
| Triazole-derivate-metabolites (TDMs) | | | | | |
| Triazole alanine (TA) – metabolite | | | | | |
| ADI | EFSA | 2018 | 0.3 mg/kg bw/d | rabbit developmental study | 100 |
| ARfD | EFSA | 2018 | 0.3 mg/kg bw | rabbit developmental study | 100 |
| Triazole lactic acid (TLA) – metabolite | | | | | |
| ADI | EFSA | 2018 | 0.3 mg/kg bw/d | bridging from TA | -- |
| ARfD | EFSA | 2018 | 0.3 mg/kg bw | bridging from TA | -- |
| Triazole acetic acid (TAA) – metabolite | | | | | |
| ADI | EFSA | 2018 | 1 mg/kg bw/d | rat 2-generation +  rabbit developmental studies | 100 |
| ARfD | EFSA | 2018 | 1 mg/kg bw | rat 2-generation +  rabbit developmental studies | 100 |
| 1,2,4-triazole– metabolite | | | | | |
| ADI | EFSA | 2018 | 0.023 mg/kg bw/d | rat 12-month study | 300 |
| ARfD | EFSA | 2018 | 0.1 mg/kg | rabbit developmental study | 300 |
| **Spiroxamine** | | | | | |
| ADI | EFSA | 2010 | 0.025 mg/kg bw/d | 1-year dog | 100 |
| ARfD | EFSA | 2010 | 0.1 mg/kg bw | Acute neurotox, rat | 100 |

#### 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? |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1-3 | Wheat (winter/spring) | Yes | Yes (13) | Yes | Yes | Yes | No | No |
| 4 | Barley (winter/spring) | Yes | Yes (15) | 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

\*\* Extrapolated from wheat

13 and 15 trials in spring and winter wheat and barley are available of two seasons.

As residues of prothioconalzole 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.

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.

#### Summary for spiroxamine

Table 7.1‑4: Summary for spiroxamine

| 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? |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1-3 | Wheat (winter/spring) | Yes | Yes (14)\*\* | Yes | Yes | Yes | No | No |
| 4 | Barley (winter/spring) | Yes | Yes (13)\*\* | 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

\*\* overdosed trials (2x 375 g as/ha, BBCH 69 (wheat) or BBCh 61 (barley)

14 and 13 trials in spring and winter wheat and barley are available in two seasons.

As residues of spiroxamine 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.

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.

#### Summary for ULTRACENT 460 EC

Table 7.1‑5: Information on ULTRACENT 460 EC (KCA 6.8)

| Crop | PHI for ULRTACENT 460 EC  proposed by applicant | PHI sufficiently supported for \* | | PHI for ULRTACENT 460 EC  proposed by zRMS | zRMS Comments  (if different PHI proposed) |
| --- | --- | --- | --- | --- | --- |
| Prothioconazole\*\* | Spiroxamine\*\*\* |
| Wheat | 35 | 35 | 35 | -- |  |
| Barley | 35 | 35 | 35 | -- |  |

\* F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop). Growth stage dependent (last application up to BBCH 69)

\*\* UK 2004, DAR Prothioconazole, B.7 (refer to 7.5 References)

\*\*\* DE 2009a, DAR Spiroxamine, B.7 (refer to 7.5 References)

Table 7.1‑6: Waiting periods before planting succeeding crops

|  |  |  |  |
| --- | --- | --- | --- |
| Waiting period before planting succeeding crops | | | Overall waiting period proposed by zRMS ULRTACENT 460 EC |
| Crop group | Led by Prothioconazole | Led by Spiroxamine |
| Not relevant |  |  |  |

Prothioconazole

In the peer review (EFSA 2007 and EFSA 2014) it was concluded that field studies on rotational crops are not necessary, as based on the results of the submitted confined metabolism study, residues of prothioconazole in parts of rotational crops intended for human consumption are expected to stay below the LOQ.

EFSA (EFSA 2018) has recommended new data for triazole derivative metabolites (TDMs), but this should be part of the new active substance renewal. Therefore no new data are presented in this product submission.

Spiroxamine

In the peer review (EFSA 2010) it was concluded that residues in rotational crops are negligible.

Assessment

Article 12 (1) of Regulation (EC) No 396/2005 are available for both substances.

Within the scope of these evaluations, no new studies on the magnitude of residues in plants have been conducted. The evaluation is based on unprotected data. Although summary tables of unprotected data are not required to be presented according to the dRR template, short summary tables will be included in Appendix 2 for better clarity and completeness.

## Prothioconazole

General data on prothioconazole are summarized in the table below (last updated 2021-01-26)

**Table 7.2‑1: General information on prothioconazole**

|  |  |
| --- | --- |
| Active substance (ISO Common Name) | Prothioconazole |
| IUPAC | (*RS*)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-  2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-  thione |
| Chemical structure |  |
| Molecular formula | C14H15Cl2N3OS |
| Molar mass | 344.26 g/mol |
| Chemical group | Triazolithiones |
| Mode of action (if available) | DMI-fungicides (DeMethylation Inhibitors) |
| Systemic | Yes |
| Company (ies) | Bayer CropScience AG\* |
| Rapporteur Member State (RMS) | PL (The original RMS was UK.) |
| Approval status | Approved  Date of 01.08.2008 and reference to decision (COMMISSION DIRECTIVE 08/44/EC - REGULATION (EU) No 2023/918) |
| Restriction | fungicide |
| Review Report | SANCO/3923/07  10/12/2007  26/01/2021 (update) |
| 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 | Yes (EFSA Scientific Report (2007) 106, 1-98) |
| EFSA Journal: conclusion on article 12 | Yes (EFSA Journal 2014;12(5):3689) |
| Current MRL applications on intended uses | EFSA, Journal 2014; 12(5):3689 |

\* Notifier in the EU process to whom the a.s. belong(s)

### Stability of Residues (KCA 6.1)

#### Stability of residues during storage of samples

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

Stability studies of prothioconazole and prothioconazole-desthio (metabolite M04) residues were carried out on wheat samples (considering whole plant, straw and grain). The samples were analysed by HPLC-MS/MS. The method's limit of quantification was 0.05 mg/kg for straw and green material and 0.01 mg/kg for grain (Heinemann 2001). It was found that there was no decrease in prothioconazole residue levels for 180 days, when stored at -18 ºC. The stability of prothioconazole-desthio was also demonstrated for more than 540 days. The concentrations of both substances tested during storage were within the required limits (70 - 110% of initial concentrations). The results showed that the storage time of the samples to be analysed in field trials was acceptable.

The storage stability of prothioconazole-desthio in plant samples stored under frozen conditions was investigated in the framework of the MRL review (EFSA, 2014; EFSA, 2020).

The freezer storage stability of various TDMs (Triazole Derivative Metabolites) was investigated in the framework of the peer review of TDMs (EFSA, 2018).

New data for the determination of storage stability with regard to TDMs and hydroxy metabolites of prothioconazole in honey and bee products has been submitted in the framework of this application.

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

| Matrix | Characteristics  of the matrix | Acceptable Maximum Storage duration | Compound covered | Reference |
| --- | --- | --- | --- | --- |
| Data relied on in EU | | | | |
| Plant products | | | | |
| Wheat green matter | High water content | 18 months | Prothioconazole-desthio | EFSA (2014) |
| Spinaches, sugar beet, tomatoes | 24 months | Prothioconazole-desthio | EFSA (2014) |
| Apples, tomatoes,  mustard leaves,  wheat forage,  radishes tops/roots,  turnips roots,  sugar beet roots,  cabbages, lettuces | 6 months  53 months  53 months  48 months (lettuce) | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Rapeseeds | High oil content | 24 months | Prothioconazole-desthio | EFSA (2014) |
| Soya beans | 12  26  53  48 | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Rapeseeds | not stable  not stable  53  48 | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Cereals grain | Dry/high starch content | 18 months | Prothioconazole-desthio | EFSA (2014) |
| Barley, wheat | 12 months  26 months  26 months  48 months | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Peas, dry;  Navy beans | High protein | no data  15 months  25 months  48 months | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Oranges | High acid | no data  no data  no data  48 months | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Cereal straw | Others | 18 months | Prothioconazole-desthio | EFSA (2014) |
| 12 months  53 months  40 months  no data | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2018) |
| Oilseed rape straw | 24 months  53 months | Prothioconazole-desthio  Triazole acetic acid | EFSA (2014) |
| **Animal products** |  |  |  |  |
| Honey |  | 6 months | Prothioconazole  Prothioconazole-desthio | EFSA (2023b) |
|  |  | 6 months | Prothioconazole-a-hydroxy-desthio,  Prothioconazole-3-hydroxy-desthio,  Prothioconazole-4-hydroxy-desthio,  Prothioconazole-5-hydroxy-desthio,  Prothioconazole-6-hydroxy-desthio  1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2023b) |
|  |  | 5 months | 1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | EFSA (2023b) |
| **New data** | | | | |
| Honey |  | 6 months | Prothioconazole  Prothioconazole-desthio | KCA 6.1/01  Peris D (2024) |
|  |  | 6 months | Prothioconazole-a-hydroxy-desthio,  Prothioconazole-3-hydroxy-desthio,  Prothioconazole-4-hydroxy-desthio,  Prothioconazole-5-hydroxy-desthio,  Prothioconazole-6-hydroxy-desthio  1,2,4-triazole  Triazole alanine  Triazole acetic acid  Triazole lactic acid | KCA 6.1/02  Jooß S. (2024) |

Conclusion on stability of residues during storage

In high starch commodities stabilities, relevant for cereal uses, stability of 18 months has been confirmed (EFSA, 2014).

The freezer storage stability of various TDMs was investigated in the framework of the peer review of TDMs (EFSA, 2018).

New data has been submitted to determine the storage stability in honey and bee products (KCA 6.1/01 and KCA 6.1/02) for all relevant substances. Results demonstrated stability of all compounds for a maximum of 6 months when stored at ≤ 18°C.

#### Stability of residues in sample extracts (KCA 6.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC. ~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

Not relevant. Samples have been analysed within 24 hours after extraction.

### Nature of residues in plants, livestock and processed commodities

#### Nature of residue in primary crops (KCA 6.2.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOL

Metabolism studies were carried out in samples of wheat (spraying, seed treatment) and peanuts (spraying).

For metabolism studies in succeeding crops, wheat, botanicals and turnips were selected. Prothioconazole is rapidly metabolised in plants. The first step is the oxidation of sulphur in the triazolinothione ring and the formation of the corresponding sulphonic acid (metabolite M02), from which the main metabolite, prothioconazole-desthio (metabolite M04), is formed by elimination of the sulphonic acid. This is followed by hydroxylation and binding to glucose. The unchanged active substance is excreted in < 4 %.

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Prothioconazole"

Ordinance of the Minister of Health of 16 October 2006 on the maximum permissible levels of residues of agricultural chemicals which may (Journal of Laws of 2006, No. 242, item. 2047).

Proposal for a residue definition (Bayer):

Definition of residue for plant material:

"Sum of prothioconazole and prothioconazole-desthio (M04)".

The nature of residues of prothioconazole in primary crops has been investigated in the framework of the EU pesticides peer review (EFSA, 2007) and have been re-evaluated in the framework of MRL review in accordance to Art. 12 of Regulation (EC) No. 396/2005 (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(a) | Rate  (kg a.s./ha) | No | Sampling (DAT) | Remarks |
| **EU data** | | | | | | | | |
| Root and tuber vegetables | Sugar beet | [U-14C-phenyl]  prothioconazole | Foliar, F | 0.29 | 4 | Roots & top leaves:  DAT 7 | -- | EFSA (2014) |
| [3,5-14C-triazole]  prothioconazole | Foliar, F | 0.29 | 4 | Roots & top leaves:  DAT 7 | -- | EFSA (2014) |
| Pulses and oilseeds | Peanut | [U-14C-phenyl]  prothioconazole | Foliar, G | 0.30 | 3 | Hay & nuts without shells: DAT 14 | -- | EFSA (2014) |
| [3,5-14C-triazole]  prothioconazole | Foliar, G | 0.30 | 3 | Hay & nuts without shells: DAT 14 | -- | EFSA (2014) |
| Cereals | Wheat | [U-14C-phenyl]  prothioconazole | Foliar, G | 0.22 | 2 | Forage: DAT 6  Hay: DAT 26  Grain & straw: DAT 48 | -- | EFSA (2014) |
| [3,5-14C-triazole]  prothioconazole-  desthio | Foliar, G | 0.25 | 2 | Forage: DAT 0, 14  Grain & straw: DAT 48 | -- | EFSA (2014) |
| [3,5-14C-triazole]  prothioconazole | Foliar, F | 0.18 and 0.29 | 2 | Forage, hay, grain, straw | -- | EFSA (2014) |
| [U-14C-phenyl]  prothioconazole | Seed, G | 0.02 or 0.10 kg  /100 kg seeds | 1 | Forage: DAT 57  Hay: DAT 110  Grain & straw: DAT 153 | ca. 220 kg  seeds/ha | EFSA (2014) |
| **New data** | | | | | | | | |
| No new data | | | | | | | | |

Summary of plant metabolism studies reported in the EU

In accordance to EFSA, 2023b, in wheat grain following foliar spray application with phenyl- and triazole-labelled prothioconazole, the total radioactive residue (TRR) accounted for 0.08 mg eq./kg and 4.97 mg eq./kg respectively. In studies with phenyl-label, parent prothioconazole accounted for 1% of the total radioactive residue (TRR) (0.008 mg e.q./kg) and prothioconazole-desthio for 15.9% of the total radioactive residue (TRR). For the triazole label in grain, Triazole alanine (TA) accounted for 71% of the total radioactive residue (TRR), Triazole acetic acid (TAA) for 19% of the total radioactive residue (TRR) and triazole lactic acid (TLA) for less than 1% of the total radioactive residue (TRR).

In peanut nutmeat following phenyl and triazole labelled prothioconazole application, the total residues accounted for 0.3 to 1.4 mg eq./kg, respectively. Parent prothioconazole was below 10% of the total radioactive residue (TRR). For the triazole label, in nutmeat Triazole alanine (TA) accounted for 47.8% of the total radioactive residue (TRR) (0.67 mg eq./kg), triazole lactic acid (TLA) for 24.5% of the total radioactive residue (TRR) (0.34 mg eq./kg) and Triazole acetic acid (TAA) for 1.2% total radioactive residue (TRR) (0.02 mg eq./kg).

In sugar beets, for the phenyl and triazole labels, total radioactive residue (TRR) levels were higher in leaves (4.3–5.2 mg eq./kg) than in roots (0.12–0.13 mg eq./kg). Following phenyl labelled prothioconazole application, prothioconazole–desthio accounted for 58% of the total radioactive residue (TRR) in roots. Prothioconazole was seen to be extensively degraded in both leaves and roots of sugar beet and accounted for less than 10% of the total radioactive residue (TRR).

Regarding the triazole labelling moiety, besides prothioconazole-desthio that was identiﬁed in roots (25% total radioactive residue (TRR), 0.03 mg eq./kg), Triazole alanine (TA) was found to be the predominant compound of the total residues in roots (29% total radioactive residue (TRR), 0.04 mg eq./kg). The other TDMs were not reported as quantiﬁed in sugar beet roots. In sugar beet tops TA represented 2% of the total radioactive residue (0.084 mg eq/kg) and the only other TDM quantiﬁed was triazole lactic acid (TLA) with 4% total radioactive residue (0.207 mg eq/kg).

Conclusion on metabolism in primary crops

EFSA concludes (EFSA, 2023b) that in plants, prothioconazole is extensively metabolised and the metabolic pathway is similar in all crops investigated. The main metabolic pathway consisted of the formation of prothioconazole-desthio with further hydroxylation (with the formation of several closely related metabolites) and glucosidation steps (EFSA, 2014). The studies with triazole labelled prothioconazole indicated the cleavage of triazole linkage and formation of three major TDM metabolites: Triazole alanine (TA), triazole lactic acid (TLA) and Triazole acetic acid (TAA) (EFSA, 2014).

For the intended uses on cereals, the metabolism of prothioconazole is considered sufﬁciently addressed.

#### Nature of residue in rotational crops (KCA 6.6.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOL

Metabolism studies were carried out in samples of wheat (spraying, seed treatment) and peanuts (spraying).

For metabolism studies in succeeding crops, wheat, botanicals and turnips were selected. Prothioconazole is rapidly metabolised in plants. The first step is the oxidation of sulphur in the triazolinothione ring and the formation of the corresponding sulphonic acid (metabolite M02), from which the main metabolite, prothioconazole-desthio (metabolite M04), is formed by elimination of the sulphonic acid. This is followed by hydroxylation and binding to glucose. The unchanged active substance is excreted in < 4 %.

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Prothioconazole"

Ordinance of the Minister of Health of 16 October 2006 on the maximum permissible levels of residues of agricultural chemicals which may (Journal of Laws of 2006, No. 242, item. 2047).

Proposal for a residue definition (Bayer):

Definition of residue for plant material:

"Sum of prothioconazole and prothioconazole-desthio (M04)".

The nature of residues in rotational crops was investigated in the framework of the MRL review (EFSA, 2014).

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

| Crop group | Crop | Label position | Application and sampling details | | | | | Reference |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Method,  F or G \* | Rate  (kg a.i./ha) | Sowing intervals  (DAT) | Harvest  Intervals (DAT) | Remarks |
| **EU data** | | | | | | | | |
| Leafy vegetables | Swiss chard | [U-14C-phenyl]  prothioconazole | Bare soil  application | 580 | 28, 146, 269 | 80, 188, 348 | -- | EFSA (2014) |
| Root and tuber vegetables | Turnip | Roots, tops:  94, 201, 349 |
| Cereals | Spring wheat | Green material: 73, 178, 327  Hay: 111, 231, 377  Grain, straw: 145, 269, 412 |
| Leafy vegetables | Swiss chard | [triazole-3,5-14C] prothioconazole | Bare soil  application | 4 x 0.20 | 30, 125, 366 | Leaves: 77, 169, 406 | -- |
| Root and tuber vegetables | Turnip | Roots, tops: 113, 195, 420 |
| Cereals | Wheat | Grain, straw: 121, 209, 450  Green material: 62, 154, 388  Hay: 80, 171, 420 |
| **New data** | | | | | | | | |
| No new data | | | | | | | | |

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

Summary of plant metabolism studies reported in the EU

The nature of residues in rotational crops has been evaluated within the review of existing MRLs in accordance to Article 12 of Regulation No 396/2005 (EFSA 2014).

In the rotational crop metabolism, the major residues identiﬁed were prothioconazole-desthio and its hydroxylated derivative metabolites, either free or conjugated. In studies with triazole labelled prothioconazole, the main residues in rotational crops were TDMs, namely TA, TAA and TLA whereby 1,2,4-T was not detected.

During the peer review of TDMs in light of conﬁrmatory data, the metabolism of various triazole compounds in rotational and primary crops was investigated. It was concluded that for TDMs similar metabolic patterns were depicted both in primary and rotational crops (EFSA, 2018).

Conclusion on metabolism in rotational crops

Based on the studies presented above, the metabolism in primary and rotational crops was found to be similar and a specific residue definition for rotational crops is not deemed necessary.

#### Nature of residues in processed commodities (KCA 6.5.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOL

Metabolism studies were carried out in samples of wheat (spraying, seed treatment) and peanuts (spraying).

For metabolism studies in succeeding crops, wheat, botanicals and turnips were selected. Prothioconazole is rapidly metabolised in plants. The first step is the oxidation of sulphur in the triazolinothione ring and the formation of the corresponding sulphonic acid (metabolite M02), from which the main metabolite, prothioconazole-desthio (metabolite M04), is formed by elimination of the sulphonic acid. This is followed by hydroxylation and binding to glucose. The unchanged active substance is excreted in < 4 %.

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Prothioconazole"

Ordinance of the Minister of Health of 16 October 2006 on the maximum permissible levels of residues of agricultural chemicals which may (Journal of Laws of 2006, No. 242, item. 2047).

Proposal for a residue definition (Bayer):

Definition of residue for plant material:

"Sum of prothioconazole and prothioconazole-desthio (M04)".

A study on the nature of prothioconazole residues in processed commodities was submitted in the framework of the EU pesticides peer review (EFSA, 2007) and has been evaluation in the framework of the revised MRL review (EFSA, 2020).

Determination of the nature of residues for various TDMs was investigated in the framework of the peer review of TDMs (EFSA, 2018).

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

| Conditions (Duration, Temperature, pH) | Identified compound(s) (%) | Reference |
| --- | --- | --- |
| **EU data** | | |
| **Pasteurisation**  (20 minutes, 90°C, pH 4) | Prothioconazole-desthio (99.4 %) | UK (2004), EFSA (2020) |
| Triazole alanine (100.4 %)  Triazole acetic acid (99.4 %)  Triazole lactic acid (102.6 %)  1,2,4-triazole (103.5 %) | EFSA (2018) |
| **Baking, boiling, brewing**  (60 minutes, 100°C, pH 5) | Prothioconazole-desthio (99.9 %) | UK (2004), EFSA (2020) |
| Triazole alanine (100.0 %)  Triazole acetic acid (101.0 %)  Triazole lactic acid (104.1 %)  1,2,4-triazole (104.0 %) | EFSA (2018) |
| **Sterilisation**  (20 minutes, 120°C, pH 6) | Prothioconazole-desthio (99.8 %) | UK (2004), EFSA (2020) |
| Triazole alanine (99.8 %)  Triazole acetic acid (100.5 %)  Triazole lactic acid (96.4 %)  1,2,4-triazole (99.4 %) | EFSA (2018) |

Conclusion on nature of residues in processed commodities

All compounds are stable under hydrolysis studies simulating baking/brewing/boiling, pasteurisation and sterilisation (EFSA, 2018; EFSA, 2020).

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOL

Metabolism studies were carried out in samples of wheat (spraying, seed treatment) and peanuts (spraying).

For metabolism studies in succeeding crops, wheat, botanicals and turnips were selected. Prothioconazole is rapidly metabolised in plants. The first step is the oxidation of sulphur in the triazolinothione ring and the formation of the corresponding sulphonic acid (metabolite M02), from which the main metabolite, prothioconazole-desthio (metabolite M04), is formed by elimination of the sulphonic acid. This is followed by hydroxylation and binding to glucose. The unchanged active substance is excreted in < 4 %.

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Prothioconazole"

Ordinance of the Minister of Health of 16 October 2006 on the maximum permissible levels of residues of agricultural chemicals which may (Journal of Laws of 2006, No. 242, item. 2047).

Proposal for a residue definition (Bayer):

Definition of residue for plant material:

"Sum of prothioconazole and prothioconazole-desthio (M04)".

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

|  |  |
| --- | --- |
| **Endpoints** | |
| Plant groups covered | Root crops (sugar beet)  Cereals/grass (wheat)  Pulses/Oilseeds (peanuts) |
| Rotational crops covered | Root and tuber vegetables (turnips)  Leafy crops (swiss chards)  Cereals (spring wheat) |
| Metabolism in rotational crops similar to metabolism in primary crops? | Yes |
| Processed commodities | a.i. is stable under standard hydrolysis conditions |
| Residue pattern in processed commodities similar to pattern in raw commodities? | Yes |
| Plant residue definition for monitoring | Prothioconazole-desthio (M04) (sum of isomers) for all categories of crops (EFSA, 2020) |
| Plant residue definition for risk assessment | 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), with separate assessment of:  - Triazole alanine (TA) and triazole lactic acid (TLA)  - Triazole acetic acid (TAA)  - 1,2,4-triazole (1,2,4-T)  (EFSA, 2020) |
| Conversion factor from enforcement to RA | 2 for cereal grain and oilseeds  3 for cereal straw  (EFSA, 2014; EFSA, 2020) |

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTIOCONAZOL

Metabolism studies were carried out in goats and egg-laying hens. The animals were mainly exposed to prothioconazole-desthio (metabolite M04), the main component of residues in agricultural material. In addition, metabolism studies of the parent substance were also performed. 90% of the prothioconazole dose administered to the animals is rapidly excreted from their bodies. The main processes involved in the animals are desulfuration, oxidative hydroxylation and binding to glycuronic acid. The main metabolites in animals are M04 (prothioconazole-desthio), M14 and M15 (hydroxydestio isomers).

Conclusion:

Metabolism studies have shown that there is no risk of residue accumulation in food of animal origin. Total radioactive residues in eggs, milk and edible animal parts were detected at very low levels.

Definition of residues for animal material:

Proposed residue definition (Bayer):

"Prothioconazole-desthio (M04)".

The nature of prothioconazole residues in commodities of animal origin was investigated in the framework of the EU pesticides peer review (EFSA, 2007) and have been re-evaluated in the framework of MRL review in accordance to Art. 12 of Regulation (EC) No. 396/2005 (EFSA, 2014).

The metabolism of prothioconazole in commodities of animal origin was investigated in two studies in lactating goats using [phenyl-UL-14C]-labelled prothioconazole and prothioconazole-desthio and one study using [3,5-14C-triazole]-labelled prothioconazole-desthio. One study was performed in laying hens using [phenyl-UL-14C]-labelled prothioconazole.

The magnitude of the TDM in processed commodities relevant to animal feed items was investigated in the framework of the peer review of TDMs (UK, 2018).

Table 7.2‑7: Summary of animal metabolism studies

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Group | Species | Label position | No of  animal | Application details | | Sample details | | Reference |
| Rate  (mg/kg bw/d) | Duration  (days) | Commodity | Time of sampling |
| **EU data** | | | | | | | | |
| Lactating  ruminants | Goat | [U-14C-phenyl]  prothioconazole | 1 | 10  (250 mg a.i./kg feed) | 3 | Milk | twice daily | EFSA (2014) |
| Urine and faeces | daily |
| Tissues | at sacrifice |
| [U-14C-phenyl]  prothioconazole-desthio | 1 | 10  (195 mg a.i./kg feed) | 3 | Milk | twice daily |
| Urine and faeces | daily |
| Tissues | at sacrifice |
| [3,5-14C-triazole]  prothioconazole | 1 | 10 | 3 | Milk | twice daily |
| Urine and faeces | daily |
| Tissues | at sacrifice |
| [triazole-UL-14C]triazole alanine | 1 | 0.7  (15.24 mg a.i./kg feed) | 7 | Milk | twice daily | UK (2018) |
| Plasma, urine and faces | Daily  At sacrifice |
| Tissues | at sacrifice |
| Laying  poultry | Hens | [U-14C-phenyl]  prothioconazole | 6 | 10 | 3 | Eggs | Once daily | EFSA (2014) |
| Excreta | At regular intervals |
| Tissues | At sacrifice |
| [3,5-14C-triazole]  prothioconazole | 6 | 10 | 3 | Eggs | Once daily |
| Excreta | At regular intervals |
| Tissues | At sacrifice |
| [triazole-UL-14C]triazole alanine | 6 | 0.81 | 14 | Eggs | Daily | UK (2018) |
| Excreta | Daily |
| Muscle  Fat  Liver  Kidney  Skin | At sacrifice |
| **New data** | | | | | | | | |
| No new data in the framework of this application | | | | | | | | |

Summary of plant metabolism studies reported in the EU

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).

The compilation of the poultry and ruminant metabolism studies conducted with the triazole pesticide active substances with the 14C labelling on the triazole moiety showed that beside the parent compound that was detected in signiﬁcant proportions in all animal matrices ranging between 27% and 81% TRR in milk, eggs and tissues, 1,2,4-T was also found to be a predominant compound of the total residues with levels ranging from 31% to 86% TRR in those matrices. TA was identiﬁed at very low levels in poultry muscle only (< 10% TRR) and at levels between 22% and 39% TRR in ruminant matrices.

Summary of new animal metabolism studies

No new data in the framework of this application

Conclusion on metabolism in livestock

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.

For risk assessment, the residue is 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).

Based on the finding of the livestock metabolism studies with the parent triazole fungicides and triazole alanine, the following triazole metabolites are considered for inclusion in the residue definition for products of animal origin for risk assessment purposes: T, TA, TAA and TLA.

On consideration of the toxicological profile of the four TDMs and how the residue definition relates to the parent triazole active, the residue definition for risk assessment is defined as follows:

1. prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2- chloro-phenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers);
2. TA and TLA since these compounds share the same toxicity;
3. TAA,
4. 1,2,4-Triazole

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTIOCONAZOL

Metabolism studies were carried out in goats and egg-laying hens. The animals were mainly exposed to prothioconazole-desthio (metabolite M04), the main component of residues in agricultural material. In addition, metabolism studies of the parent substance were also performed. 90% of the prothioconazole dose administered to the animals is rapidly excreted from their bodies. The main processes involved in the animals are desulfuration, oxidative hydroxylation and binding to glycuronic acid. The main metabolites in animals are M04 (prothioconazole-desthio), M14 and M15 (hydroxydestio isomers).

Conclusion:

Metabolism studies have shown that there is no risk of residue accumulation in food of animal origin. Total radioactive residues in eggs, milk and edible animal parts were detected at very low levels.

Definition of residues for animal material:

Proposed residue definition (Bayer):

"Prothioconazole-desthio (M04)".

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 | Milk: 1 - 1.3 days  Eggs: not reached within test period of 53 hours |
| Animal residue definition for monitoring | Prothioconazole-desthio (sum of isomers) |
| Animal residue definition for risk assessment | 1) prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2- chloro-phenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers);  2) TA and TLA since these compounds share the same toxicity;  3) TAA,  4) 1,2,4-Triazole |
| Conversion factor | 2 (liver & fat)  3 (muscle & kidney)  Conversion factors not calculated for poultry and milk where <LOQ residues expected. |
| Metabolism in rat and ruminant similar | Yes |
| Fat soluble residue | Yes |

### Magnitude of residues in plants (KCA 6.3)

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

Unprotected data (higher number of applications) are summarized in the Table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.2‑9: Summary of EU reported and new data supporting the intended uses of ULTRACENT 460 EC and conformity to existing MRL

| Commodity | Source | Residue zone (EUN, EUS, EU, outside EU) | Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition  RA = according to risk assessment residue definition | STMR (mg/kg) | HR (mg/kg) | Unrounded OECD calculator MRL  (rounded) (mg/kg) | Current EU MRL  (mg/kg)  \* | MRL compliance |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Residue definition for enforcement (E): prothioconazole-desthio (sum of isomers)  Residue deﬁnition for risk assessment (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) (“E” values multiplied with conversion factor 2 for cereal grain; 3 for cereal straw (EFSA, 2014; EFSA, 2020)) | | | | | | | | |
| Wheat  (0500090)  *intended use:*  *1x 160 g a.i./ha,*  *BBCH max. 59, PHI 35 days* | DAR 2004  EFSA 2007  EFSA 2014  EFSA 2020 | EUN | GAP on which EU a.i. assessment is based: 3 x 200 g a.i./ha, BBCH 69, 14-d-interval, outdoor, PHI 35  grain: E: 11x < 0.01  straw: E: 0.08; 0.09; 0.11; 0.14; 0.15; 0.19; 0.20; 0.27; 0.31; 0.66; 0.72  grain: RA:11x < 0.02  straw: RA: 0.24; 0.27; 0.33; 0.42; 0.45; 0.57; 0.60; 0.81; 0.93; 1.98; 2.16 | N/A | | | | |
| EFSA 2014\*\*\*  EFSA 2020 | EUN | GAP on which EU a.i. assessment is based: information not available  grain: E: <0.01; 0.02  straw: E: 0.09; 0.42; 0.48; 1.60  grain: RA: <0.02; 0.04  straw: RA: 0.27; 1.26; 1.44; 4.80 |
| Overall supporting data for cGAP | EUN | grain: E: 12x < 0.01; 0.02  straw: E: 0.08; 2x 0.09; 0.11; 0.14; 0.15; 0.19; 0.20; 0.27; 0.31; 0.42; 0.48; 0.66; 0.72; 1.60 | grain: 0.010  straw: 0.200 | grain: 0.020  straw: 1.600 | grain: 0.022 (0.03) | 0.1 | Yes |
|  |  |  | grain: RA: 12x < 0.02; 0.04  straw: RA: 0.24; 2x 0.27; 0.33; 0.42; 0.45; 0.57; 0.60; 0.81; 0.93; 1.26; 1.44; 1.98; 2.16; 4.80 | grain: 0.020  straw: 0.600 | grain: 0.040  straw: 4.800 | n.r. | n.r. | -- |
| Barley  (0500010)  *intended use:*  *1x 160 g a.i./ha,*  *BBCH max 51, PHI 35 days* | DAR 2004  EFSA 2007  EFSA 2014  EFSA 2020 | EUN | GAP on which EU a.i. assessment is based: 2 x 200 g a.i./ha, BBCH 59-69, 14-d-interval,outdoor, PHI 35  grain: E: 9x < 0.01  straw: E: 0.05; 0.08; 2x 0.1; 2x 0.13; 2x 0.14; 0.3  grain: RA: 9x < 0.02  straw: RA: 0.15; 0.24; 2x 0.3; 2x 0.39; 2x 0.42; 0.9 | N/A | | | | |
| EFSA 2014\*\*\*  EFSA 2020 | EUN | GAP on which EU a.i. assessment is based: information not available  grain: E: 2x <0.01; 0.01; 0.02  straw: E: 0.11; 0.36; 0.56  grain: RA: 2x <0.02; 0.02; 0.04  straw: RA: 0.33; 1.08; 1.68 |
| EFSA 2020\*\* | EUN | GAP on which EU a.i. assessment is based: 2 x 200 g a.i./ha, BBCH 69, 14-d-interval,outdoor  grain: E: 2 <0.01  straw: E: 0.11; 0.54  grain: RA: 2 <0.02  straw: RA: 0.33; 1.62 |
| Overall supporting data for cGAP | EUN | grain: E: 13x < 0.01; 0.01; 0.02  straw: E: 0.05; 0.08; 2x 0.1; 2x 0.11; 2x 0.13; 2x 0.14; 0.3; 0.36; 0.54; 0.56 | grain: 0.010  straw: 0.130 | grain: 0.020  straw: 0.560 | grain: 0.021 (0.02) | 0.2 | Yes |
|  |  |  | grain: RA: 13x < 0.02; 0.02; 0.04  straw: RA: 0.15; 0.24; 2x 0.3; 2x 0.33; 2x 0.39; 2x 0.42; 0.9; 1.08; 1.62; 1.68 | grain: 0.020  straw: 0.390 | grain: 0.040  straw: 1.680 | n.r. | n.r. | -- |
| Honey, bee products  (1040000) | EFSA (2023) | EUN | GAP on which EU a.i. assessment is based: 2 x < 0.10 kg a.i./ha, PHI 7 days  E: 6 x < 0.01; 2 x 0.012  RA: 6x < 0.06; 2x 0.062  *trials still unter protection, not considered for MRL calculation* |  |  |  |  |  |
|  |  | EUS | GAP on which EU a.i. assessment is based: 2 x < 0.10 kg a.i./ha, PHI 7 days  E: 7x < 0.01  RA: 6x < 0.07  *trials still unter protection, not considered for MRL calculation* |  |  |  |  |  |
|  | New trials | EUN | Tested GAP: 2x 200 g a.i./ha, BBCH 63-65, PHI 7-14, tunnel  E: 2x < 0.01  RA: < 0.01; 0.011 |  |  |  |  |  |
|  |  | EUS | Tested GAP: 2x 200 g a.i./ha, BBCH 63-65, PHI 7-14, tunnel  E: 1x < 0.0025, 1x < 0.01  RA: < 0.0025, 0.154 |  |  |  |  |  |
|  | Overall supporting data for cGAP | EU | E: 1x < 0.0025, 3x < 0.01  RA: < 0.0025; < 0.01; 0.011; 0.154 | E: 0.01  RA: 0.011 | E: 0.01  RA: 0.154 | E: 0.01  (0.01)  RA: -- | 0.05 | Yes |

\* Source of EU MRL: Reg. (EU) 2024/1318

\*\* new trials, evaluated under EFSA 2020

\*\*\* Trials assessed by FR (France, 2014) performed at a similar or less critical GAP than the authorised European cGAP and leading to similar or higher residue levels than the ones assessed in the peer-review

As the parent compound was only present in minor amounts and prothioconazole-desthio was shown to more toxic than the parent compound, it was concluded to define prothioconazole-desthio as the relevant residue for enforcement. Based on metabolism study results, the MRL review derived the following tentative conversion factors to account for hydroxy metabolites of prothioconazole-desthio: 2 in cereal grains and 3 in cereal straw (EFSA, 2014)

#### Conclusion on the magnitude of residues in plants

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC~~.

Wheat:

The intended critical use of prothioconazole is with a maximum of one application of 160 g a.i./ha as foliar application during the growing period of the crop (BBCH 30-59) and a PHI of 35 days.

Overall, 13 EU evaluated trials on wheat are available for the northern zone.

Trials submitted in the framework of EU pesticide peer review (EFSA, 2007), testing residues after 3 applications with 200 g a.i./ha at a BBCH of 69 represent an overestimated exposure of the crop to the plant protection product (higher number and amount of application), compared to the intended GAP.

Residues in grains were low, ranging from below the LOQ of 0.01 mg/kg to 0.02 mg/kg, resulting in an MRL of 0.03 mg/kg, which is clearly below the current MRL of 0.1 mg/kg. Since these overdosed results were observed, after 3 instead of the intended 1 application, these results can be regarded as worst-case.

Exceedance of the current MRL is therefore not expected.

The uses in wheat are considered acceptable.

Barley:

Use of prothioconazole is intended in barley with a maximum of one applications of 160 g a.i./ha as foliar application during the growing period of the crop (BBCH 30-51) and a PHI of 35 days.

Overall, 15 EU evaluated trials on barley are available for the northern zone.

Trials submitted in the framework of EU pesticide peer review (EFSA, 2007), testing residues after 2 applications with 200 g a.i./ha at a BBCH between 59 and 69 represent an overestimated exposure of the crop to the plant protection product (higher number and amount of application), , compared to the intended GAP.

Residues in grains were low, ranging from below the LOQ of 0.01 mg/kg to 0.02 mg/kg, resulting in an MRL of 0.02 mg/kg, which is clearly below the current MRL of 0.2 mg/kg. Since these overdosed results were observed, after 2 instead of the intended 1 application, these results can be regarded as worst-case.

Exceedance of the current MRL is therefore not expected.

The uses in barley are considered acceptable.

### Magnitude of residues in livestock

By-products of cereals might be used for feed purposes. Hence, it is necessary to conduct dietary burden calculations.

Since the residue data available to the pesticide peer review on the TDM conﬁrmatory data were affected by uncertainties related to storage stability and the number of residue trials, the livestock dietary burden to TDMs cannot be currently estimated. Moreover, the peer review on the TDM conﬁrmatory data identiﬁed a data gap related to the lack of poultry and ruminant feeding studies with triazole lactic acid (TLA). EFSA recommends that the livestock exposure to TDMs originating from the use of prothioconazole is further assessed in the framework of the renewal of the approval of active substance. (EFSA, 2018).

#### Dietary burden calculation

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

Table 7.2‑10: Input values for the dietary burden calculation (EFSA, 2020)

| Feed Commodity | Median dietary burden | | Maximum dietary burden | |
| --- | --- | --- | --- | --- |
| Input value (mg/kg) | Comment | Input value (mg/kg) | Comment |
| **Risk assessment residue definition:** Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers) | | | | |
| Barley grain | 0.07 | STMR x CF(2) | 0.07 | STMR x CF(2) |
| Brewer´s grain | 0.23 | STMR x CF(2) x PF(3.3) \* | 0.23 | STMR x CF(2) x PF(3.3) \* |
| Oat grain | 0.02 | STMR x CF(2) | 0.02 | STMR x CF(2) |
| Wheat grain | 0.04 | STMR x CF(2) | 0.04 | STMR x CF(2) |
| Wheat gluten meal | 0.04 | STMR x CF(2) x PF(1.8) \* | 0.04 | STMR x CF(2) x PF(1.8) \* |
| Wheat milled by-products | 0.28 | STMR x CF(2) x PF(7) \* | 0.28 | STMR x CF(2) x PF(7) \* |
| Rye grain | 0.02 | STMR x CF(2) | 0.02 | STMR x CF(2) |
| Barley straw | 1.96 | STMR x CF(3) | 7.50 | HR x CF(3) |
| Oats straw | 1.26 | STMR x CF(3) | 7.50 | HR x CF(3) |
| Wheat straw | 2.69 | STMR | 5.52 | HR x CF(3) |
| Rye straw | 2.25 | STMR x CF(3) | 5.52 | HR x CF(3) |

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

\* For brewer’s grain, wheat gluten meal and wheat milled by-products in the absence of processing factors supported by data, default processing factors were, included in the calculation to consider the potential concentration of residues in these commodities.

Table 7.2‑11: Results of the dietary burden calculation

| Animal species | Median  dietary burden  (mg/kg bw/d) | Maximum dietary  burden  (mg/kg bw/d) | Highest contributing  commodity | | Max dietary  burden  (mg/kg DM) | Trigger exceeded  (Y/N) |
| --- | --- | --- | --- | --- | --- | --- |
| **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) | | | | | | |
| Cattle (all diets) | 0.030 | 0.102 | Barley | straw | 2.66 | Yes |
| Cattle (dairy only) | 0.030 | 0.102 | Barley | straw | 2.66 | Yes |
| Sheep (all diets) | 0.062 | 0.220 | Barley | straw | 5.18 | Yes |
| Sheep (ewe only) | 0.048 | 0.173 | Barley | straw | 5.18 | Yes |
| Swine (all diets) | 0.006 | 0.006 | Wheat | milled bypdts | 0.20 | Yes |
| Poultry (all diets) | 0.029 | 0.051 | Wheat | straw | 0.75 | Yes |
| Poultry (layer only) | 0.029 | 0.051 | Wheat | straw | 0.75 | Yes |

The calculated livestock dietary burden exceeded the trigger value of 0.004 mg/kg bw/d for all relevant animal groups. Further livestock feeding studies are necessary.

#### Livestock feeding studies (KCA 6.4.1-6.4.3)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOLE

As no significant residues (>0.1 mg/kg) are found in cereal grains, testing of animals fed with feed containing residues is not required. However, residues of M04 in straw and green parts of cereals may exceed this value. Metabolic studies in goats indicate that residues above 0.01 mg/kg may occur in the edible parts of the animal or in its milk. Therefore, tests were performed on dairy cows fed with feed containing residues. Tissue and milk samples were analysed by HPLC/MS/MS to determine the metabolites M14, M15 and M04. No residues above the limits of quantification of the analytical methods (0.01mg/kg for meat, kidney, liver and fat and 0.004 mg/kg for milk) were found in the samples tested.

Conclusion:

No residues of these compounds are expected in foodstuffs of animal origin animal origin. This conclusion is supported by the results of metabolism studies in animals. Consumer exposure to dietary residues will not increase due to the consumption of foodstuffs of animal origin, taking into account data on the intake of residues by animals with feed.

Livestock feeding studies have been evaluated in the framework of MRL review according Art. 12 of Regulation (EC) No. 396/2005 (EFSA, 2014).

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

| Commodity | Dietary burden | | Results of the livestock feeding study | | | | | | Median residue  (mg/kg)(c) | Highest residue  (mg/kg)(d) | Calculated MRL  (mg/kg) | CF for RA(e) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Med. (mg/kg bw/d) | Max. (mg/kg bw/d) | Dose Level (mg/kg bw/d)(a) | No | Result for enforcement | | Result for RA (b) | |
| Mean (mg/kg) | Max. (mg/kg) | Mean (mg/kg) | Max. (mg/kg) |
| **EU data (EFSA, 2014)** | | | | | | | | | | | | |
| **Risk assessment residue definition:** Sum of prothioconazole-desthio and all metabolites containing the 2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl-2H-1,2,4-triazole moiety, expressed as prothioconazole-desthio (sum of isomers) | | | | | | | | | | | | |
| Pig muscle | 0.006 | 0.006 | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 1.0 |
| 0.91 | 3 | < 0.01 | < 0.01 | n.a. | n.a. |
| 3.64 | 3 | < 0.01 | < 0.01 | n.a. | n.a. |
| Pig fat | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 1.0 |
| 0.91 | 3 | < 0.01 | 0.01 | n.a. | n.a. |
| 3.64 | 3 | 0.02 | 0.04 | n.a. | n.a. |
| Pig liver | 0.15 | 3 | 0.02 | 0.03 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 2.0 |
| 0.91 | 3 | 0.14 | 0.18 | n.a. | n.a. |
| 3.64 | 3 | 0.68 | 1.20 | n.a. | n.a. |
| Pig kidney | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 9.0 |
| 0.91 | 3 | 0.03 | 0.03 | n.a. | n.a. |
| 3.64 | 3 | 0.13 | 0.24 | n.a. | n.a. |
| Milk | 0.030 | 0.102 | 0.15 | 42 | < 0.05(f) | N/A | n.a. | n.a. | < 0.05 | < 0.05 | 0.05\*  (tentative) | 1.0 |
| 0.91 | 42 | < 0.05(f) | N/A | n.a. | n.a. |
| 3.64 | 42 | < 0.05(f) | N/A | n.a. | n.a. |
| Ruminant muscle | 0.030 | 0.102 | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 1.0 |
| 0.91 | 3 | < 0.01 | < 0.01 | n.a. | n.a. |
| 3.64 | 3 | < 0.01 | < 0.01 | n.a. | n.a. |
| Ruminant fat | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | < 0.01 | 0.01\*  (tentative) | 1.0 |
| 0.91 | 3 | < 0.01 | 0.01 | n.a. | n.a. |
| 3.64 | 3 | 0.02 | 0.04 | n.a. | n.a. |
| Ruminant liver | 0.15 | 3 | 0.02 | 0.03 | n.a. | n.a. | 0.01 | 0.042 | 0.05  (tentative) | 2.0 |
| 0.91 | 3 | 0.14 | 0.18 | n.a. | n.a. |
| 3.64 | 3 | 0.68 | 1.20 | n.a. | n.a. |
| Ruminant kidney | 0.15 | 3 | < 0.01 | < 0.01 | n.a. | n.a. | < 0.01 | 0.012 | 0.02  (tentative) | 9.0 |
| 0.91 | 3 | 0.03 | 0.03 | n.a. | n.a. |
| 3.64 | 3 | 0.13 | 0.24 | n.a. | n.a. |
| **New data** | | | | | | | | | | | | |
| No new data in the framework of this application | | | | | | | | | | | | |

N/A: Not applicable.

n.a.: Not analysed.

(a): Based on a 560 kg animal consuming approximately 20 kg feed DM/day.

(b): In the feeding study, residues were not determined according to the residue definition for risk assessment. Indeed, only prothioconazole-desthio, M14 and M15 were analysed.

(c): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009b).

(d): Highest residue value (tissues) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009b).

(e): The tentative conversion factors for enforcement to risk assessment in liver and kidney were derived on the basis of the available metabolism study on ruminants. For muscle, fat and milk, no CF was derived as residue levels are expected at the maximum meat ruminant dietary burden in these matrices are negligible (<0.01 mg/kg).

(f): Mean residue level from day 1 or 4 until day 29 (3 cows, 13 or 14 sampling days).

(\*): Indicates that the MRL is set at the limit of analytical quantification.

Conclusion on feeding studies

The available livestock feeding studies demonstrated that residues of prothioconazole are not expected in products of pig origin and milk. Values > LOQ have been determined in ruminant liver and kidney.

Since the requested uses do not modify the theoretical maximum daily intake for animals, a change of the existing MRLs for products of animal origin is not required.

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

PROTHIOCONAZOLE

Studies on the effects of processing and home food preparation on residues are not required due to the low residues in the plant material (TMDI < 10% ADI, residues lower than 0.1 mg/kg).

Testing is not required as residues of the test substances occur at levels below the limit of quantification of analytical methods (<0.02 mg/kg).

Despite the lack of requirements, a study of the effect of hydrolysis on residues (pH 6, 120 ºC) was performed. No significant effect of hydrolysis conditions on residues of this compound was found.

Conclusion:

No aggregation of residues was found under the influence of the processing and domestic food preparation process.

Speciﬁc studies investigating the magnitude of prothioconazole-desthio, its hydroxy metabolites and TDMs residues in processed commodities have not been submitted and are not necessary, considering that the total theoretical maximum daily intake (TMDI) is below the trigger value of 10% of the ADI for the crops under assessment.

#### Available data for all crops under consideration

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

#### Conclusion on processing studies

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

Speciﬁc studies investigating the magnitude of prothioconazole-desthio, its hydroxy metabolites and TDMs residues in processed commodities have not been submitted and are not necessary, considering that the total theoretical maximum daily intake (TMDI) is below the trigger value of 10% of the ADI for the crops under assessment.

### Magnitude of residues in representative succeeding crops

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

Metabolism in succeeding crops (wheat, turnips, beets) proceeds in the same way as in the main crop. The product decomposes very quickly in soil without posing a risk to succeeding crops. No residues above the limit of quantification of analytical methods were found in samples taken from succeeding crops.

Conclusion:

There are no restrictions for succeeding crops.

In the framework of the EU pesticides peer review (EFSA, 2007) and re-evaluation in the framework of MRL review in accordance to Art. 12 of Regulation (EC) No. 396/2005 (EFSA, 2014) it was concluded that rotational crop studies were not necessary. The confined rotational crop studies indicate that prothioconazole residues in food and feed rotational commodities are expected to be covered by the residue levels in primary crops.

Nevertheless, residue data for prothioconazole in rotational crops are available from field rotational crop trials conducted on barley (cereal), carrot and turnip (root crop), lettuce (leafy crop). Studies were performed in an effort to address the assessment of consumer exposure to triazole derivative metabolites (TDMs) in rotational crops; prothioconazole-desthio was also determined. (EFSA, 2018).

No residues of prothioconazole-desthio above the LOQ (0.01 mg/kg) were detected in control samples. At all plant-back intervals and for all matrices, no residues of prothioconazole-desthio were detected above the LOQ (0.01 mg/kg). It can be concluded that prothioconazole-desthio residue levels in food and feed rotational commodities are expected to be covered by the residue levels in primary crops. Therefore, no risk mitigation measures (plant back restrictions) need to be proposed with regard to prothioconazole-desthio.

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.

This should be part of the processes of renewal of active substances.

#### Field rotational crop studies (KCA 6.6.2)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC. ~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

In accordance to the technical guideline SANTE/11956/2016 rev. 9, Appendix II, cereals do not belong to the crops with melliferous capacity.

However, non-target plants can be affected during flowering, which might be attractive for bees.

15 EU evaluated Studies on the determination of residues of prothioconazole and its metabolites in pollen and bee products are available for the southern (7x) and northern zone (8x) (EFSA, 2023a), however, these studies might still be under protection.

Therefore, 4 new tunnel studies (2x EUS, 2x EUN), to determine the residues in honey under semi-field conditions have been investigated by the applicant in the framework of the current application (KCA 6.10/01: *Peris D 2024, E23-0116* for a.i. and prothioconazole-desthio).

No residues > LOQ have been reported in these trials after 2 applications of 200 g a.i./ha, at BBCH 63-65.

According to the MRL calculation presented in Table 7.2‑9 the current default MRL of 0.05\* mg/kg was not exceeded; no adaptation of the MRL in honey is required.

Storage stability data for honey are presented under Table 7.2‑2 (KCA 6.1/01 *Peris D 2024, E23-0116* for a.i. and prothioconazole-desthio and KCA 6.1/02 *Jooß S 2024, S23-102955* for TDMs).

A summary of all studies are presented in in Appendix 2.

*~~The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:~~*

~~PROTHIOCONAZOLE~~

~~Residues, field trials (selected trials for assessment - up to 2000) (Annex IIA, point 6.3, Annex IIIA, point 8.2)~~

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **~~STMR [mg/kg]~~** | **~~0.01~~**  **~~0.01~~** | | **~~0.01~~** | **~~0.01~~** | **~~0.01~~** | **~~0.01~~** |
| **~~MRL [mg/kg]~~** | **~~0.01~~** | | **~~0.05~~** | | **~~0.05~~** | |
| **~~Comments~~** | **~~GAP~~** | | **~~GAP~~** | | **~~GAP~~** | |
| **~~Results in accordance with critical points of Good Agricultural Practice [mg/kg]~~** | **~~11 x <0.01~~** | **~~8 x <0.01~~** | **~~9 x <0.01~~** | **~~8: 3 x 0.02, 3 x 0.01, 2 x < 0.01~~** | **~~8: 2 x 0.02, 1 x 0.01, 5 x < 0.01~~** | **~~4: 2 x 0.01, 2 x < 0.01~~** |
| **~~Region~~** | **~~North~~** | **~~South~~** | **~~North~~** | **~~South~~** | **~~North~~** | **~~South~~** |
| **~~Crop~~** | **~~Wheat~~** | | **~~Barley~~** | | **~~Rapeseed~~** | |

~~In 2000, an additional four tests were carried out in wheat in the Northern European region and two in Southern Europe. In all samples tested, no residues were found above the analytical method limit of quantification (0.01 mg/kg). All tests were performed in accordance with the GAP~~.

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

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

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

The metabolites included in the residue deﬁnition of prothioconazole were assumed to be covered by the toxicological reference values of prothioconazole-desthio (EFSA, 2014).

~~However, a~~ A new PRIMo version 3.1 is available now, therefore, new consumer risk assessments are provided in the following.

#### Input values for the consumer risk assessment

The residue data of ULTRACENT 460 EC is believed to be identical to the formulation of INPUT 460 EC (authorisation no.: R-61/2011) by Bayer AG. All information on metabolites and residues are believed to be identical to that of INPUT 460 EC for which all data protection has now expired.

For this reason, the applicant fully refers to the unprotected data of INPUT 460 EC. No new MRLs are required nor proposed.

In order to evaluate the potential acute and chronic exposure to prothioconazole residues through the diet, the Theoretical Maximum Dietary Intakes (TMDI) for chronic and the International Estimated Short-Term Intake (IESTI) for acute calculations were estimated using the actual EFSA PRIMo model 3.1.

The presented current MRLs for prothioconazole are stated in the Regulation (EU) 2019/552. The whole MRL list is presented in Annex II of Regulation (EU) 2019/552.

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

~~The toxicological reference values relevant for the dietary risk assessments are reported in the following[[1]](#footnote-1):~~

|  |  |  |
| --- | --- | --- |
| ~~ADI~~ | ~~0.01 mg/kg bw/day~~ | ~~Source: EFSA Scientific Report (2007) 106, 1-98~~  ~~SANCO/3923 /07 – final on 10 December 2007 (updated on 26 January 2021)~~ |
| ~~ARfD~~ | ~~0.01 mg/kg bw~~ |

The exposure values calculated were compared to the toxicological reference values for prothioconazole.

The input data (current MRLs) are presented in Appendix 3.

The risk assessment is performed for the parent prothioconazole; while for the additional residue deﬁnitions related to the TDMs, an indicative exposure assessment is performed, considering only the crops under consideration.

Prothioconazole-desthio:

Since no new MRLs have been proposed in the framework of this submission, and MRL is based on evaluated EU data, the chronic risk assessment (TMDI) is derived based on existing EU MRLs as set in Reg. (EU 2024/1318), which are presented in the table in Appendix 3.

The acute exposure assessment was performed only with regard to the commodity under consideration assuming the consumption of a large portion of the food item as reported in the national food surveys and that these items contained residues at the highest residue level (HR).

Triazole derivate metabolites (TDMs):

A comprehensive risk assessment, including all crops in which TDMs might be present from the uses of all pesticides belonging to the class of triazole fungicides, could not be performed. A separate risk assessment for TDMs has been performed in line with the conﬁrmatory data assessment for triazole compounds in the framework of Regulation (EC) No 1107/2009 (EFSA, 2018). In the framework of the present assessment, an indicative exposure assessment was performed for cereals, considering the additional residue deﬁnitions derived in the framework of the conclusion on TDMs (EFSA, 2018). The input values (HR/STMR values) were as derived from residue trials on cereals, which have been evaluated in the addendum to the conclusion on TDMs (EFSA, 2018).

Table 7.2‑13: Input values for the consumer risk assessment (IEDI and IESTI calculation) - prothioconazole-desthio

| 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) | | | | |
| Barley | 0.020 | STMR | 0.040 | HR |
| Wheat | 0.020 | STMR | 0.040 | HR |
| **Risk assessment residue definition:** Triazole alanine (TA) | | | | |
| Cereals | 1.039 | STMR (EFSA, 2018) | 2.826 | HR (EFSA, 2018) |
| **Risk assessment residue definition:** Triazole lactic acid (TLA) | | | | |
| Cereals | 0.065 | STMR (EFSA, 2018) | 0.192 | HR (EFSA, 2018) |
| **Risk assessment residue definition:** Triazole acetic acid (TAA) | | | | |
| Cereals | 0.120 | STMR (EFSA, 2018) | 0.680 | HR (EFSA, 2018) |
| **Risk assessment residue definition:** 1,2,4-triazole (1,2,4-T) | | | | |
| Cereals | 0.050 | STMR (EFSA, 2018) | 0.100 | HR (EFSA, 2018) |

#### Conclusion on consumer risk assessment

~~ULTRACENT 460 EC is believed to be identical to the formulation of INPUT 460 EC (authorisation no.: R-61/2011) by Bayer AG. All information on metabolites and residues are believed to be identical to that of INPUT 460 EC (authorisation no.: R-61/2011), for which all data protection has now expired.~~

~~For this reason, the applicant fully refers to the unprotected data of INPUT 460 EC.~~

The input data (current MRLs) are presented in Appendix 3.

TMDI (chronic) and IESTI (acute) were calculated with PRIMo revision 3.1 (2021/01/06). Taking into consideration the current MRLs.

Extensive calculations sheets are presented in Appendix 3 (A 3.1 TMDI calculations, A 3.3 IESTI calculations – Raw commodities and A 3.4 IESTI calculations – Processed commodities).

Table 7.2‑14: Consumer risk assessment

|  |  |  |
| --- | --- | --- |
| ~~TMDI (% ADI) according to EFSA PRIMo vers. 3.1~~ | ~~32 % NL toddler~~  ~~23 % GEMS/Food G11~~ |  |
| ~~IESTI (% ARfD) according to EFSA PRIMo vers. 3.1~~ | ~~Unprocessed commodities (children)~~  ~~14 % Wheat~~  ~~11 % Barley~~  ~~Processed commodities (children)~~  ~~12 % Wheat / milling (flour)~~  ~~7 % Barley / cooked~~  ~~6 % Wheat / milling (wholemeal)~~  ~~4 % Barley / milling (flour)~~ | ~~Unprocessed commodities (adults)~~  ~~10 % Barley~~  ~~8 % Wheat~~  ~~Processed commodities (adults)~~  ~~14 % Barley / beer~~  ~~4 % Wheat / bread/pizza~~  ~~4 % Wheat / pasta~~  ~~3 % Wheat / bread (wholemeal)~~ |

|  |  |  |  |
| --- | --- | --- | --- |
| **Prothioconazole-desthio** | | | |
| TMDI (% ADI) according to EFSA PRIMo | 30%(based on NL toddler) | | |
| IEDI (% ADI) according to EFSA PRIMo | 27 % (based on NL toddler) | | |
| IESTI (% ARfD) according to EFSA PRIMo | Unprocessed | | |
| Children  3 % Wheat (0.29 µg/kg bw)  1 % Barley (0.11 µg/kg bw) | | Adults  2 % Wheat (0.17 µg/kg bw)  1.0 % Barley (0.10 µg/kg bw) |
| Processed | | |
| Children  2 % Wheat/milling (flour)  1 % Wheat/milling wholemeal)  0.7 % Barley/cooked  0.4 % Barley/milling (flour) | | Adults  1 % Barley/beer  0.9 % Wheat/bread/pizza  0.8 % Wheat/pasta  0.7 % Wheat/bread (wholemeal) |
| **Triazole alanine (TA)** | | | |
| TMDI (% ADI) according to EFSA PRIMo | | Has not been calculated | |
| IEDI (% ADI) according to EFSA PRIMo | | 3 % (based on GEMS/Food G06) | |
| IESTI (% ARfD) according to EFSA PRIMo | | Unprocessed | |
| Children  5 % Wheat (15 µg/kg bw)  2 % Barley (5.8 µg/kg bw) | Adults  3 % Wheat (8.7 µg/kg bw)  2 % Barley (5.0 µg/kg bw) |
| Processed | |
| Children  4 % Wheat/milling (flour)  2 % Wheat/milling wholemeal)  1 % Barley/cooked  0.6 % Barley/milling (flour) | Adults  2 % Barley/beer  2 % Wheat/bread/pizza  1 % Wheat/pasta  1 % Wheat/bread (wholemeal) |
| **Triazole lactic acid (TLA)** | | | |
| TMDI (% ADI) according to EFSA PRIMo | | Has not been calculated | |
| IEDI (% ADI) according to EFSA PRIMo | | 0.2 % (based on GEMS/Food G06) | |
| IESTI (% ARfD) according to EFSA PRIMo | | Unprocessed | |
| Children  0.3 % Wheat (0.94 µg/kg bw)  0.1 % Barley (0.36 µg/kg bw) | Adults  0.2 % Wheat (0.55 µg/kg bw)  0.1 % Barley (0.31 µg/kg bw) |
| Processed | |
| Children  0.3 % Wheat/milling (flour)  0.1 % Wheat/milling wholemeal)  0.1 % Barley/cooked  0.0% Barley/milling (flour) | Adults  0.2 % Barley/beer  0.10 % Wheat/bread/pizza  0.08% Wheat/pasta  0.08 % Wheat/bread (wholemeal) |
| **Triazole acetic acid (TAA)** | | | |
| TMDI (% ADI) according to EFSA PRIMo | | Has not been calculated | |
| IEDI (% ADI) according to EFSA PRIMo | | 0.1 % (based on GEMS/Food G06) | |
| IESTI (% ARfD) according to EFSA PRIMo | | Unprocessed | |
| Children  0.2 % Wheat (1.7 µg/kg bw)  0.07 % Barley (0.67 µg/kg bw) | Adults  0.1 % Wheat (1.0 µg/kg bw)  0.06 % Barley (0.58 µg/kg bw) |
| Processed | |
| Children  0.1 % Wheat/milling (flour)  0.1 % Wheat/milling wholemeal)  0.0 % Barley/cooked  0.0% Barley/milling (flour) | Adults  0.1 % Barley/beer  0.05 % Wheat/bread/pizza  0.05 % Wheat/pasta  0.04 % Wheat/bread (wholemeal) |
| **1,2,4-triazole (1,2,4-T)** | | | |
| TMDI (% ADI) according to EFSA PRIMo | | Has not been calculated | |
| IEDI (% ADI) according to EFSA PRIMo | | 2 % (based on GEMS/Food G06)) | |
| IESTI (% ARfD) according to EFSA PRIMo | | Unprocessed | |
| Children  0.7 % Wheat (0.72 µg/kg bw)  0.3 % Barley (0.28 µg/kg bw) | Adults  0.4 % Wheat (0.42 µg/kg bw)  0.2 % Barley (0.24 µg/kg bw) |
| Processed | |
| Children  0.6 % Wheat/milling (flour)  0.3 % Wheat/milling (wholemeal)  0.2 % Barley/cooked  0.1 % Rye/milling (wholemeal) | Adults  0.4 % Barley/beer  0.2 % Wheat/bread/pizza  0.2 % Wheat/pasta  0.2 % Wheat/bread (wholemeal) |

The proposed uses of prothioconazole in the formulation ULTRACENT 460 EC do not represent unacceptable acute and chronic risks for the consumer with regard to prothioconazole-desthio and the TDMs.

TMDI and IESTI values were all below the Trigger of 100 % of ADI and ARfD, respectively. No acute or consumer risk for consumer is expected.

## Spiroxamine

General data on spiroxamine are summarized in the table below (last updated 2011-06-17)

**Table 7.3‑1: General information on spiroxamine**

|  |  |
| --- | --- |
| Active substance (ISO Common Name) | Spiroxamine |
| IUPAC | 8-*tert*-butyl-1,4-dioxaspiro[4.5]decan-2-  ylmethyl(ethyl)(propyl)amine (ISO)  *N*-{[8-(1,1-dimethylethyl)-1,4-dioxaspiro[4.5]dec-2-yl]methyl}-*N-*ethylpropan-1-amine (ACD software) |
| Chemical structure |  |
|  |  |
| Molecular formula | C18H35NO2 |
| Molar mass | 297.5 g/mol |
| Chemical group | Spiroketal-amines |
| Mode of action (if available) | Amines (“morpholines”)  Sterol biosynthesis in membranes# |
| Systemic | Yes |
| Company (ies) | Bayer CropScience \* |
| Rapporteur Member State (RMS) | AT |
| Approval status | Approved  Date of (01/01/2012) and reference to decision (Reg. (EU) No 2019/29, Reg. (EU) No 540/2011, Reg. (EU) No 797/2011 (old Legislation: 2007/21/EC, 99/73/EC))  ~~Date of 01.01.2012 and reference to decision (COMMISSION DIRECTIVE 99/73/EC - REGULATION (EU) No 2019/291)~~ |
| Restriction | fungicide |
| Review Report | SANCO/10889/2011 Rev 2  17/06/2011 |
| Current MRL regulation | Regulation (EC) No 2016/452 |
| Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed | Yes |
| EFSA Journal : Conclusion on the peer review | Yes (EFSA Journal 2010;8(10):1719) |
| EFSA Journal: conclusion on article 12 | Yes (EFSA Journal 2015;13(1):3992) |
| Current MRL applications on intended uses | EFSA-Q-2008-629  All commodities  Status: Reasoned opinion available (EFSA Journal 2015;13(1)3992) |

\* Notifier in the EU process to whom the a.s. belong(s)

\*\* If yes: EFSA, Journal 2015;13(1)3992) - see list of references

# FRAC Code List 2018: Fungicides sorted by mode of action (including FRAC Code numbering)

### Stability of Residues (KCA 6.1)

#### Stability of residues during storage of samples

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. ~~It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

Stability studies of spiroxamine and N-oxide metabolite (M3) residues were carried out on wheat samples (considering whole plant, straw and grain). Test samples were fortified at 0.5 mg/kg and stored at -20ºC for 434 days. No decrease in residue levels was observed during storage of the samples.

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 |  |  |  |
| Spiroxamine, N-oxide (M03) and incurred residues) | | | |
| Cereals (grain) | High protein content | ≥ 516-566 days | DE 1997  EFSA 2010 |
| Cereals (forage, straw) | -- |  |  |
| Spiroxamine and aminodiol | | | |
| Grapes (grapes, raisins, juice) | High acid content | ≥ 529-585 days | DE 1997  EFSA 2010 |
| Banana | -- | ≥ 21 months | EFSA 2010 |
| Animal Products | | | |
| No data |  |  |  |
|  |  |  |  |
| **No New data** | | | |
| \* Please refer to point 7.5 References | | | |

Conclusion on stability of residues during storage

Spiroxamine residues were stable under frozen storage conditions (-18 C°) in cereal samples over the study period (up to >14 months in grain, straw and forage).

This time period covers all of the storage periods of the samples for the residue trials presented within this submission.

In the framework of the peer review, the storage stability of the total spiroxamine residues under frozen conditions was determined in dry commodities (barley straw, grain) for 14 months. Degradation of the total spiroxamine residues during storage of the trial samples is therefore not expected.

However, in the Art. 12 evaluation (EFSA 2015) it is recommended that in dry and acidic commodities, the analysis was performed only using the common moiety methods. A possible degradation of spiroxamine to the metabolites covered by the analytical methods used is not excluded. Therefore, a new storage stability study where samples are specifically analysed for spiroxamine in acidic and dry commodities and covering the maximum storage time interval of the residue samples from the reported trials is required. This is only recommended on for the active substance evaluation level and not relevant for this product submission.

#### Stability of residues in sample extracts (KCA 6.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC. ~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

### Nature of residues in plants, livestock and processed commodities

#### Nature of residue in primary crops (KCA 6.2.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Studies on the metabolism of spiroxamine in wheat have been performed. The parent substance was detected (after the waiting period) at a level of 14.3% of the administered dose. In addition, the following metabolites were detected in the crop samples tested: N-formyl-desethyl- spiroxamine (M4), hydroxy-spiroxamine (M5), desethyl-spiroxamine (M1), depropyl-spiroxamine (M2) and N-oxydo-spiroxamine(M3).

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, 2004, item 801). Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑3: Summary of plant metabolism studies

| Crop Group | Crop | Label position | Application and sampling details | | | | | Reference |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Method,  F or G (a) | Rate  (kg a.s./ha) | No | Sampling (DAT) | Remarks |
| **EU data** | | | | | | | | |
| Fruits and fruiting vegetable | Grape | 1-14C-cyclohexyl and  4-14C-dioxolane | Foliar spray, F | 0.4  +  1.2 | 1  +  1 | 0, 35 (berries, stalks) | Only bunches of grapes were sprayed. | DE 2009  EFSA 2015 |
|  | Banana | 1-14C-cyclohexyl and  4-14C-dioxolane | Foliar spray, G | 3.2 | 3 | 0 (small fruit),  17 (medium size),  71 (at harvest) | One tree was used for each labelling form. | DE 2009  EFSA 2015 |
| Cereals | Spring wheat | 1-14C-cyclohexyl | Foliar spray, F | 0.4  +  0.431 | 1  +  1 | 0, 14 (forage),  61 (straw, grain) | Applications at BBCH 30 & 51 | DE 2009  EFSA 2015 |
|  | Winter wheat | 4-14C-dioxolane | Foliar spray, F | 1.65 | 2 | 0, 14 (forage),  56 (straw, grain) | Applications at BBCH 30 & 51 | DE 2009  EFSA 2015 |
| **No New data** | | | | | | | | |

Summary of plant metabolism studies reported in the EU

Metabolism of spiroxamine was investigated for foliar application on cereals (wheat) and on fruit crops (grapes, banana), using [1-14C-cyclohexyl] and [4-14C-dioxolane]-labelled spiroxamine. In both crop groups, spiroxamine was found to be the major compound of the total residues, accounting in mature crops for 3–25 % TRR in wheat grain and straw and 25–60 % TRR in grapes and banana for both the labelling forms. Significant differences were however observed in the metabolism of spiroxamine in the two crop groups.

In cereals, the metabolism proceeds mainly by oxidation and de-alkylation at the amine group and by hydroxylation at the *tert*-butyl group of the parent molecule with the formation of metabolites structurally related to the parent compound (group A metabolites) identified mainly as M03 (18 %–22 % TRR; 0.012–7.7 mg eq/kg) in wheat grain and straw. No cleavage of the parent molecule occurred.

EFSA (EFSA 2015) proposed the following residue definitions for the risk assessment: 

Cereals: sum of spiroxamine and all metabolites containing the *tert*-butyl-cyclohexanone moiety, expressed as spiroxamine,

Summary of new plant metabolism studies

No new data available.

Conclusion on metabolism in primary crops

No new data are required for the intended uses in cereals.

#### Nature of residue in rotational crops (KCA 6.6.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. ~~It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Studies on the metabolism of spiroxamine in wheat have been performed. The parent substance was detected (after the waiting period) at a level of 14.3% of the administered dose. In addition, the following metabolites were detected in the crop samples tested: N-formyl-desethyl- spiroxamine (M4), hydroxy-spiroxamine (M5), desethyl-spiroxamine (M1), depropyl-spiroxamine (M2) and N-oxydo-spiroxamine(M3).

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, 2004, item 801). Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑4: Summary of metabolism studies in rotational crops

| Crop group | Crop | Label position | Application and sampling details | | | | | Reference |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Method,  F or G \* | Rate  (kg a.s./ha) | Sowing intervals  (DAT) | Harvest  Intervals (DAT) | Remarks |
| **EU data** | | | | | | | | |
| Leafy vegetables | Swiss chard | 1-14C-cyclohexyl and  4-14C-dioxolane | F  G | 1.58  1.62 | 30, 161  30, 196, 294 | -- | Bare soil application  Plants sown after soil ageing for 30, 161, 193 and 294 days – Crop interception: 0 % | DE 2009,  EFSA 2010,  EFSA 2015 |
| Root and tuber vegetables | Turnips | 1-14C-cyclohexyl and  4-14C-dioxolane | F  G | 1.58  1.62 | 30, 161  30, 196, 294 | -- |
| Cereals | Wheat | 1-14C-cyclohexyl and  4-14C-dioxolane | F  G | 1.58  1.62 | 30, 161  30, 196, 294 | -- |
| **No New data** | | | | | | | | |

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

Summary of plant metabolism studies reported in the EU

Spiroxamine is authorised for use on cereals that might be grown in rotation. According to the soil degradation studies evaluated in the framework of the peer review, the DT90 field value of spiroxamine is 466 days which is higher than the trigger value of 100 days (EFSA 2010). The major soil metabolites were identified as M01 and M02 (DT90 field values of 321 and 318 days, respectively). According to the European guidelines on rotational crops (EC 1997), further investigation of residues in rotational crops is relevant.

The metabolism of spiroxamine in rotational crops (Swiss chard, turnips, wheat) has been determined on EU level (DE 2009, EFSA 2010). A field and a confined rotational crop studies were conducted both with [1-14C-cyclohexyl] and [4-14C-dioxolane]-labelled spiroxamine and investigated the nature of residues at different plant back intervals.

In EFSA 2015 it was concluded that the metabolic pathway of spiroxamine in the edible parts of the rotational crops was considered as sufficiently investigated and was found to be similar to that observed in cereals as primary crops. The main degradation routes involved the desalkylation of the parent compound yielding the metabolites M01 and M02, and the oxidation of the tert-butyl group leading to hydroxy and carboxylic acid derivatives, especially present as hexose conjugates. A minor degradation pathway consisted of parent molecule cleavage. This metabolic pathway was also found to be similar to the metabolism of spiroxamine depicted in soil suggesting a potential uptake by these plants of major soil metabolites M01 and M02. The residue definition proposed for cereals as primary crops and relying on the tert-butylcyclohexanone moiety for risk assessment is also appropriate to cover the residues in rotational crops. Finally, based on this metabolism study and considering that the total annual application rate of spiroxamine within the EU is 1.5 kg a.s./ha (cereals) and the fact that bare soil treatment was applied (interception of spiroxamine residues by the primary crops is in practice expected at a rate of up to 90 %), lower levels of total residues may be expected in the edible parts of the rotated crops, provided that spiroxamine is applied in compliance with the intended GAPs.

Summary of new plant metabolism studies

No new data available.

Conclusion on metabolism in rotational crops

No new data are required for the intended uses in cereals.

#### Nature of residues in processed commodities (KCA 6.5.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. ~~It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Studies on the metabolism of spiroxamine in wheat have been performed. The parent substance was detected (after the waiting period) at a level of 14.3% of the administered dose. In addition, the following metabolites were detected in the crop samples tested: N-formyl-desethyl- spiroxamine (M4), hydroxy-spiroxamine (M5), desethyl-spiroxamine (M1), depropyl-spiroxamine (M2) and N-oxydo-spiroxamine(M3).

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, 2004, item 801). Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑5: Nature of the residues in processed commodities

| Conditions (Duration, Temperature, pH) | Identified compound(s) (%) | Reference |
| --- | --- | --- |
| **EU data** | | |
| **Pasteurisation** (20 minutes, 90°C, pH 4) | Not relevant for cereals | DE 2009  EFSA 2015 |
| **Baking, boiling, brewing** (60 minutes, 100°C, pH 5) |  |
| **Sterilisation** (20 minutes, 120°C, pH 6) |  |
| **No New data** | | |

In the framework of the peer review (DE 2009) no processing studies in cereals are required. Very low residue levels are expected in cereal grains. Based on the two processing trials in barley it can be concluded that residues in processed products are below those in grain and that no residues are expected in beer when barley is treated according to the critical GAP.

In view of the low levels of residues in wheat or rye grain studies on the effects of processing on wheat or rye grain are not considered necessary.

EFSA (EFSA 2015) concluded that the nature of the residues in processed commodities has been sufficiently investigated and it is proposed to apply the same residue definition for enforcement and risk assessment as for primary crops. A robust processing factor for enforcement and risk assessment could be derived only for peeled banana. Further processing studies are not required as they are not expected to affect the outcome of the risk assessment.

Conclusion on nature of residues in processed commodities

In view of the low levels of residue of spiroxamine in wheat or barley grain determined from field residue trials performed according to the critical GAP, considering the low contribution of residues to the ADI and ARfD and the likely reduction of residues by processing operations, studies on the effects of processing on wheat or barley grain are not required.

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Studies on the metabolism of spiroxamine in wheat have been performed. The parent substance was detected (after the waiting period) at a level of 14.3% of the administered dose. In addition, the following metabolites were detected in the crop samples tested: N-formyl-desethyl- spiroxamine (M4), hydroxy-spiroxamine (M5), desethyl-spiroxamine (M1), depropyl-spiroxamine (M2) and N-oxydo-spiroxamine(M3).

Conclusions:

1) Prothioconazole and spiroxamine are rapidly eliminated from the crop and do not accumulate.

2) Radioactive residues were found in very low concentrations.

Definition of residues for plant-derived material:

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, 2004, item 801). Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑6: Summary of the nature of residues in commodities of plant origin

|  |  |
| --- | --- |
| **Endpoints** | |
| Plant groups covered | Fruits (grapes, banana),  cereals (wheat) |
| Rotational crops covered | Cereals (wheat), leafy crops (Swiss chard, turnip leaves) and root crops (turnip root) |
| Metabolism in rotational crops similar to metabolism in primary crops? | Yes |
| Processed commodities | Spiroxamine. is stable stable under standard hydrolysis conditions |
| Residue pattern in processed commodities similar to pattern in raw commodities? | Yes |
| Plant residue definition for monitoring | Spiroxamine (parent only) (EFSA 2010) |
| Plant residue definition for risk assessment | **Cereals and rotational crops:** Sum of spiroxamine and metabolites containing the tert.-butylcyclohexanone moiety, expressed as spiroxamine  **Fruits:** Sum of spiroxamine and metabolites containing the N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane moiety, expressed as spiroxamine (provisional) (EFSA 2010)  Spiroxamine (sum of isomers) (Commission Regulation (EU) 2016/452)\*  **Fruits:** Sum of spiroxamine and metabolites containing the aminodiol (N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane) and the tert.-butylcyclohexanone moiety, expressed as spiroxamine (provisional)  (EFSA 2010, LoE Revision RMS 2017) |
| Conversion factor from enforcement to RA | Cereal grain: 4.3 (1/0.23)  Cereal straw: 5.9 (1/0.17)  Grapes: 2.0 (1/0.50) (provisional)  Banana: 1.7 (1/0.61) (provisional)  (EFSA 2010)  Grapes: 4.3 (1 + 2 x 1.0 x TEF 0.1/0.06)  Banana: 2.7 (1 + 2 x 0.5 x TEF 0.1/0.06)  (EFSA 2010, LoE Revision 2017) |

\* The EU reference labs identified the reference standard for spiroxamine carboxylic acid metabolite M06 as commercially not available. When re-viewing the MRL, the Commission will take into account the commercial availability of the reference standard referred to in the first sentence by 30 March 2017, or, if that reference standard is not commercially available by that date, the unavailability of it..

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Rapid metabolism was found in goats. The highest levels of residues were detected in the liver and kidney. However, in the milk of the test animals, the test compounds were at very low levels. Rapid elimination of spiroxamine also occurred in hens. The lowest levels of residues were found in muscle and eggs.

Conclusion:

Metabolism studies have shown that there is no risk of residue accumulation in food of animal origin. Total radioactive residues in eggs, milk and edible animal parts were detected at very low levels.

Definition of residues for animal material:

Proposed residue definition (Bayer):

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, item 801).

"Spiroxamine carboxylic acid expressed as spiroxamine".

Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑7: 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 | 1-14C-cyclohexyl | 1 | 10 | 3 | Milk | twice daily | DE 2009,  EFSA 2010,  EFSA 2015 |
| Urine and faeces | daily |
| Tissues | at sacrifice  (7 h after third dosing) |
| Laying  poultry | Hens | 1-14C-cyclohexyl | 2 x 5 | 10 | 3 | Eggs | twice daily | DE 2009,  EFSA 2010,  EFSA 2015 |
| Excreta | daily |
| Tissues | at sacrifice  (5 h after third dosing) |
| **No New data** | | | | | | | | |

Summary of plant metabolism studies reported in the EU

The nature of spiroxamine residues in commodities of animal origin was investigated in the framework of Directive 91/414/EEC (DE 2009, EFSA 2010). Reported metabolism studies included one study in lactating goats and one study in laying hens using [1-14C-cyclohexyl]-labelled spiroxamine.

EFSA (EFSA 2010) concludes that the livestock metabolism studies in goat and hen have shown very high percentages of residues with uncleaved spiroketal structure in all organs, tissues and in milk and eggs. Only very low amounts of cleaved metabolites and conjugates of cleaved metabolites were observed (glucuronide of the t-butylcyclohexanol (M22) at a level of 0.4 % of TRR in the kidneys of the goat). Therefore, no substantial new information would be expected from new livestock metabolism studies using [dioxolane-4-14C] labelled spiroxamine. The metabolism of spiroxamine in livestock animals is considered as sufficiently understood.

During the Article 12 review EFSA (EFSA 2015) proposed two different residue definitions for risk assessment purposes:

* *Ruminants matrices*: sum of spiroxamine, spiroxamine carboxylic acid (M06), its glucuronide conjugate (M19) and hydroxy acid spiroxamine (M07), expressed as spiroxamine (sum of isomers)
* *Poultry matrices*: sum of spiroxamine, desethyl-spiroxamine (M01), despropyl-spiroxamine (M02) and spiroxamine carboxylic acid (M06) expressed as spiroxamine (sum of isomers).

Summary of new animal metabolism studies

No new data submitted in the framework of this application.

Conclusion on metabolism in livestock

No new data are required.

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Rapid metabolism was found in goats. The highest levels of residues were detected in the liver and kidney. However, in the milk of the test animals, the test compounds were at very low levels. Rapid elimination of spiroxamine also occurred in hens. The lowest levels of residues were found in muscle and eggs.

Conclusion:

Metabolism studies have shown that there is no risk of residue accumulation in food of animal origin. Total radioactive residues in eggs, milk and edible animal parts were detected at very low levels.

Definition of residues for animal material:

Proposed residue definition (Bayer):

"Spiroxamine"

Regulation of the Minister of Health of 16 April 2004 on the maximum permissible levels of chemical residues of plant protection products which may be present in or on foodstuffs (Journal of Laws No. 85, item 801).

"Spiroxamine carboxylic acid expressed as spiroxamine".

Directive 2000/81/EC of 18.12.2000 amending the Annexes to Council Directives 86/362/EEC, 86/363/EEC and 90/642/EEC on the fixing of maximum levels for pesticide residues in and on cereals, animal products and relevant products of plant origin, including fruit and vegetables (OJ L 326/56 of 22.12.2000).

Table 7.3‑8: 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 | 2 days in milk |
| No applicable (eggs, no residues) |
| Animal residue definition for monitoring | **Ruminants**: Spiroxamine carboxylic acid (M06), expressed as spiroxamine (EFSA 2010)  **Poultry:** Sum of spiroxamine and spiroxamine carboxylic acid (M06), expressed as spiroxamine (sum of isomers); proposal: provisional pending confirmatory information from a poultry feeding study (data requirement under Reg. (EU) 396/2005  (EFSA 2010 LoE, Revision RMS 2017) |
| Animal residue definition for risk assessment | **Ruminants:** Sum of spiroxamine, spiroxamine carboxylic acid (M06), its glucuronide conjugate (M19) and hydroxy acid spiroxamine (M07), expressed as spiroxamine (sum of isomers)  spiroxamine carboxylic acid (M06), its glucuronide conjugate (M19) and -hydroxy acid (M07) and acid glucuronide (M19), expressed as spiroxamine  **Poultry:** Sum of spiroxamine, desethyl-spiroxamine (M01), despropyl-spiroxamine (M02) and spiroxamine carboxylic acid (M06) expressed as spiroxamine (sum of isomers)  (EFSA 2010 LoE, Revision RMS 2017) |
| Conversion factor | Ruminant/pig muscle: 1.4  Ruminant/pig liver: 2.8  Ruminant/pig kidney: 3.8  Ruminant/pig fat: 1.8  Milk: 1.2  Poultry liver: 7.6  Poultry muscle: 2.0  Poultry fat: 53.5  (EFSA 2010) |
| Metabolism in rat and ruminant similar | Yes (but major ruminant metabolite M07 was not found in rat excreta. Toxicologists suggest, that reference values for spiroxamine are applicable to M07) |
| Fat soluble residue | No |

### Magnitude of residues in plants (KCA 6.3)

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

Unprotected overdosed data are summarized in the table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.3‑9: Summary of EU reported and new data supporting the intended uses of ULTRACENT 460 EC and conformity to existing MRL

| Commodity | Source | Residue zone | 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 (winter, spring)  Intended cGAP 1x 300 g a.i./ha, BBCH 30-59, PHI 35 | DE 2009  ER 2014a (RMS: DE),  EFSA 2015 | N-EU, outdoor | Fall-back GAP on which MRL/EU a.s. assessment is based: 2x 0.375 kg as/ha, BBCH 69, PHI 42d  E/RA: Grain: 10 × <0.05, 2x <0.01 0.02, 0.03  E/RA: Straw: 0.24, 0.31, 0.39, 0.4, 0.47, 0.50, 2x 0.69, 0.70, 0.81, 0.99, 2x 1.1, 1.2 | N/A | | | | |
| Overall supporting data for cGAP | N-EU, outdoor | E/RA: Grain: 10 × <0.05, 2 x <0.01, 0.02, 0.03 | E/RA: 0.05 | E/RA: 0.05 | 0.05 | 0.05 | Yes |
| E/RA: Straw: 0.24, 0.31, 0.39, 0.4, 0.47, 0.50, 2x 0.69, 0.70, 0.81, 0.99, 2x 1.1, 1.2 | E/RA: 0.69 | E/RA: 1.2 | -- | -- | -- |
| Barley  Intended cGAP 1x 300 g a.i./ha, BBCh 30-51, PHI 35 | DE 2009  ER 2014a (RMS: DE),  EFSA 2015 | N-EU, outdoor | Barley (winter/spring)  Critical GAP on which MRL/EU a.s. assessment is based: 2 x 0.75 kg as/ha, upt to BBCH 61, PHI 35d, outdoor (  E: Grain: 0.106, 0.107, 0.127, 0.172  Straw: 0.416, 0.635, 0.65, 0.669  RA: Grain: 0.312, 0.5, 0.901, 0.923  Straw: 2.58, 3.9, 3.99, 4.4 | N/A | | | | |
| DE 2009  ER 2014a (RMS: DE),  EFSA 2015 | N-EU, outdoor | Fall-Back GAP on which MRL/EU a.s. assessment is based: 2 x 0.375 kg as/ha, upt to BBCH 61, PHI 42d, outdoor  E/RA: Grain: 10 × <0.05, 0.01, 2 x 0.02  E/RA: Straw: 0.61, 0.59, 0.23, 0.41, 0.47, 0.36, 0.54, 0.49, 0.12, 0.09, 0.57, 0.59, 1.1 |
| Overall supporting data for cGAP | N-EU, outdoor | E/RA: Grain: 10 × <0.05, 0.01, 2 x 0.02  E/RA: Straw: 0.61, 0.59, 0.23, 0.41, 0.47, 0.36, 0.54, 0.49, 0.12, 0.09, 0.57, 0.59, 1.1 | 0.02  0.49 | 0.05  1.1 | 0.05  -- | 0.05 | Yes |

\* Source of EU MRL: Commission Regulation (EU) 2016/452 of 29 March 2016 amending Annexes II and III to Regulation (EC) No. 396/2005

LOQ: 0.01 mg/kg

LOD: 0.003 mg/kg

#### Conclusion on the magnitude of residues in plants

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

**Wheat**

14 unprotected trials (grain, straw) from the northern zone are available and already evaluated by EFSA (EFSA 2015). All trials were conducted with a higher application rate, 2 instead of 1 application and on a later BBCH level.

The data indicate that even with this more critical GAP, an exceedance of the current MRL is not expected. This also applies to the less critical intended product application submitted.

An exceedance of the current MRL is not expected after the intended application of ULTRACENT 460 EC on wheat.

**Barley**

13 unprotected trials (grain, straw) from the northern zone are available and already evaluated by EFSA (EFSA 2015). All trials were conducted with a higher application rate, 2 instead of 1 application and on a later BBCH level.

The data indicate that even with this more critical GAP, an exceedance of the current MRL is not expected. This also applies to the less critical intended product application submitted.

An exceedance of the current MRL is not expected after the intended application of ULTRACENT 460 EC on barley.

### Magnitude of residues in livestock

#### Dietary burden calculation

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

A dietary burden calculation made by EFSA in the framework of the Art. 12 evaluation is available and is presented completely in the table below (EFSA 2015).

Spiroxamine is authorised for use on cereals that might be fed to livestock. The median and maximum dietary burdens were therefore calculated for different groups of livestock using the agreed European methodology (EC 1996). For cereal bran, the default processing factor of 8 was included in the calculation in order to consider the potential concentration of residues in these commodities.

Table 7.3‑10: 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:** sum of spiroxamine and all metabolites containing the *tert*-butylcyclohexanone moiety, expressed as spiroxamine (sum of isomers) | | | | |
| Barley & oats grain | 0.6 | Median residue x CF (EFSA 2015) | 0.6 | Median residue x CF (EFSA 2015) |
| Barley & oats straw | 3.96 | Median residue x CF (EFSA 2015) | 4.5 | Highest residue x CF (EFSA 2015) |
| Wheat & rye grain | 0.25 | Median residue x CF (EFSA 2015) | 0.25 | Median residue x CF (EFSA 2015) |
| Wheat & rye bran | 2 | Median residue x 8 x CF (EFSA 2015) | 2 | Median residue x 8 x CF (EFSA 2015) |
| Wheat & rye straw | 4.27 | Median residue x CF (EFSA 2015) | 12.4 | Highest residue x CF (EFSA 2015) |

Table 7.3‑11: Results of the dietary burden calculation – Art 12

| Animal species | Median  dietary burden (mg/kg bw/d) | Maximum dietary burden  (mg/kg bw/d) | Highest contributing commodity | Max dietary burden (mg/kg DM) | Trigger exceeded (Y/N) |
| --- | --- | --- | --- | --- | --- |
| **Risk assessment residue definition:** sum of spiroxamine and all metabolites containing the *tert*-butylcyclohexanone moiety, expressed as spiroxamine (sum of isomers) | | | | | |
| Dairy ruminants | 0.046 | 0.116 | Wheat straw | 3.2 | Y |
| Meat ruminants | 0.122 | 0.326 | Wheat straw | 7.57 | Y |
| Poultry | 0.030 | 0.030 | Barley grain | 0.48 | Y |
| Pigs | 0.022 | 0.022 | Barley grain | 0.55 | Y |

The calculated dietary burdens for all groups of livestock were found to exceed the trigger value of 0.1 mg/kg DM. Further investigation of residues is therefore required in all commodities of animal origin.

#### Livestock feeding studies (KCA 6.4.1-6.4.3)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Tests were performed on dairy cows and hens. No residues were found in meat, fat or milk of cows above the limit of quantification of the analytical method. In the liver, which according to studies of spiroxamine metabolism is the organ most exposed to high levels of residues, concentrations of up to 0.05 mg/kg were found. In the kidney of cows, residues up to 0.045 mg/kg were detected. These data show that cows have very low penetration into internal organs such as the liver and kidneys. No residues above the analytical limit of quantification (0.02 mg/kg for meat, eggs; 0.05 mg/kg for liver and fat) were found in samples from hens. liver and fat).

Conclusion:

No residues of these compounds are expected in foodstuffs of animal origin animal origin. This conclusion is supported by the results of metabolism studies in animals. Consumer exposure to dietary residues will not increase due to the consumption of foodstuffs of animal origin, taking into account data on the intake of residues by animals with feed.

During the peer review under Council Directive 91/414/EEC, the magnitude of Spiroxamine carboxylic acid (M06) residues in ruminants was investigated in a feeding study with lactating cows (DE 2009, EFSA 2010). Four groups of lactating cows, each consisting of three animals were dosed for 28 consecutive days with spiroxamine at levels of 0 (control), 2, 6 and 20 mg/kg in the diet (equivalent to 0, 0.072, 0.218 and 0.727 mg/kg bw/d).

Furthermore, a poultry feeding study was also submitted in the framework of the peer review (DE 2009, EFSA 2010), but EFSA (EFSA 2015) requires a new poultry feeding study.

For a respective overview please refer to the following table:

Table 7.3‑12: Overview of the values derived from livestock feeding studies

| Commodity | Dietary burden | | Results of the livestock feeding study | | | | | | Median residue  (mg/kg)(b) | Highest residue  (mg/kg)(c) | Calculated MRL  (mg/kg) | CF for RA(d) |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Med. (mg/kg bw/d) | Max. (mg/kg bw/d) | Dose Level (mg/kg bw/d)(a) | No | Result for enforcement | | Result for RA | |
| Mean (mg/kg) | Max. (mg/kg) | Mean (mg/kg) | Max. (mg/kg) |
| **EU data (DE 2009, EFSA 2015)** | | | | | | | | | | | | |
| **Residue definition for enforcement:** sum of spiroxamine and spiroxamine carboxylic acid (M06), expressed as spiroxamine (sum of isomers)  **Residue definition for risk assessment:** sum of spiroxamine, spiroxamine carboxylic acid (M06), its glucuronide conjugate (M19) and hydroxy acid spiroxamine (M07), expressed as spiroxamine (sum of isomers) | | | | | | | | | | | | |
| Pig muscle | 0.022 | 0.022 | 0.0727 | 3 | <0.02 | <0.02 | - | - | 0.020 | 0.020 | 0.02\* (tentative)(f) | 1.4 |
| 0.2182 | 3 | <0.02 | 0.021 | - | - |
| 0.7272 | 3 | 0.054 | 0.057 | - | - |
| Pig fat | 0.022 | 0.022 | 0.0727 | 3 | <0.02 | <0.02 | - | - | 0.020 | 0.020 | 0.02\* (tentative)(f) | 1.8 |
| 0.2182 | 3 | <0.02 | <0.02 | - | - |
| 0.7272 | 3 | 0.088 | 0.154 | - | - |
| Pig liver | 0.022 | 0.022 | 0.0727 | 3 | 0.053 | 0.060 | - | - | 0.020 | 0.020 | 0.02\* (tentative)(f) | 2.8 |
| 0.2182 | 3 | 0.16 | 0.177 | - | - |
| 0.7272 | 3 | 0.27 | 0.308 | - | - |
| Pig kidney | 0.022 | 0.022 | 0.0727 | 3 | 0.045 | 0.054 | - | - | 0.020 | 0.020 | 0.02\* (tentative)(f) | 3.8 |
| 0.2182 | 3 | 0.10 | 0.106 | - | - |
| 0.7272 | 3 | 0.22 | 0.306 | - | - |
| Ruminant muscle | 0.121 | 0.326 | 0.0727 | 3 | <0.02 | <0.02 | - | - | 0.020 | 0.029 | 0.03\* (tentative)(f) | 1.4 |
| 0.2182 | 3 | <0.02 | 0.021 | - | - |
| 0.7272 | 3 | 0.054 | 0.057 | - | - |
| Ruminant fat | 0.121 | 0.326 | 0.0727 | 3 | <0.02 | <0.02 | - | - | 0.020 | 0.048 | 0.05 (tentative)(f) | 1.8 |
| 0.2182 | 3 | <0.02 | <0.02 | - | - |
| 0.7272 | 3 | 0.088 | 0.154 | - | - |
| Ruminant liver | 0.121 | 0.326 | 0.0727 | 3 | 0.053 | 0.060 | - | - | 0.100 | 0.205 | 0.3 (tentative)(f) | 2.8 |
| 0.2182 | 3 | 0.16 | 0.177 | - | - |
| 0.7272 | 3 | 0.27 | 0.308 | - | - |
| Ruminant kidney | 0.121 | 0.326 | 0.0727 | 3 | 0.045 | 0.054 | - | - | 0.072 | 0.148 | 0.15 (tentative)(f) | 3.8 |
| 0.2182 | 3 | 0.10 | 0.106 | - | - |
| 0.7272 | 3 | 0.22 | 0.306 | - | - |
| Milk | 0.046 | 0.116 | 0.0727 | 3 | <0.01 | N/A | - | - | 0.01 | 0.011 | 0.015 (tentative)(f) | 1.2 |
| 0.2182 | 3 | 0.014 | N/A | - | - |
| 0.7272 | 3 | 0.035 | N/A | - | - |
|  | | | | | | | | | | | | |
| **No New data** | | | | | | | | | | | | |

N/A: Not applicable – only the mean values are considered for calculating MRLs in milk.

(a): Based on a 550 kg animal consuming 20 kg feed DM/day.

(b): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009).

(c): Highest residue value (tissues, eggs) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009).

(d): The median conversion factor for enforcement to risk assessment.

(e): Mean residue level from 3 cows, 6 sampling days for the low dose group; 3 cows, 7 sampling days for the medium dose group; 3 cows, 11 sampling days for the high dose group.

(f): MRL proposal is tentative because an analytical method for enforcement of spiroxamine in commodities of animal origin is still required.

(\*): Indicates that the MRL is set at the limit of analytical quantification.

Conclusion on feeding studies

The requested uses (or the new mode of calculation) modify the theoretical maximum daily intake for animals, but regarding available feeding data, there is no risk for animal MRL to be exceeded.

However, EFSA (EFSA 2015) considered that the available data are sufficient for deriving MRLs in ruminants and pigs. These MRLs were derived in compliance with the latest recommendations on this matter (FAO 2009). Significant residues in ruminant tissues and milk are expected and MRLs for these commodities can be proposed. Considering however that an analytical method is still required for enforcement of spiroxamine in commodities of animal origin, these MRLs are tentative only. Furthermore, since no feeding study was submitted for poultry, MRLs for poultry matrices could not be proposed.

Based on the available metabolism studies, EFSA also derived conversion factors for enforcement to risk assessment in ruminants and poultry tissues, eggs and milk. Although it is preferable to derive conversion factors for risk assessment from the livestock feeding studies, the conversion factors are considered appropriate in the framework of the Art. 12 review because the contribution from products of animal origin to the acute and chronic exposure is minor.

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

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

SPIROXAMINE

Study not required. A study of the effect of the brewing process on residues has been carried out. No increase in residue levels was found in the processed products. Residues below the limits of quantification of analytical methods were found in all samples tested.

Conclusion:

No aggregation of residues was found under the influence of the processing and domestic food preparation process.

#### Available data for all crops under consideration

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

The effect of processing on the nature of spiroxamine has not been investigated in the framework of the peer review (DE 2009, EFSA 2010). However, a processing study 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) was submitted in the framework of the Art. 12 (ER 2014b). Since the metabolic pattern of spiroxamine was shown to be similar in primary crops and in processed products, it is proposed to apply the same residue definition for enforcement and risk assessment as for primary crops.

A robust processing factor for enforcement and risk assessment could be derived only for peeled banana (DE 2009, EFSA 2010). Further processing studies are not required as they are not expected to affect the outcome of the risk assessment. However, if more robust processing factors were to be required by risk managers, in particular for enforcement purposes, additional processing studies would be needed.

Table 7.3‑13: Overview of the available processing studies

| Processed commodity | Number of studies | Median PF \* | Median CF \*\* | Comments | Reference |
| --- | --- | --- | --- | --- | --- |
| **EU data** | | | | | |
| **Enforcement residue definition:** spiroxamine (sum of isomers)  **Risk assessment residue definition:** sum of spiroxamine and all metabolites containing the N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane moiety, expressed as spiroxamine (sum of isomers) | | | | |  |
| Banana, peeled | 6 | 0.07 | 1.44 |  | DE 2009  EFSA 2015 |
| Cereals | -- | -- | -- | - | -- |
| **No New data** | | | | | |

\* The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.

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

#### Conclusion on processing studies

No further processing studies are required.

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

### 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 7.3.2.2), no study dealing with magnitude of residues in succeeding crops is needed.

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

*The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:*

Metabolism in succeeding crops (wheat, turnips, beets) follows the same pattern as in the primary crops. The product decomposes very quickly in soil without posing a risk to succeeding crops. No residues above the limit of quantification of analytical methods were found in samples taken from succeeding crops.

Conclusion:

There are no restrictions for succeeding crops.

#### Field rotational crop studies (KCA 6.6.2)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

~~Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC~~.

Table 7.3‑14: Summary of available studies in field rotational crops

| Primary crop | Rate (kg a.s./ha)  (GS at application or PHI) | Residue levels in succeeding crops | | | |
| --- | --- | --- | --- | --- | --- |
| Succeeding crop group | Succeeding crop | Sowing intervals  (DAT) | Reference /  Remarks |
| **EU data** | | | | | |
| Bare soil (Sandy loam soil) | 1.58 kg ai/ha (2N) | Leafy vegetables | Swiss chard | 30  161 | DE 2009 |
| Root vegetables | Turnips | 30  161 |  |
| Cereals | Wheat | 30  161 |  |
| Bare soil (sandy loam, greenhouse) | 1.62 kg as/ha (2N) | Leafy vegetables | Swiss chard | 30  193  294 | DE 2009 |
| Root vegetables | Turnips | 30  193  294 |  |
| Cereals | Wheat | 30  193  294 |  |
| Spring barley (DE, UK outdoor, field trial) | 2x 0.75 kg as/ha (2N)  BBCH 31-37  (1st application  58-61  (2nd application) | Leafy vegetables | Spinach | 30 | DE 2009 |
|  | Root vegetables | Turnips | 30 |  |
|  | Cereals | Wheat | 30 |  |
| **No New data** | | | | | |

Conclusion on rotational crops studies

All values were similar or below 0.05 mg/kg. The results of the field studies with rotational crops show that under field conditions no residue in food and feed commodities are to be expected in practice.

### Other / special studies (KCA 6.10, 6.10.1)

No new data is submitted in support of the application for authorization of ULTRACENT 460 EC.

Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

In accordance to the technical guideline SANTE/11956/2016 rev. 9, Appendix II, cereals do not belong to the crops with melliferous capacity.

*~~The following information can be found in the evaluation reports that were compiled for the authorization of INPUT 460 EC (R-61/2011) in Poland:~~*

~~SPIROXAMINE  
Residues, field trials (selected trials for assessment - up to 2000) (Annex IIA, point 6.3, Annex IIIA, point 8.2)~~

|  |  |  |  |
| --- | --- | --- | --- |
| **~~STMR [mg/kg]~~** | **~~0.05~~** | **~~0.10~~** | **~~0.05~~** |
| **~~MRL [mg/kg]~~** | **~~0.05~~** | **~~0.3~~** | **~~0.05~~** |
| **~~Comments~~** | **~~GAP~~**  **~~500 EC, 383 EW~~** | **~~GAP~~**  **~~500 EC, 383 EW~~** | **~~GAP~~**  **~~500 EC, 383 EW~~** |
| **~~Results in accordance with critical points of Good Agricultural Practice [mg/kg]~~** | **~~13 x <0.05; 1x 0.09~~** | **~~12 x <0.05 – 0.3~~** | **~~3: x <0.05~~** |
| **~~Region~~** | **~~North~~** | **~~North~~** | **~~North~~** |
| **~~Crop~~** | **~~Whaet~~** | **~~Barley~~** | ~~Rye~~ |

~~In 2000, an additional four tests were carried out in wheat in the Northern European region and two in Southern Europe. In all samples tested, no residues were found above the analytical method limit of quantification (0.05 mg/kg).~~

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

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

~~However,~~ A new PRIMo version 3.1 is available now, therefore, new consumer risk assessments are provided in the following.

#### Input values for the consumer risk assessment

The residue data of ULTRACENT 460 EC is believed to be identical to the formulation of INPUT 460 EC (authorisation no.: R-61/2011) by Bayer AG. All information on metabolites and residues are believed to be identical to that of INPUT 460 EC for which all data protection has now expired.

For this reason, the applicant fully refers to the data as mentioned in Appendix 1. No new MRLs are required nor proposed.

In order to evaluate the potential acute and chronic exposure to spiroxamine residues through the diet, the Theoretical Maximum Dietary Intakes (TMDI) for chronic and the International Estimated Short-Term Intake (IESTI) for acute calculations were estimated using the actual EFSA PRIMo model 3.1.

The presented current MRLs for spiroxamine are stated in the Regulation (EU) 2016/452. The whole MRL list is presented in Annex II of Regulation (EU) 2016/452.

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

~~The toxicological reference values relevant for the dietary risk assessments are reported in the following:~~

|  |  |  |
| --- | --- | --- |
| ~~ADI~~ | ~~0.025 mg/kg bw/day~~ | ~~Source: EFSA Journal 2010;8(10)1719 SANCO/10889/2011 Rev 3 on 19 May 2020~~ |
| ~~ARfD~~ | ~~0.1 mg/kg bw~~ |

The exposure values calculated were compared to the toxicological reference values for spiroxamine.

The input data (current MRLs) are presented in Appendix 3.

#### Conclusion on consumer risk assessment

ULTRACENT 460 EC is believed to be identical to the formulation of INPUT 460 EC (authorisation no.: R-61/2011) by Bayer AG. All information on metabolites and residues are believed to be identical to that of INPUT 460 EC (authorisation no.: R-61/2011), for which all data protection has now expired.

For this reason, the applicant fully refers to the unprotected data of INPUT 460 EC.

TMDI (chronic) and IESTI (acute) were calculated with PRIMo revision 3.1 (2021/01/06). Taking into consideration the current MRLs.

Extensive calculations sheets are presented in Appendix 3 (A 3.5 TMDI calculations, A 3.7 IESTI calculations – Raw commodities and A 3.8 IESTI calculations – Processed commodities).

Table 7.3‑15: Consumer risk assessment

|  |  |  |
| --- | --- | --- |
| TMDI (% ADI) according to EFSA PRIMo vers. 3.1 | 76 % NL toddler  30 % NL child |  |
| IESTI (% ARfD) according to EFSA PRIMo vers. 3.1 | Unprocessed commodities (children)  0.7 % Wheat  0.3 % Barley  Processed commodities (children)  0.6 % Wheat / milling (flour)  0.3 % Wheat / milling (wholemeal)  0.2 % Barley / cooked  0.1 % Barley / milling (flour) | Unprocessed commodities (adults)  0.4 % Wheat  0.2 % Barley  Processed commodities (adults)  0.4 % Barley / beer  0.2 % Wheat / bread/pizza  0.2 % Wheat / pasta  0.2 % Wheat / bread (wholemeal) |

TMDI and IESTI values were all below the Trigger of 100 % of ADI and ARfD, respectively. . No acute or consumer risk for consumer is expected.

## Combined exposure and risk assessment

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.

However, the product is a mixture of two active substances and for both an acute reference dose has been allocated. Therefore, combined acute exposure can be considered.

### Acute consumer risk assessment from combined exposure

~~In a first step,~~ D~~d~~ose-addition of residues of the active substances prothioconazole and spiroxamine is assumed by making use of the Hazard Index (HI) concept. The Hazard Quotient (HQ) is calculated for the active substances in the product ULTRACENT 460 EC that are acutely toxic by performing deterministic IESTI calculations with the calculation models EFSA PRIMO (rev. 3.1) and dividing the individual exposure levels by the respective ARfD. Addition of the individual HQs irrespective of any considerations on phenomenological effects or mode(s)/mechanisms of action results in the HI. The results of the HQ/HI calculations are summarized in the following table 7.4-2.

In a first step all HQs for Prothioconazole-desthio und TDMs were calculated and summed up. For details please refer to the following table:

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

|  | **IESTI** | | | | **ArfD** | **HQ** | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **children** | | **adults** | |  | **children** | **adults** |
|  | **[µg/kg bw]** | **[mg/kg bw]** | **[µg/kg bw]** | **[mg/kg bw]** | **[mg/kg bw]** |  |  |
| **Wheat** |  |  |  |  |  |  |  |
| Protio-destio | 0.28 | 0.00028 | 0.17 | 0.00017 | 0.01 | 0.028 | 0.017 |
| TA | 15.00 | 0.01500 | 8.70 | 0.00870 | 0.30 | 0.050 | 0.029 |
| TLA | 0.94 | 0.00094 | 0.55 | 0.00055 | 0.30 | 0.003 | 0.002 |
| TAA | 1.70 | 0.00170 | 1.00 | 0.00100 | 1.00 | 0.002 | 0.001 |
| 124 triazole | 0.72 | 0.00072 | 0.42 | 0.00042 | 0.10 | 0.007 | 0.004 |
| **Sum** |  |  |  |  |  | **0.090** | **0.053** |
| **Barley** |  |  |  |  |  |  |  |
| Protio-destio | 0.11 | 0.00011 | 0.10 | 0.00010 | 0.01 | 0.011 | 0.010 |
| TA | 5.80 | 0.00580 | 5.00 | 0.00500 | 0.30 | 0.019 | 0.017 |
| TLA | 0.36 | 0.00036 | 0.31 | 0.00031 | 0.30 | 0.001 | 0.001 |
| TAA | 0.67 | 0.00067 | 0.58 | 0.00058 | 1.00 | 0.001 | 0.001 |
| 124 triazole | 0.28 | 0.00028 | 0.24 | 0.00024 | 0.10 | 0.003 | 0.002 |
| **Sum** |  |  |  |  |  | **0.035** | **0.031** |

Table 7.4‑2: Acute consumer risk assessment from combined exposure – ULTRACENT 460 EC

| Crop | Active Ingredient | HQ\* (based on IESTI children) | HQ\* (based on IESTI adults) |
| --- | --- | --- | --- |
| Wheat | Prothioconazole\*\* | ~~0.140~~  0.090 | ~~0.084~~  0.053 |
| Spiroxamine | 0.007 | 0.004 |
| Cumulative risk wheat (HI) | ~~0.147~~  0.097 | ~~0.088~~  0.057 |
| Barley | Prothioconazole\*\* | ~~0.110~~  0.035 | ~~0.097~~  0.031 |
| Spiroxamine | 0.003 | 0.002 |
| Cumulative risk barley (HI) | ~~0.113~~  0.038 | ~~0.099~~  0.033 |

\*HQ= IESTI / ArfD

\*\* Sum of Prothioconazole-destio, TA, TLA, TAA, 1,2,4-triazole

The Hazard Index for all commodities is < 1. Thus, combined exposure to the active substances in ULTRACENT 460 EC is not expected to present a consumer risk. No further refinement of the assessment is required.

### 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.

## References

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

**Prothioconazole**

EFSA (European Food Safety Authority), 2007: Conclusion regarding the peer review of the pesticide risk assessment of the active substance prothioconazole. EFSA Scientific Report (2007) 106, 1-98, Conclusion on the peer review of prothioconazole

EFSA (European Food Safety Authority), 2014: Reasoned opinion on the review of the existing maximum residue levels (MRLs) for prothioconazole according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2014;12(5):3689, 72 pp. doi:10.2903/j.efsa.2014.3689

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

EFSA (European Food Safety Authority), 2020: Reasoned Opinion on the evaluation of conﬁrmatory data following the Article 12 MRLreview and modiﬁcation of the existing maximum residue levels for Prothioconazole in celeriacs and rapeseeds. EFSA Journal 2020;18(2):5999, 50 pp.

EFSA (European Food Safety Authority), 2023a : Reasoned Opinion on the modiﬁcation of the existing maximum residue levels for Prothioconazole in garlic, onions and shallots. EFSA Journal 2023;21(1):7717, 48 pp.

EFSA (European Food Safety Authority), 2023b : Modiﬁcation of the existing maximum residue levels for prothioconazole in sugar beet and chicory roots. EFSA Journal, 21(8), 1–49. http://doi.org.10.2903/j.efsa.2023.8198.

France, 2014: Evaluation Report prepared under Article 12 of Regulation (EC) No 396/2005. Authorised uses to be considered for the review of the existing MRLs for prothioconazole, January 2014.

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

UK, 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, further revised following discussions at the toxicology and residues expert meetings (Pesticides Peer Review Meetings nos. 162 and 171 respectively) (February 2018).

**Spiroxamine**

DE 1997. Monograph, Spiroxamine, Volume 3, B6; RMS DE [in the context of the application for first inclusion of the as in Annex I to Council Directive 91/414/EEC], 29. January 1997

DE 2009, Spiroxamine. Assessment report – public version – Initial risk assessment provided by the rapporteur Member State Germany for the existing active substance Spiroxamine upon submission in the framework of the renewal of the inclusion of a first group of active substance in Annex I to Council Directive 91/414/EEC in accordance with Commission Regulation (EC) No. 737/2007, Re-Assessment for Annex-I-renewal, Volume 3, Annex B7, September 2009

ER 2014a (RMS: DE), Spiroxamine. Evaluation Report prepared under Article 12.2 of Regulation (EC) No. 396/2005. Authorized uses to be considered for the review of the existing MRLs for Spiroxamine, September 2014.

ER 2014b (RMS: DE), Spiroxamine. Amendment to Additional Evaluation Report prepared under Article 12.2 of Regulation (EC) No 396/2005. Review of the existing MRLs for spiroxamine, October 2014.

EFSA 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance Spiroxamine, EFSA Journal 2010;8(10):1719

EFSA 2010, Revision RMS 2017. Draft Re-Assessment Report, revised – 05 April 2017 and 08 August 2017. Spiroxamine, Vol. 3, Annex B.7. RMS: Germany.

EFSA 2010, LoE, Revision RMS 2017. Draft Re-Assessment Report, revised – 05 April 2017 and 08 August 2017. Spiroxamine, List of Endpoints. RMS: Germany.

EFSA 2015. Reasoned Opinion on the review of the existing maximum residue levels (MRLs) for Spiroxamine according to Article 12 of Regulation (EC) No 396/2005, EFSA Journal 2015; 13(1):3992, 1-48,

1. Lists of data considered in support of the evaluation

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

List of data submitted by the applicant and relied on

| Data point | Author(s) | Year | Title Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
| KCA 6.1/01  *Submitted under KCA 6.10/01* | Peris Mestre D. | 2024 | Determination of Residues of Prothioconazole and its metabolites in Honey after Two Applications of Prothioconazole 250g/L EC to Phacelia tanaceti-folia under Semi-Field Conditions in Northern and Southern Europe in 2023  Agrotox Research Services, S.L, Spain  Report No.: E23-0116  GLP, unpublished | N | CROPNOSYS INDIA PRIVATE LIMITED |
| **KCA 6.1/02** | Jooß S. | 2024 | Storage Stability of Prothioconazole OH-desthio Metabolites (alpha-, 3-, 4-, 5- and 6-hydroxy desthio) and Triazole Derivative Metabolites (TDMs) in Honey under Deep Frozen Conditions  Eurofins Agroscience Services EAG Laboratories GmbH  Report No.: S23-102955  GLP, unpublished | N | CROPNOSYS INDIA PRIVATE LIMITED |
| **KCA 6.10/01** | Peris Mestre D. | 2024 | Determination of Residues of Prothioconazole and its metabolites in Honey after Two Applications of Prothioconazole 250g/L EC to Phacelia tanaceti-folia under Semi-Field Conditions in Northern and Southern Europe in 2023  Agrotox Research Services, S.L, Spain  Report No.: E23-0116  GLP, unpublished  *also referred to under KCA 6.1/01* | N | CROPNOSYS INDIA PRIVATE LIMITED |
|  |  |  |  |  |  |

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

| Data point | Author(s) | Year | Title Company Report No.  Source (where different from company) GLP or GEP status Published or not | Vertebrate study  Y/N | Owner |
| --- | --- | --- | --- | --- | --- |
| **Prothioconazole** | | | | | |
| KCA 6.1 | Heinemann O. | 2001 | 18 months storage stability of residues of JAU 6476 and JAU 6476-Desthio during frozen storage in on wheat matrices  Bayer AG. Leverkusen. Germany  Bayer CropScience.  Report No.: MR-282/00,  GLP, unpublished | N | BAY |
| KCA 6.1 | Freitag T. | 2007 | Storage stability of protliioconazole-desthio in/on canola, spinach, sugar beet, tomato, and pea during freezer storage for 24 months  Bayer CropScience.  Report No.: MR-07/282  GLP, unpublished | N | BAY |
| KCA 6.1 | Murphy I. | 2008 | Stability of 1,2,4-Triazole, Triazolyl alanine, and Triazolyl acetic acid in Various Crop Matrices and Processed Commodities during Frozen Storage  Bayer CropScience.  Report No.: RAJAY006  GLP, unpublished | N | BAY |
| KCA 6.2.1 | Haas M.,  Bornatsch W. | 2000 | Metabolism of JAU6476 in spring wheat (after foliar application)  Bayer AG. Leverkusen. Germany  Report No.: MR-198/99.  GLP, unpublished | N | BAY |
| KCA 6.2.1 | Duah F. K.,  Lopez R.T. | 2004 | The metabolism of [triazole-3,5-14C]-JAU 6476 in wheat  Bayer CropScience LP. Stilwell. KS. USA  Report No.: 200733  GLP, unpublished | N | BAY |
| KCA 6.2.1 | Haas M. | 2001 | Metabolism of JAU 6476 in spring wheat after seed dressing  Bayer AG. Leverkusen. Germany  Report No.: 110881.  GLP, unpublished | N | BAY |
| KCA 6.2.1 | Vogeler K.,  Sakamoto H.  Brauner A. | 1993 | Metabolism of SXX 0665 in summer wheat  Bayer AG. Leverkusen. Germany  Report No.: PF3906.  GLP, unpublished | N | BAY |
| KCA 6.2.1 | Haas M. | 2001 | Metabolism of [phenyl-UL-14C]JAU6476 in peanuts  Bayer Crop Science  Report No.: MR-193/01  GLP, unpublished | N | BAY |
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| KCA 6.2.1 | Beedle E.C.,  Ying S.L. | 2004 | The metabolism of [triazole-UL-14C]JAU6476 in sugar beets  Bayer Crop Science  Report No.: 200467  GLP, unpublished | N | BAY |
| KCA 6.2.2 | *sanitized information* | 2001 | [Phenyl-UL-14C]JAU6476 - Absorption, distribution, excretion, and metabolism in laying hens  XXXX  Report No.: MEF-309/01  GLP, unpublished | Y | BAY |
| KCA 6.2.2 | *sanitized information* | 2003 | [Triazole-UL-14C]JAU6476: Absorption, distribution, excretion, and metabolism in laying hens  XXXX  Report No.: MEF-005/03  GLP, unpublished | Y | BAY |
| KCA 6.2.2 | *sanitized information* | 2010 | [Triazole-UL-14C]Triazole Alanine: Metabolism in the Laying Hen  XXXX  Report No.: MEF-09/839  GLP, unpublished | Y | BAY |
| KCA 6.2.3 | *sanitized information* | 2001 | [Phenyl-UL-14C]JAU6476 - Absorption, distribution, excretion, and metabolism in the lactating goat  XXXX  Report No.: MR-092/01  GLP, unpublished | Y | BAY |
| KCA 6.2.3 | *sanitized information* | 2003 | [Triazole-UL-14C]JAU6476 - Absorption, distribution, excretion, and metabolism in the lactating goat  XXXX  Report No.: MR-448/02  GLP, unpublished | Y | BAY |
| KCA 6.2.3 | *sanitized information* | 2002 | [Phenyl-UL-14C]JAU6476 - Absorption, distribution, excretion, and metabolism in the lactating goat  XXXX  Report No.: MR-091/01  GLP, unpublished | Y | BAY |
| KCA 6.2.3 | *sanitized information* | 2010 | [Triazole-UL-14C]Triazole Alanine: Metabolism in the lactating goat  XXXX  Report No.: MEF-09/699  GLP, unpublished | Y | BAY |
| KCA 6.2.3 | *sanitized information* | 2011 | [Triazole-UL-14C]JAU 6476-desthio: Metabolism in the lactating goat  XXXX  Report No.: MEF-11/011  GLP, unpublished | Y | BAY |
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| KCA 6.3.1/04 | Heinemann O. | 2001 | Determination of residues of JAU 6476-desthio on spring wheat and winter wheat following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, Northern France, and Great Britain  Bayer Crop Science  Report No.:RA-2003/99  GLP, unpublished | N | BAY |
| KCA 6.3.1/05  (KCA 6.3.3) | Heinemann O. | 2001 | 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 Crop Science  Report No.: RA-2104/00  GLP, unpublished | N | BAY |
| KCA 6.3.2/01 | Heinemann O. | 2001 | Determination of residues of JAU 6476-desthio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany  Bayer Crop Science  Report No.: RA-2150/98  GLP, unpublished | N | BAY |
| KCA 6.3.2/02 | Heinemann O., Elke K. | 2001 | Determination of residues of JAU 6476-desthio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, France and Great Britain  Bayer Crop Science  Report No.: RA-2140/98  GLP, unpublished | N | BAY |
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| KCA 6.4.1 | *sanitized information* | 2008 | Prothioconazole - Magnitude of the residue in laying hens  XXXX  Report No.: RAJAL001  GLP, unpublished | Y | BAY |
| KCA 6.4.2 | *sanitized information* | 2001 | JAU 6476-desthio - Dairy cattle feeding study  XXXX  Report No.: MR-535/00  GLP, unpublished | Y | BAY |
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| KCA 6.1  (KIIA 6.2.3) | XXXX | 1995 | KWG 4168: Evaluation of the significance of the goat metabolite KNO 2212  Report No. MR 1017/95; M-010086-01-1; 1797650  GLP, unpublished | Y | BAY |
| KCA 6.1  (KIIA 6.2) | Klein, O., Leicht, W. Diesing, L. | 1998 | Position paper on the metabolic and toxicological aspects of the spiroxamine-N-oxide metabolites Aminodiol, Aminodio-N-oxide, Desethyl- and Despropylaminodiol  Report No. M-008167-02-1; 1849750  No GLP, unpublished | N | BAY |
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| KCA 6.3.1  (KIIA 6.3) | Allmendinger, H. | 1994 | Determination of residues of HWG 1608 & KWG 4168 383 EW in/on winter rye, winter wheat, spring barley, spring wheat, winter barley under actual use conditions in the Federal Republic of Germany and France  Report No. RA-2077/93; M-010788-01-1; 1797662  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Allmendinger, H. | 1995 | Determination of residues of HWG 1608 & KWG 4168 383 EW in/on spring barley, spring wheat, winter rye, winter wheat and winter barley in the Federal Republic of Germany and France  Report No. RA-2004/94; M-010783-01-1; 1797664  GLP, unpublished | N | BAY |
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| KCA 6.3.1  (KIIA 6.3) | Allmendinger, H. | 1995 | Determination of residues of KWG 4168 500 EC in/on spring barley, spring wheat, winter rye, winter wheat and winter barley in the Federal Republic of Germany, Great Britain and France  Report No. RA-2003/94; M-010687-01-1; 1797668  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Allmendinger, H. | 1995 | Determination of residues of KWG 4168 500 EC in/on spring barley in the Federal Republic of Germany  Report No. RA-2148/94; M-010764-01-1; 1797660  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.5.4) | Allmendinger, H. | 1995 | Determination of residues of KWG 4168 500 EC in/on spring barley in the Federal Republic of Germany  Report No. RA-2148/94; M-010764-01-1; 1797674  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Anonymous | 1992 | HWG 1608 & KWG 4168; 417 EC, winter wheat, Germany BBA  Report No. 0640-90; M-010809-01-2; 1797989  No GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Anonymous | 1992 | HWG 1608 & KWG 4168; 417 EC, winter barley, Germany BBA  Report No. 0641-90; M-010806-01-2; 1798005  No GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Freitag, T; Wolter, A. | 2006 | Determination of the residues of JAU 6476, Tebuconazle and KWG 4168 in/on winter wheat after spraying of JAU 6476 & HWG 1608 & KWG 4168 (450 EC) in the field in Northern France, Germany, UK and Sweden  Report No. RA-2574/05; M-271973-01-1, 1797997  GLP, unpublished | N | BAY |
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| KCA 6.3.1  (KIIA 6.3) | Heinemann, O. | 1999 | Determination of the residues of KWG 4168 & ICI A 5504 400 SE in/on spring barley and winter wheat  Following spray application in Germany, Sweden and Great Britain  Report No. RA-2002/97; M-010782-01-1, 1797991  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Heinemann, O. | 1999 | Determination of the residues of KWG 4168 & ICI A 5504 400 SE in/on spring barley and winter wheat  Following spray application in Germany, Sweden and Great Britain  Report No. RA-2002/97; M-010782-01-1, 1798007  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Heinemann, O. | 1999 | Determination of the residues of KWG 4168 500 EC in/on spring and winter barley following spray application in Germany and Great Britain  Report No. RA-2157/98; M-010652-01-2, 1798019  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Heinemann, O. | 1999 | Determination of the residues of KWG 4168 500 EC in/on spring and winter barley following spray application in France  Report No. RA-2158/98; M-010906-01-1, 1798021  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Heinemann, O., Elke, K. | 2001 | Determination of the residues of JAU 6476-desthio & KWG 4168 500 EC in/on spring wheat following spray application of JAU 6476 & KWG 4168 460 EC in Great Britain, France, Germany and Italy  Report No. RA-2092/00; M-087669-01-1, 1797993  GLP, unpublished | N | BAY |
| KCA 6.3.1  (KIIA 6.3) | Heinemann, O., Elke, K. | 2001 | Determination of the residues of JAU 6476-desthio & KWG 4168 500 EC in/on spring barley following spray application of JAU 6476 & KWG 4168 460 EC in Germany, France and Great Britain  Report No. RA-2096/00; M-088981-01-1, 1798009  GLP, unpublished | N | BAY |
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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 |
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| II A, 4.1.2  /01 | Ruengeler, W. | 2001b | JAU 6476 - By-products - HPLC -external standard  Bayer AG,  Report No.: 2005-0011401-01,  Date: 2001-06-20 | N | BCS |
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| II A, 4.2.1.1  /08 | Dubey, L. | 2001 | Independent laboratory validation of bayer methods 00655 and 00655/M001 for the determination of residues of JAU6476-3-hydroksy-detio, JAU6476-4-hydroksy-detio, and JAU6476-detio in/on matreces of animal origin by  HPLC-MS/MS  Battelle, Geneva Research Centres, Carouge/Geneva, Switzerland  Bayer AG,  Report No.: A-14-01-01,  Date: 2001-10-16 | N | BCS |
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| II A, 4.2.4.1  /02 | Maasfeld, W. | 2002b | Method for the determination of JAU 6476-detio in air by HPLCMS/MS  Bayer AG,  Report No.: 00731,  Date: 2002-02-13 | N | BCS |
| II A,4.2.3.1  /01 | Sommer, H. | 1999 | Method for the determination of JAU 6476 and SXX 0665 in test water from aquatic toxicity tests by HPLC [Tox/Ecotox method]  Bayer AG,  Report No.: 00586,  Date:1999-05-28 | N | BCS |
| II A,4.2.3.1  /02 | Sommer, H. | 2001a | Tox/Ecotox method: Method for determination of JAU6476-S-metyl in test water from aquatic toxicity tests by HPLC-UV  Bayer AG,  Report No.: 00699,  Date: 2001-06-21 | N | BCS |
| II A,4.2.3.1  /03 | Sommer, H. | 2001b | Enforcement method 00684 for determination of JAU 6476 and JAU 6476-detio in drinking and surface water by HPLC-MS/MS  Bayer AG,  Report No.: 00684,  Date: 2001-10-23 | N | BCS |
| AII, 4.2.1/06 | Allmendinger, H. | 1998 | Method for the gaschromatographic determination of KWG 4168 residues in grapes (berries), wheat and barley (grain)  Generated by: Bayer AG,  Submitted by: Bayer AG,  Bayer file No.: MR-1090/97  Method No.:00506,  Date: January 07, 1998  GLP | N | BCS |
| AII, 4.2.2  /03 | Sommer, H. | 1995 | Confirmatory procedure for the determination of residues of spiroxamine in/on wheat, barley and grape  Generated by: Bayer AG,  Submitted by: Bayer AG,  Bayer file No.: MR-567/98,  Study No. P62283012,  Date: September 09, 1998  GLP | N | BCS |
| AII; 4.2.5  /05 | Allmendinger, H | 1997 | Method for the gas chromatographic determination of the residue of KWG 4168 carboxylic acid in eggs, modification for eggs.  Generated by: Bayer AG,  Submitted by: Bayer AG,  Bayer file No.: MR-563/93,  Method no.: 00395/M001  Date: September 24, 1997  GLP | N | BCS |
| III A, 5.2 /02 | Nuesslein, F | 2001 | Method 00709 for the determination of residues of KWG 4168 in/on sample materials of wheat and barley  Bayer AG,  Raport N.: 00709,  GLP,  not published | N | BCS |
| IIA, 4.2.2 | Sommer, H | 1994a | Validation of the method 00352 (RA-294/94) for gaschromatographic determination of KWG 4168 and the metabolites KWG 4557 and KWG 4669 in soil  Met96-00164 | N | BCS |
| IIA, 4.2.2 | Sommer, H | 1994b | Validation of the method 00374 (RA-294/94) for gaschromatographic determination of KWG 4168 and the metabolites KWG 4557 and KWG 4669 in soil  Met. 96-00165 | N | BCS |
| IIA, 4.2.1 | König, T | 1993 | Determination of tebuconazole and KWG 4168 in water, modification M001 of method 00252, RA-259/91,  Dr. H Allmendinger, method for gaschromatographic determination of residues of the fungicides Folicur and  KWG 4168in cereals;  RA-575/93.  Met.96-00166 | N | BCS |
| IIA, 4.2.3 | König, T | 1994 | Validation of the analitycal methods for the determination of plant protectants in water; RA-660/93 Folicur and KWG 4168 in cereals;  RA-575/93.  Met.96-00167 | N | BCS |
| IIA, 4.2.4 | Riegner, K | 1995 | Method for the determination of KWG 4168 in air; MR-746/95; Method 00408 Folicur and KWG 4168 in cereals; RA-575/93.  Met.96-00168 | N | BCS |
| AII; 4.2.1 | Allmendinger, H | 1995 | Method for the determination of KWG 4168 carboxylic acid in bovine tissues and milk with LC/MS/MS; MR 683/95;  Method 00355.  Met.96-00161 | N | BCS |
| AII; 4.2.1 | XXXX | 1995a | Method for the gas chromatographic determination of the total residue of the fungicidal active ingredient KWG 4168 in hen tissues and eggs; MR 628/95;  Method 00392.  Met.96-00160 | N | BCS |
| AII; 4.2.1 | Allmendinger, H | 1991 | Method for the gas chromatographic determination of residues of the fungicides Folicur and KWG 4168 in cereals; RA-259/91;  Method 00252.  Met.96-00155 | N | BCS |
| AII; 4.2.1 | Allmendinger, H | 1993 | Method for the gas chromatographic determination of the total residue of the fungicidal active ingriedient KWG 4168 in cereals  RA-310/93;  Method 00312.  Met.96-00156 | N | BCS |
| III A, 8.2.1  /01 | Heinemann, O.;  Elke, K. | 2001 | Determination of residues of JAU 6476-detio & KWG 4168 on spring wheat following spray application of JAU 6476 & KWG 4168 460 EC in Great Britain, France, Germany and Italy  Bayer AG,  Report No.: RA-2092/00,  Report includes Trial Nos.:  R 2000 0434/6  R 2000 0433/8  R 2000 0431/1  R 2000 0430/3  R 2000 0082/0  R 2000 0081/2  Date: 2001-11-28  GLP, unpublished | N | BCS |
| III A, 8.2.2  /01 | Heinemann, O.;  Elke, K. | 2001 | Determination of residues of JAU 6476-detio & KWG 4168 on spring barley following spray application of JAU 6476 & KWG 4168 460 EC in Germany, France and Great Britain  Bayer AG,  Report No.: RA-2096/00,  Report includes Trial Nos.:  R 2000 0428/1  R 2000 0427/3  R 2000 0426/5  R 2000 0425/7  R 2000 0084/7  R 2000 0083/9  Date: 2001-12-07  GLP, unpublished | N | BCS |
| VVII A, 6.0  /01 | Heinemann, O. | 2001a | 18 months storage stability of residues of JAU 6476 and JAU 6476-Detio during frozen storage in/on wheat matrices  Bayer AG,  Report No.: MR-282/00,  Date: 2001-09-13 | N | BCS |
| II A, 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,  Date: 2000-07-10 | N | BCS |
| II A, 6.1.1 /02 | Haas, M. | 2001a | Metabolism of JAU 6476 in spring wheat after seed dressing  Bayer AG,  Report No.: MR-467/99,  Date: 2001-05-10 | N | BCS |
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| 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,  Date: 2001-05-15 | N | BCS |
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| IIA, 6.2.2.1  /01 | XXXX | 2001a | [Phenyl-UL-14C]JAU6476 Absorption, distribution, excretion and metabolism in the lactating goat  XXXX,  Report No.: MR-092/01,  Date: 2001-09-19 | N | BCS |
| IIA, 6.2.2.2  /01 | XXXX | 2002a | [Phenyl-UL-14C]JAU6476-detio Absorption, distribution, excretion, and metabolism in the lactating goat  XXXX,  Report No.: MR-091/01,  Date: 2002-02-28 | N | BCS |
| IIA, 6.2.2.2.1  /01 | XXXX | 2002b | Validation of the residue analytical method for the determination of JAU6476-detio, JAU6476-3-hydroksy-detio and JAU6476-4-hydroksy-detio residues in animal matrices using aged radioactive residues  XXXX,  Report No.: MR-091/01 Part 2,  Date: 2002-02-28 | N | BCS |
| IIA, 6.2.2.3  /01 | XXXX | 2001b | [Phenyl-UL-14C]JAU6476 Absorption, distribution, excretion and metabolism in laying hens  XXXX,  Report No.: MR-309/01,  Date: 2001-10-29 | N | BCS |
| IIA, 6.3.2.1.1  /01 | Heinemann, O. | 2001b | Determination of residues of JAU 6476-Detio on spring wheat following seed treatment of JAU 6476 200 FS in Great Britain, Germany and France  Bayer AG,  Report No.: RA-2010/99,  Report includes Trial Nos.:  R 1999 0173/9  R 1999 0174/7  R 1999 0175/5  R 1999 0176/3  Date: 2001-09-18 | N | BCS |
| IIA, 6.3.2.1.1  /02 | Heinemann, O. | 2001c | Determination of residues of JAU 6476-detio on spring wheat following seed treatment of JAU 6476 200 FS in Germany and France  Bayer AG,  Report No.: RA-2091/00,  Report includes Trial Nos.:  R 2000 0002/2  R 2000 0424/9  Date: 2001-09-28 | N | BCS |
| IIA, 6.3.2.1.1  /03 | Heinemann, O. | 2001d | Determination of residues of JAU 6476-detio in/on spring wheat following seed treatment of JAU 6476 200 FS in Italy and France  Bayer AG,  Report No.: RA-2090/00,  Report includes Trial Nos.:  R 2000 0003/0  R 2000 0423/0  Date: 2001-09-17 | N | BCS |
| IIA, 6.3.2.1.2  /01 | Heinemann, O. | 2001h | Determination of residues of JAU 6476-detio on spring wheat and winter wheat following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, Northern France, and Great Britain  Bayer AG,  Report No.: RA-2003/99,  Report includes Trial Nos.:  R 1999 0023/6  R 1999 0025/2  R 1999 0026/0  R 1999 0027/9  R 1999 0266/2  Date: 2001-10-04 | N | BCS |
| IIA, 6.3.2.1.2  /02 | Heinemann, O. | 2001i | Determination of residues of JAU 6476-detio 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  R 2000 0475/3  R 2000 0476/1  Date: 2001-11-29 | N | BCS |
| IIA, 6.3.2.1.2  /03 | Heinemann, O.;  Elke, K. | 2001c | Determination of residues of JAU6476-Detio on winter wheat following seed treatmen of JAU6476 200 FS and spray application of JAU6476 250 EC in France, Spain and Italy  Bayer AG,  Report No.: RA-2149/98,  Report includes Trial Nos.:  R 1998 1314/1  R 1998 1586/1  R 1998 1588/8  R 1998 1589/6  R 1998 1725/2  Date: 2001-11-13 | N | BCS |
| IIA, 6.3.2.1.2  /04 | Heinemann, O. | 2001  l | Determination of residues of JAU 6476-detio 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  Date: 2001-12-06 | N | BCS |
| IIA, 6.3.2.1.3  /01 | Heinemann, O. | 2001e | Determination of residues of JAU 6476-detio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany  Bayer AG,  Report No.: RA-2150/98,  Date: 2001-09-24 | N | BCS |
| IIA, 6.3.2.1.3  /02 | Heinemann, O.;  Elke, K. | 2001a | Determintion of residues of JAU 6476-detio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, France and Great Britain  Bayer AG,  Report No.: RA-2140/98,  Report includes Trial Nos.:  R 1998 1582/9  R 1998 1581/0  R 1998 1580/2  R 1998 1247/1  Date: 2001-09-24 | N | BCS |
| IIA, 6.3.2.1.3  /03 | Heinemann, O. | 2001j | Determination of residues of JAU 6476-detio on spring barley after spray application of JAU 6476 250 EC in Sweden, Germany, Nothern 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  Date: 2001-11-21 | N | BCS |
| IIA, 6.3.2.1.3  /04 | Heinemann, O. | 2001f | Determination of residues of JAU 6476-detio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Southern France  Bayer AG,  Report No.: RA-2079/98,  Report includes Trial Nos.:  R 1998 1249/8  Date: 2001-09-27 | N | BCS |
| IIA, 6.3.2.1.3  /05 | Heinemann, O.;  Elke, K. | 2001b | Determination of residues of JAU 6476-detio 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  Date: 2001-09-24 | N | BCS |
| IIA, 6.3.2.1.3  /06 | Heinemann, O. | 2001  k | Determination of residues of JAU 6476-detio 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  Date: 2001-11-21 | N | BCS |
| IIA, 6.3.2.2  /01 | Heinemann, O. | 2002a | Determination of residues of JAU 6476-detio 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  Date: 2002-01-14 | N | BCS |
| IIA, 6.3.2.2  /02 | Heinemann, O. | 2001g | Determination of residues of JAU 6476-detio 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  Date: 2001-09-27 | N | BCS |
| IIA, 6.3.2.2  /03 | Heinemann, O. | 2002c | Determination of residues of JAU 6476-detio 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  Date: 2002-02-08 | N | BCS |
| IIA, 6.3.2.2  /04 | Heinemann, O. | 2002b | Determination of residues of JAU 6476-detio 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  Date: 2002-01-28 | N | BCS |
| II A, 6.4 /01 | XXXX | 2001 | JAU 6476-detio - Dairy cattle feeding study  XXXX,  Report No.: MR-535/00,  Report includes Trial Nos.:  P 673003007  Date: 2001-10-15 | N | BCS |
| II A, 6.5 /01 | Gilges, M. | 2001 | Hydrolysis of JAU 6476 under conditions of processing  Bayer AG,  Report No.: MR-166/00,  Date: 2001-01-29 | N | BCS |
| II A, 6.6 /01 | Haas, M. | 2001c | Confined rotational crop study with JAU6476  Bayer AG,  Report No.: MR-159/00,  Date: 2001-05-14 | N | BCS |
| II A, 6.1 | Reiner, H.,  Vogeler, K.,  Braunem, A | 1995 | Metabolism of KWG 4168 in Spring Wheat.  RIP96-00170 | N | BCS |
| II A, 6.2 | XXXX | 1995 | KWG 4168: Evaluation of the significance of the goat metabolite KNO 2212.  RIP96-00179 | N | BCS |
| II A, 6.2 | XXXX | 1995 | [Cyclohexyl-1-14C] KWG 4168: Absorption, Distribution, Excretion and Metabolism in Laying Hens  RIP96-00177 | N | BCS |
| II A, 6.2 | Reiner, H. | 1995 | Metabolism of KWG 4168 in Spring Wheat; validation of the residue method for the total KWG 4168 residue in Wheat using radioactive residues  RIP96-00454 | N | BCS |
| II A, 6.2 | XXXX | 1995 | [Cyclohexyl-1-14C] KWG 4168: Absorrption, Distribution, Excretion and Metabolism in Laying Hens  RIP96-00178 | N | BCS |
| II A, 6.3 | Allmendinger, H | 1994 | Determination of Storage Stability of KWG 4168 in/on Barley  RIP96-00185 | N | BCS |
| II A, 6.3 | Allmendinger, H | 1994 | Determination of residues of KWG4168 500 EC in/on winter rye, winter wheat, spring barley, spring wheat and winter barley under actual use conditions in England, France, and Germany  RIP96-00180 | N | BCS |
| II A, 6.3 | Allmendinger, H | 1994 | Determination of residues of HWG4168 and KWG 4168 383 EW in/on winter rye, winter wheat, spring barley, spring wheat and winter barley under actual use conditions in the Federal Republic of Germany and France  RIP96-00181 | N | BCS |
| II A, 6.3 | Allmendinger, H | 1995 | Determination of residues of KWG4168 500 EC in/on spring barley, spring wheat, winter rye, winter wheat winter barley in the Federal Republic of Germany, Great Britain and France  RIP96-00182 | N | BCS |
| II A, 6.3 | Allmendinger, H | 1995 | Determination of residues of HWG4168 and KWG 4168 383 EW in/on spring barley, spring wheat, winter rye, winter wheat winter barley in in the Federal Republic of Germany and Germany and France  RIP96-00184 | N | BCS |
| II A, 6.2 | XXXX | 1995 | KWG4168 – Laying Hen Feeding Study.  RIP96-00175 | N | BCS |
| II A, 6.2 | XXXX | 1995 | KWG4168 – Cattle Hen Feeding Study.  RIP96-00175 | N | BCS |
| II A, 6.3 | Allmendinger,  H., Walz-Tylla | 1995 | 1995 Determination of residues of KWG4168 500 EC in/on spring barley in the Federal Republic of Germany  RIP96-00183 | N | BCS |
| II A, 6.6 | Sommer, H. | 1995 | Field Rotational Crop Studies with KWG 4  RIP96-00187 | N | BCS |
| II A, 6.6 | Vogeler, K. | 1994 | [Cyclohexyl-1-14C] KWG 4168 residues in Following Crops  RIP96-00187 | N | BCS |

1. Detailed evaluation of the additional studies relied upon
   1. Prothioconazole
      1. Stability of residues

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Stability of residues during storage of samples

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Storage stability of residues in plant products

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Storage stability of residues in animal products

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC~~.

KCA 6.1/01 Peris Mestre (2024)\_ E23-0116

|  |  |
| --- | --- |
| Reference: | KCA 6.1/01  *Submitted under KCA 6.10/01* |
| Report | Determination of Residues of Prothioconazole and its metabolites in Honey after Two Applications of Prothioconazole 250g/L EC to *Phacelia tanacetifolia* under Semi-Field Conditions in Northern and Southern Europe in 2023  Peris Mestre D. (2024)  Report No.: E23-0116 |
| Guideline(s): | Yes  SANTE/2020/12830 Rev. 2  OECD ENV/JM/MONO/(2007)17  OECD 506 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

The aim of the study phase was to determine the residue levels of prothioconazole and its metabolite prothioconazole-desthio in honey specimens collected in the field (biological) phase of the study according to SANTE/2020/12830 Rev. 2 and to obtain data about the storage stability of prothioconazole and its metabolite prothioconazole-desthio in honey at temperature ≤-18 °C over a six months storage period.

Materials and methods

The storage stability of prothioconazole and prothioconazole-desthio under frozen conditions (T ≤ -18°C) in honey over a 6 months storage period (181 days) was investigated according to guideline SANTE/2020/12830 rev.2 and guideline OECD 506.

Each storage stability sample was prepared at Renolab Test Site analytical laboratory by fortification of the honey blank matrix with single analyte reference item at 0.1 mg/kg (10 x LOQ level).

For each analyte four untreated matrix samplings (2 analyse and 2 back-up) were weighed into 50-mL PE centrifuge tubes, spiked at 10 x LOQ level and placed in a freezer at temperature ≤ -18°C for the specified storage period.

The two analyse storage samples were extracted and analysed after 6 months in a single analytical session, including the analysis of 4 freshly spiked single analyte samples (2 for each analyte, time zero storage samples), 1 untreated honey blank matrix, 2 procedural recoveries at LOQ (0.01 mg/kg of both analytes), two procedural recoveries at 10xLOQ (0.1 mg/kg of both analytes).

Recovery samples were spiked with both analytes since the analysis method was validated for the concurrent determination of both analytes.

Further information on the analytical methods, can be found in Part B Section 5.

Results and discussions

The results of the prothioconazole and prothioconazole-desthio storage stability in honey (primary transition) are summarized in the following tables.

Table A 1: Summary of concurrent recoveries of prothioconazole from honey.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Sample  type | Sample  code | Fortification  date | Extraction &  analysis date | Storage period  (days) | Analyte found  (mg/kg) | Analyte. added  (mg/kg) | Recovery  (%) |
| Control | 9123 | NA | 21/02/24 | NA | n.d. | NA | NA |
| Stored  T0 | 9133 | 21/02/24 | 21/02/24 | 0 | 0.1019 | 0.1011 | 100.8 |
| 9134 | 21/02/24 | 21/02/24 | 0 | 0.1062 | 0.1011 | 105.0 |
| **Mean recovery** | | | | | | | **102.9** |
| **RSD %** | | | | | | | **2.9** |
| Stored  6 months | 9137 | 24/08/23 | 21/02/24 | 181 | 0.07601 | 0.09931 | 76.5 |
| 9138 | 24/08/23 | 21/02/24 | 181 | 0.07755 | 0.09931 | 78.1 |
| **Mean recovery** | | | | | | | **77.3** |
| **RSD %** | | | | | | | **1.5** |

NA = Not applicable;

n.d. = not detectable (< 0.0025 mg/kg)

Table A 2: Summary of concurrent recoveries of prothioconazole-desthio from honey.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Sample  type | Sample  code | Fortification  date | Extraction &  analysis date | Storage period  (days) | Analyte found  (mg/kg) | Analyte. added  (mg/kg) | Recovery  (%) |
| Control | 9123 | NA | 21/02/24 | NA | n.d. | NA | NA |
| Stored  T0 | 9141 | 21/02/24 | 21/02/24 | 0 | 0.1121 | 0.1038 | 108.0 |
| 9142 | 21/02/24 | 21/02/24 | 0 | 0.1090 | 0.1038 | 105.0 |
| **Mean recovery** | | | | | | | **106.5** |
| **RSD %** | | | | | | | **2.0** |
| Stored  6 months | 9145 | 24/08/23 | 21/02/24 | 181 | 0.09219 | 0.10125 | 91.0 |
| 9146 | 24/08/23 | 21/02/24 | 181 | 0.08779 | 0.10125 | 86.7 |
| **Mean recovery** | | | | | | | **88.9** |
| **RSD %** | | | | | | | **3.4** |

NA = Not applicable;

n.d. = not detectable (< 0.0025 mg/kg)

Conclusion

According to guideline OECD 506 prothioconazole and prothioconazole-desthio can be considered stable in honey over a period of 6 months (181 days) under frozen conditions (T ≤ -18°C), as no significant degradation (≥ 30%) occurred.

For both analytes the procedural recoveries at each fortification level performed concurrently with the analysis of stored samples was in agreement with the requirements of SANTE/2020/12830 rev.2.

KCA 6.1/02 Jooß (2024)\_S23-102955

|  |  |
| --- | --- |
| Reference: | KCA 6.1/02 |
| Report | Storage Stability of Prothioconazole OH-desthio Metabolites (alpha-, 3-, 4-, 5- and 6 hydroxy desthio) and Triazole Derivative Metabolites (TDMs) in Honey under Deep Frozen Conditions  Jooß S. (2024)  Report No.: S23-102955 |
| Guideline(s): | Yes  OECD 506, 2007 (OECD guideline for the testing of chemicals / Stability of pesticide residues in stored commodities)  ENV/JM/MONO(2007)17 (OECD guidance document on pesticide residue analytical methods)  EU Guidance Document SANTE/2020/12830 rev. 2 (2023) Pesticide Analytical Methods for Risk Assessment and Post-approval Control and Monitoring Purposes |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

Materials and methods

The purpose of this study was to obtain data about the storage stability of the prothioconazole hydroxy-desthio metabolites (alpha-, 3-, 4-, 5- and 6-hydroxy desthio) and the triazole Derivative Metabolites (TDMs) 1,2,4-triazole (T), triazole acetic acid (TAA), triazole lactic acid (TLA) and triazole alanine (TA) in honey under deep frozen conditions in the dark over a storage period up to 6 months in accordance to OECD Guideline 506.

Prothioconazole-hydroxy desthio metabolites in Honey (Test Method 1)

Samples of honey were extracted with acetonitrile/water (4/1, v/v). An aliquot of the raw extract was concentrated to an aqueous remainder which was hydrolysed by heating with 5N hydrochloric acid. After neutralization the extracts were diluted with aqueous ammonium formate solution. Quantification was performed by use of LC-MS/MS detection.

1,2,4-T, TAA, TLA and TA in Honey (Test Method 2)

For 1,2,4-triazole (T), triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA) homogenized samples of honey were extracted with methanol/water (4/1, v/v). Clean-up of the extract was performed by dispersive SPE with C18 material. Quantification was performed by use of LC-DMS/MS/MS detection with isotopically labelled internal standard(s).

Further information on the analytical methods, can be found in Part B Section 5.

Results and discussions

The maximum storage interval of final sample extracts at typically 1 °C to 10 °C from extraction until injection to LC MS/MS was 8 days for the PTZ hydroxy-desthio metabolites and 3 days for the TDMs, respectively.

The stability of the analyte(s) in the final extracts of honey upon storage at typically 1 °C to 10 °C for 11 days (PTZ hydroxy-desthio metabolites, Test Method 1) was demonstrated in study S22-05884 [1].

For the TDMs (Test Method 2), isotopically-labelled internal standards were used for quantification and were added at the end of the sample extraction procedure. As the internal standards are considered to show the same degradation behaviour as the analytes themselves, prolonged storage is possible.

Table A 3: Summary of concurrent recoveries of prothioconazole-hydroxy desthio metabolites from honey.

| **Matrix** | **Fortification level  (mg/kg)** | **Recovery (%)** | | | **Mean   (%)** | **Rel. Std. Dev.  (%)** | **Overall Mean  (%)** | **Overall Rel. Std. Dev. (%)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Day 0  Testing\* | 1 Month  Testing | 3 Months  Testing |
| **Prothioconazole-3-hydroxy-desthio** | | | | | | | | |
| Honey | 0.01 | 109, 111, 104 | - | - | 108 | 3.6 | 104 | 5.2 |
| 0.1 | 104, 96.5, 98.5 | 108, 101 | 110, 97.0 | 102 | 5.2 |
| **Prothioconazole-4-hydroxy-desthio** | | | | | | | | |
| Honey | 0.01 | 119, 117, 97.3 | - | - | 111 | 11 | 103 | 9.5 |
| 0.1 | 106, 95.0, 96.0 | 90.0, 98.5 | 108, 98.0 | 98.8 | 6.4 |
| **Prothioconazole-5-hydroxy-desthio** | | | | | | | | |
| Honey | 0.01 | 110, 105, 105 | - | - | 107 | 3.0 | 101 | 5.5 |
| 0.1 | 104, 94.0, 95.0 | 93.5, 101 | 102, 97.5 | 98.0 | 4.2 |
| **Prothioconazole-6-hydroxy-desthio** | | | | | | | | |
| Honey | 0.01 | 91.5, 99.5, 83.0 | - | - | 91.3 | 9.0 | 89.5 | 7.0 |
| 0.1 | 90.5, 82.0, 80.5 | 87.5, 96.0 | 94.0, 90.5 | 88.7 | 6.5 |
| **Prothioconazole-α-hydroxy-desthio** | | | | | | | | |
| Honey | 0.01 | 110, 111, 102 | - | - | 108 | 4.9 | 110 | 6.7 |
| 0.1 | 116, 115, 113 | 104, 96.0 | 120, 113 | 111 | 7.4 |

Table A 4: Summary of concurrent recoveries of 1,2,4-T, TAA, TLA and TA metabolites from honey.

| **Matrix** | **Fortification level  (mg/kg)** | **Recovery (%)** | | | **Mean    (%)** | | **Rel. Std. Dev.  (%)** | **Overall Mean  (%)** | **Overall Rel. Std. Dev. (%)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Day 0**  **Testing** | **1 Month**  **Testing** | **3 Months**  **Testing** |
| **1,2,4-Triazole** | | | | | | | | | |
| Honey | 0.01 | 90.1, 71.2, 67.3 | - | - | 76.1 | 16 | | 82.7 | 10 |
| 0.1 | 84.4, 86.2, 87.9 | 78.9, 80.5 | 86.1, 94.3 | 85.5 | 5.9 | |
| **Triazole Acetic Acid** | | | | | | | | | |
| Honey | 0.01 | 65.1, 61.4, 60.9 | - | - | 62.5 | 3.7 | | 80.2 | 17 |
| 0.1 | 80.4, 81.4, 84.7 | 86.2, 94.8 | 87.2, 100 | 87.8 | 8.1 | |
| **Triazole Lactic Acid** | | | | | | | | | |
| Honey | 0.01 | 65.3, 58.5, 63.3 | - | - | 62.4 | 5.6 | | 101 | 5.5 |
| 0.1 | 76.6, 80.3, 85.2 | 87.5, 92.9 | 104, 108 | 90.6 | 13 | |
| **Triazole Alanine** | | | | | | | | | |
| Honey | 0.01 | 97.4, 83.3, 86.0 | - | - | 88.9 | 8.4 | | 87.2 | 5.0 |
| 0.1 | 85.6, 87.7, 85.4 | 81.1 (86.0), 89.2 (94.1) | 87.9 (92.7), 88.4 (93.2) | 86.5 | 3.2 | |

Conclusion

For all combinations of analytes and matrices the average amount of each analyte recovered relative to the initial mean recovery at day 0 and to the nominal fortification level was ≥ 70 % at any testing interval.

The study is deemed sufficient for assessing the stability of PTZ hydroxy-desthio metabolites (alpha-, 3-, 4-, 5- and 6-hydroxy desthio) and the Triazole Derivative Metabolites (TDMs) 1,2,4-triazole (T), triazole acetic acid (TAA), triazole lactic acid (TLA) and triazole alanine (TA) in homogenates of honey upon storage at ≤ 18 °C for 6 months.

* + 1. Nature of residues in plants, livestock and processed commodities

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Nature of residue in plants

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residue in primary crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residue in rotational crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residues in processed commodities

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Nature of residues in livestock

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in plants

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Cereals

No new data submitted with this submission. In general only new data should be presented and summarized in Appendix 2. However, after request and for the sake of completeness a short summary of unprotected data (RAR 2018, DAR (UK 2004)) are presented in the following.

**Please note** that the “KCA” numbering corresponds to the numbering in the RAR 2018. No K-docs are submitted again with this submission.

**Please note**, that the exact selection of values that are relevant according to EFSA 2020 or France 2014 is not comprehensible due to the lack of the respective Evaluation Report (France 2014).

RAR 2018 (CA B.7, p. 85): *“The applicant has referenced the data considered in the DAR; however it should be noted that the proposed GAPs considered for the original DAR are different to the proposed GAPs for the RAR and therefore whilst the trials considered in the DAR are presented in Table 7.3-8 to 7.3-12 those selected as pertinent to the GAP for this assessment will differ from those selected in EFSA, 2007.*

*Note: The residues values selected for use in dietary risk assessment and MRL calculations are based on a PHI of 35 days. It is noted that for many of the trials harvest is not occurring until 50-60 days post treatment. Several of the trials have 3 applications which can be considered acceptable for determining grain residues as these are <LOQ, but would be considered overdosed for the residues in straw. Trials containing both seed treatment and foliar applications can be considered acceptable for grain residues but are similarly considered overdosed for addressing residues in straw from the seed treatment use.”*

Table A 2: Comparison of intended and critical EU GAPs - Prothioconazole

| Type of GAP | Number of  applications | Application rate  per treatment  (kg as/ha) | Interval between  application | Growth stage at  last application | PHI (days) |
| --- | --- | --- | --- | --- | --- |
| Wheat |  |  |  |  |  |
| cGAP EU (DAR (UK 2004)) | 2 | 0.200 | 14 | BBCH 69 | 35 |
| cGAP EU (RAR 2018) | 2 | 0.1875 | 14 | BBCH 69 | n/a |
| cGAP EU (Art. 12 (EFSA 2014),  France 2014) | 3 | 0.200 | 14 | BBCH 69 | 35 |
| Intended cGAP (use 1-3) | 1 | 0.160 | -- | BBCH 59 | 35 |
| Barley |  |  |  |  |  |
| cGAP EU (DAR (UK 2004)) | 2 | 0.200 | 14 | BBCH 61 | 35 |
| cGAP EU (RAR 2018) | 2 | 0.150 | 14 | BBCH 61 | n/a |
| cGAP EU (Art. 12 (EFSA 2014),  France 2014) | 2 | 0.200 | 14 | BBCH 69 | 35 |
| Intended cGAP (use 4) | 1 | 0.160 | -- | BBCH 51 | 35 |

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

The following trials were evaluated in the first approval:

Previous evaluation In DAR Addendum (2006) for original approval

Report: KCA 6.3.1/01: Heinemann, O.; 2001

Title: Determination of residues of JAU 6476-Desthio on spring wheat following seed treat ment of JAU 6476 200 FS in Great Britain, Germany and France

Report No.: RA-2010/99

Guidelines: Not specified

Deviation No

GLP: Yes

and

Report: KCA 6.3.1/02; Heinemann, O.; 2001: Determination of residues of JAU 6476-desthio on spring wheat following seed treatment of JAU 6476 200 FS in Germany and France, Bayer AG, Leverkusen, Germany , Report No.: RA-2091/00

Guidelines: Not specified

Deviation No

GLP: Yes

and

Report: KCA 6.3.1/04; Heinemann, O.; 2001: Determination of residues of JAU 6476-desthio on spring wheat and winter wheat following seed treatment of JAU 6476 200 FS and spray appli cation of JAU 6476 250 EC in Germany, Northern France, and Great Britain, Report No.: RA- 2003/99

Guidelines: Not specified

Deviation No

GLP: Yes

and

Report: KCA 6.3.1/05; Heinemann, O.; 2001; 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, Report No.: RA-2104/00

Guidelines: Not specified

Deviation No

GLP: Yes

and

Report: KCA 6.3.2/01; Heinemann, O.; 2001: Determination of residues of JAU 6476-desthio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, Report No.: RA-2150/98

Guidelines: Not specified

Deviation No

GLP: Yes

and

Report: KCA 6.3.2/02; Heinemann, O.; Elke, K.; 2001: Determination of residues of JAU 6476- desthio on spring barley following seed treatment of JAU 6476 200 FS and spray application of JAU 6476 250 EC in Germany, France and Great Britain, Report No.: RA-2140/98

Guidelines: Not specified

Deviation No

GLP: Yes

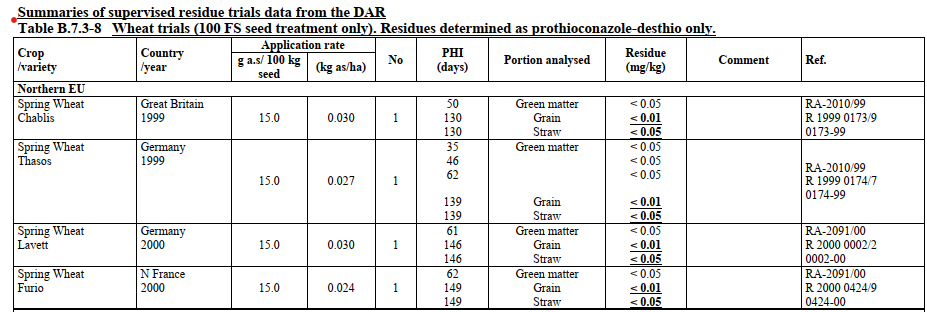
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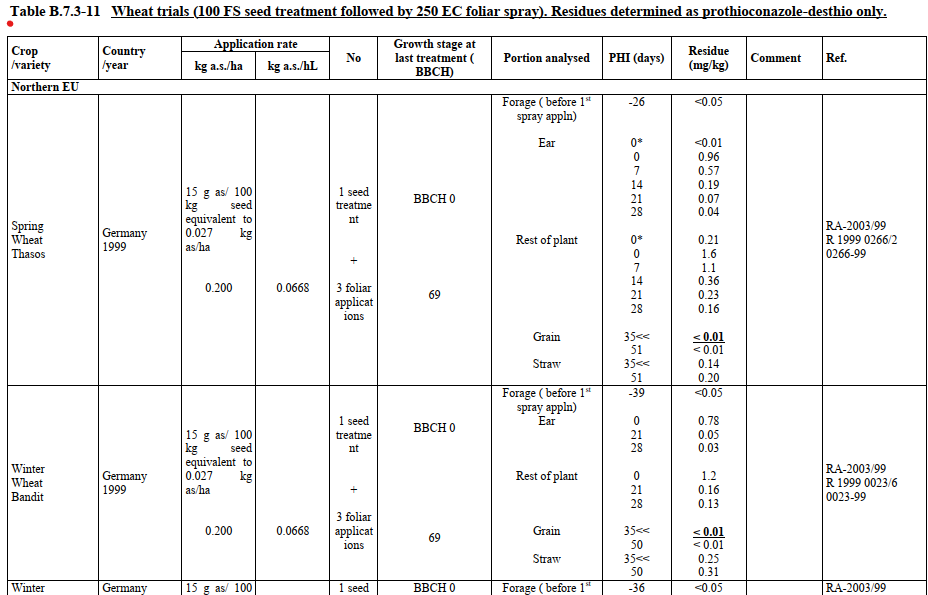
Report: KCA 6.3.2/03; Heinemann, O.; 2001: Determination of residues of JAU 6476-desthio on spring barley after spray application of JAU 6476 250 EC in Sweden, Germany, Northern France and Great Britain, Report No.: RA-2101/00

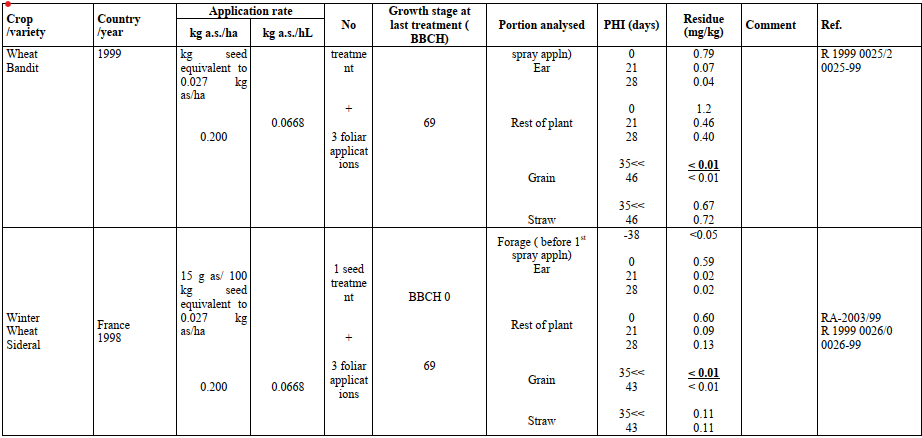
Guidelines: Not specified

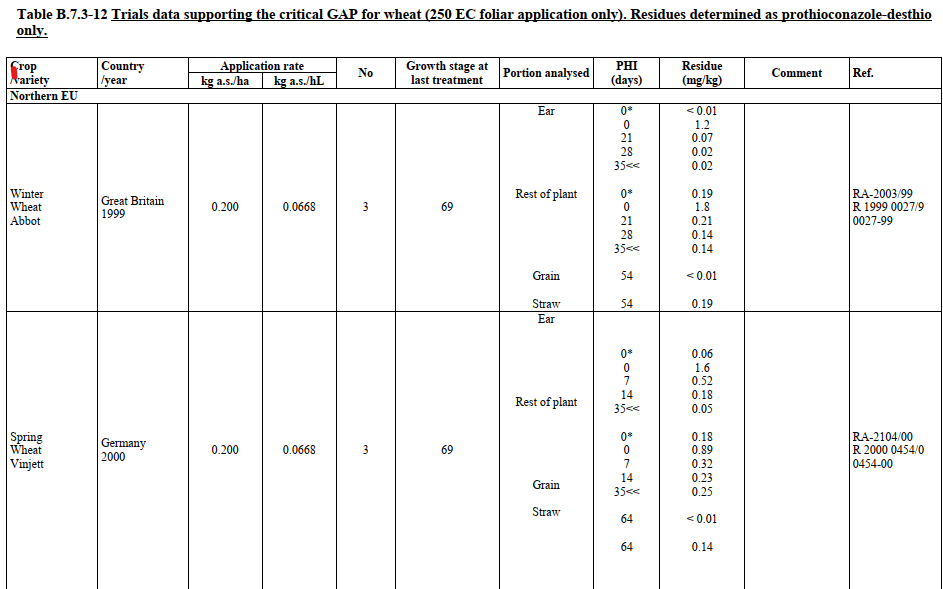
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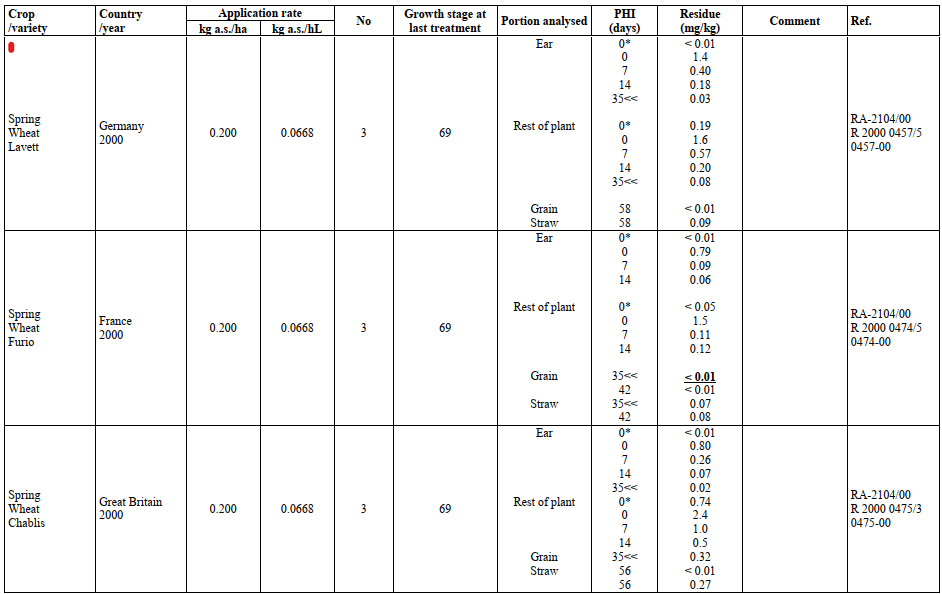
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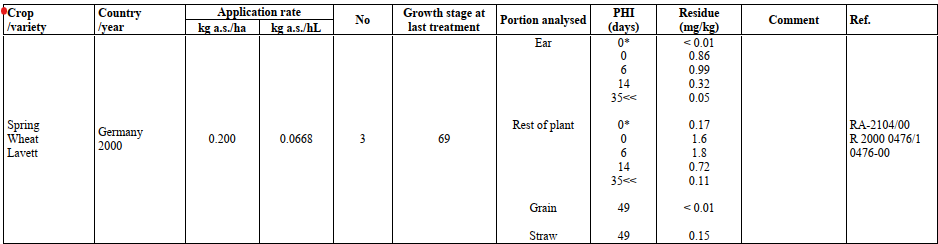


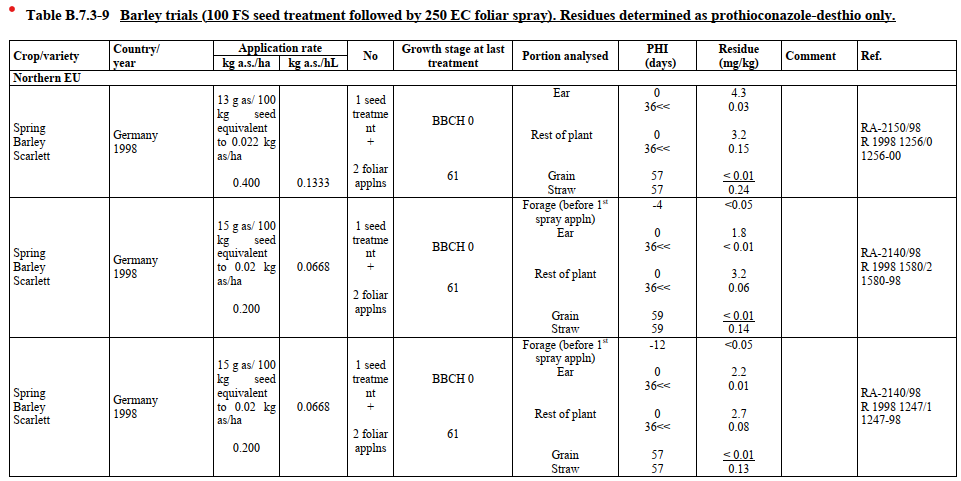


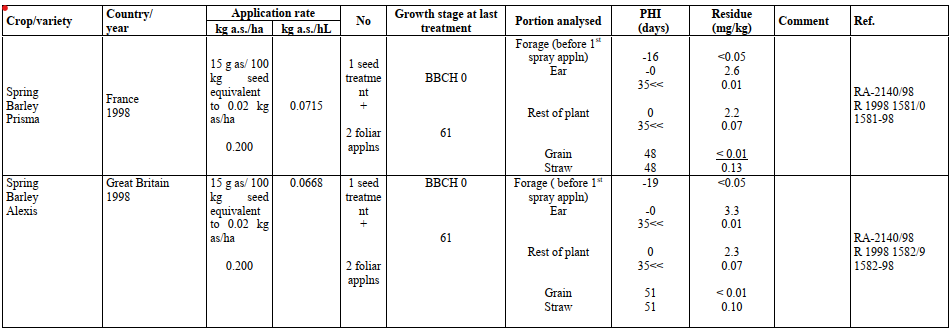


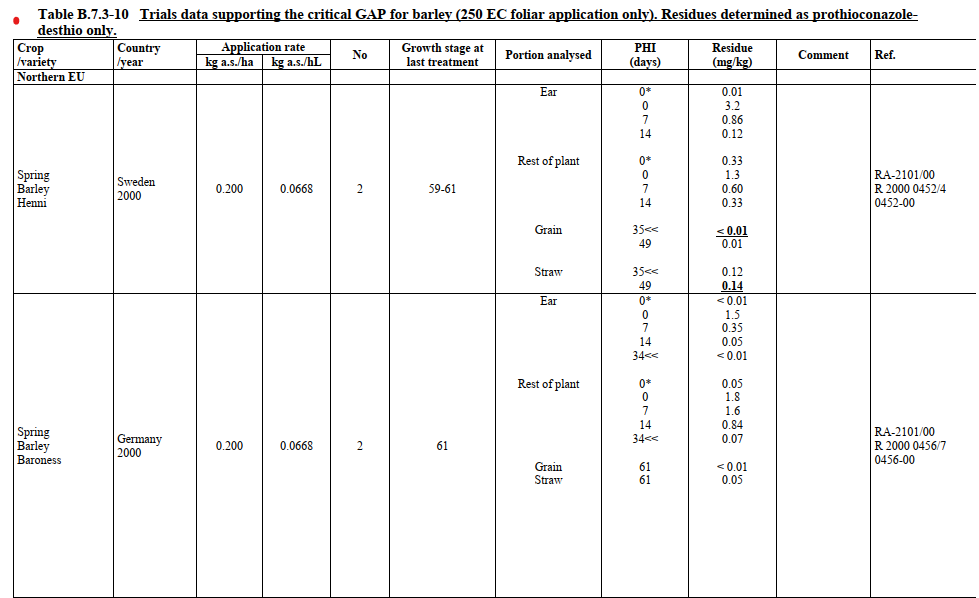


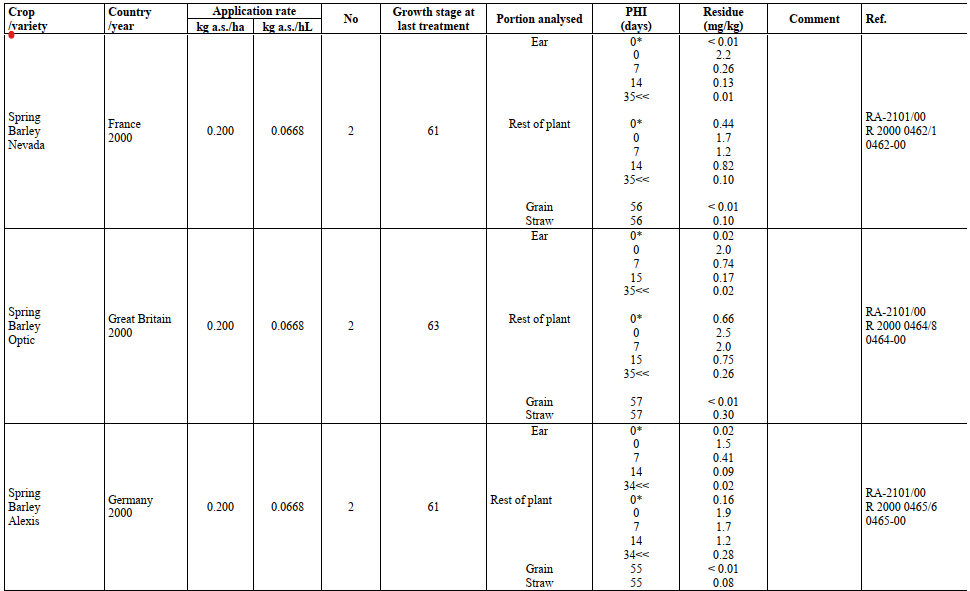












* + 1. Magnitude of residues in livestock

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Livestock feeding studies

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Distribution of the residue in peel/pulp

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Processing studies on a core set of representative processes

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in representative succeeding crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Other/Special Studies

~~No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.~~

* + - 1. KCA 6.10/01 Peris Mestre (2024)\_ E23-0116

|  |  |
| --- | --- |
| Reference: | KCA 6.10/01 (also referred to under KCA 6.1/01) |
| Report | Determination of Residues of Prothioconazole and its metabolites in Honey after Two Applications of Prothioconazole 250g/L EC to *Phacelia tanacetifolia* under Semi-Field Conditions in Northern and Southern Europe in 2023  Peris Mestre D. (2024)  Report No.: E23-0116 |
| Guideline(s): | Yes  SANTE/11956/2016 rev.9  SANTE/2020/12830, Rev.2  OECD 509 |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | Yes |

**Executive summary**

The present study was carried out to determine the residues of prothioconazole (and its metabolites) in honey after two applications of the test item Prothioconazole 250 EC in order to allow a dietary risk assessment and to establish scientifically-based maximum residue limits (MRLs). Honey was collected from combs of hives foraging on *Phacelia tanacetifolia* plants during full flowering (BBCH 63 - 65) under semi-field study conditions.

Trials were performed at four *Phacelia tanacetifolia* field sites located in Lliria (Spain), Calatorao (Spain), Langenfeld (Germany) and Kinrooi (Belgium) according to the OECD Good Laboratory Practices principles.

Each trial site consisted of a control plot and a treated plot.

The test item Prothioconazole 250 EC treatment group (T), which was applied in two application events at a nominal rate of 0.8 L/ha of Prothioconazole 250 EC at fourteen days interval and consistent with Good Agricultural Practice.

Samples were analysed for residues of prothioconazole and prothioconazole-desthio metabolite by Renolab S.r.l. Residues of prothioconazole metabolites (triazole derivative metabolites (TDMs) 1,2,4 triazole (T), triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA) as well as for residues of the prothioconazole-hydroxy desthio (PTZ-hydroxy desthio) metabolites M14, M15, M16, M17 and M18) were analysed by Eurofins Agroscience Services – EAG Laboratories GmbH.

Residues of prothioconazole and prothioconazole-desthio metabolite were analysed by LC-MS/MS.

Residues of prothioconazole-hydroxy desthio metabolites were analysed by LC-MS/MS and residues of triazole derivative metabolites (TDMs) were analysed by LC-DMS/MS/MS.

Further information on the analytical methods, can be found in Part B Section 5.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  |  |
| PPP (product name/code): | Prothioconazole 250 EC | Formulation type: | EC |
| Active substance 1: | Prothioconazole | Conc. of as 1: | 250 g/L |
| Safener: | -- | Conc. of safener: | conc. (c) |
| Synergist: | -- | Conc. of synergist: | conc. (c) |
| Applicant: | CROPNOSYS INDIA PRIVATE LIMITED | Professional use: |  |
| Zone(s): | SEU (Spain) and NEU (Germany, Belgium) | Non-professional use: |  |
| Verified by MS: | yes/no | Residues calculated as: | Prothioconazole-desthio |
| Field of use: | Fungicide |  |  |

| **Trial No./**  **Location/**  **Year** | **Commodity** | **Date of**  **harvest** | **Application rate per treatment** | | | **Dates of treatment or number and last date** | **Growth stage at each treatment** | **Portion**  **analysed** | **Residues (mg/kg)** | | | | | | **PHI (days)** | **Remarks** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **g ai/ha** | **Water (L/ha)** | **g ai/hL** | **Prothioconazole-**  **desthio** | **Prothioconazole-hydroxy**  **desthio metabolite** | **1,2,4-**  **Triazole** | **TAA** | **TA** | **TLA** |
| E23-0116-01  Lliria (Spain)  Southern Europe  2023 | Honey | 11.07.2023 | 200 | 400 | 50 | 2/28.06.2023 | BBCH 63-65 | Honey | 0.154 | < 0.015 | 0.003 (< LOQ) | n.d. | n.d. | n.d. | 13 | -- |
| E23-0116-02  Calatorao (Spain)  Southern Europe  2023 | Honey | 03.07.2023 | 200 | 400 | 50 | 2/19.06.2023 | BBCH 63 | Honey | n.d. | < 0.015 | 0.002 (< LOQ) | n.d. | 0.013 | n.d. | 14 | -- |
| E23-0116-03  Langenfeld (Germany)  Northern Europe  2023 | Honey | 11.07.2023 | 200 | 400 | 50 | 2/04.07.2023 | BBCH 65 | Honey | 0.0053 (< LOQ) | < 0.015 | n.d. | n.d. | n.d. | n.d. | 7 | -- |
| E23-0116-04  Kinrooi (Belgium)  Northern Europe  2023 | Honey | 10.07.2023 | 200 | 400 | 50 | 3/04.07.2023 | BBCH 65 | Honey | 0.011 | < 0.015 | n.d. | n.d. | n.d. | n.d. | 7 | -- |

* 1. Spiroxamine
     1. Stability of residues

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Stability of residues during storage of samples

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Storage stability of residues in plant products

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Storage stability of residues in animal products

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Nature of residues in plants, livestock and processed commodities

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Nature of residue in plants

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residue in primary crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residue in rotational crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - * 1. Nature of residues in processed commodities

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Nature of residues in livestock

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in plants

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Cereals (Wheat)

No new data submitted with this submission. In general only new data should be presented and summarized in Appendix 2. However, after request and for the sake of completeness a short summary of unprotected data (RAR 2017, DAR 2007) are presented in the following.

Please note that the “KCA” numbering corresponds to the numbering in the RAR 2017. No K-docs are submitted again with this submission.

Table A 2: Comparison of intended and critical EU GAPs - Spiroxamine

| Type of GAP | Number of  applications | Application rate  per treatment  (kg as/ha) | Interval between  application | Growth stage at  last application | PHI  (days) |
| --- | --- | --- | --- | --- | --- |
| cGAP EU (DE, 2009) | 2 | 0.375 | -- | BCH 69 | 42 |
| cGAP EU (Art. 12, DE 2014a,  EFSA, 2015) | 2 | 0.375 | -- | BCH 69 | 42 |
| Intended cGAP (use 1-3) | 1 | 0.300 | -- | BBCH 59 | 35. |

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

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/01: Allmendinger H (1994) Determination of residues of HWG1608 & KWG 4168 383 EW in/on winter rye, winter wheat, spring barley, spring wheat and winter barley under actual use conditions in the Federal Republic of Germany and France RA-2077/93 M-010788-01-1 |
| Guideline(s): | Yes  IVA Guideline, Residue Trials, Parts 1A and 1B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable. (RAR 2017) |

and

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/02: Allmendinger H (1995) Determination of residues of HWG 1608 & KWG 4168 383 EW in/on spring barley, spring wheat, winter rye, winter wheat and winter barley in the Federal Republic of Germany and France RA-2004/94 M-010783-01-1 |
| Guideline(s): | Yes  IVA Guideline, Residue Trials, Parts 1A and 1B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable. (RAR 2017) |

For wheat, 7 trials are available, where spiroxamine was applied twice as an EW formulation to wheat according to the cGAP for Northern Europe. These trials were already evaluated in the Monograph (1997). Samples were analysed for total residues of spiroxamine containing the intact 4-tert-butylcyclohexanone moiety according to method 00312 (see Vol. 3, B.5) with a limit of quantification of 0.05 mg/kg for all matrices (forage, grain, straw).

**Summary of residue data from supervised field trials (wheat, Northern Europe) analysed for total residues of spiroxamine and originally submitted for first Annex 1 inclusion**

| Trial No./  Location/  EU zone/  Year | Commodity/ Variety | Date of  1.Sowing or planting  2.Flowering  3. Harvest | Application rate per treatment | | | Dates of treatment or no. of treatments and last date | Growth stage at last treatment or date | Portion analyzed | Residues (mg/kg) | | | PHI (days) | Details on trial |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| g a.s./ ha | Water (l/ha) | g a.s./hl | Spiroxamine | | |
|  | (a) | (b) |  |  |  | (c) |  |  | Total residue (measured) | | *Parent only*  *(calculated)a* | (d) | (e) |
| KIIA 6.3.1/01  N-EU N-France 1993  RA-2077/93 0080-93 300802 | Winter wheat | -- | 375 | 280 |  | 2 | BBCH 65 | green m.  straw  ear  grain | 0.62  4.1  1.2  1.0  1.4  1.4  0.12  <0.05 | | *-*  *-*  *-*  *-*  *[0.24]*  *-*  *-*  *[<0.012]* | 0  0  14  28  35  56  35  56 |  |
|  |  | -- |  |  |  |  |  |  |  |  |  |  |  |
| KIIA 6.3.1/01  N-EU Germany 1993  RA-2077/93 0134-93 301345 | Winter wheat | -- | 375 | 300 |  | 2 | BBCH 61 | green m.  straw  ear  grain | 1.4  6.8  2.7  2.1  0.26  < 0.05 | | *-*  *-*  *[0.46]*  *-*  *-*  *[<0.012]* | 0  0  35  56  35  56 |  |
|  | Winter wheat |  |  |  |  |  |  |  |  |  |  |  |  |
| KIIA 6.3.1/01  N-EU Germany 1993  RA-2077/93 0135-93 301353 | Winter wheat | -- | 375 | 300 |  | 2 | BBCH 61 | green m.  straw  ear  grain | 3.2  9.1  5.4  4.4  0.50  < 0.05 | | *-*  *-*  *[0.92]*  *-*  *-*  *[<0.012]* | 0  0  35  51  35  51 |  |
| KIIA 6.3.1/01  N-EU N-France 1993  RA-2077/93 0300-93 303003 | Winter wheat | -- | 375 | 280 |  | 2 | BBCH 65 | green m.  straw  ear  grain | 0.56  4.4  1.2  0.89  1.3  1.3  0.21  <0.05 | | *-*  *-*  *-*  *-*  *[0.22]*  *-*  *-*  *[<0.012]* | 0  0  14  28  35  56  35  56 |  |
| KIIA 6.3.1/02  N-EU Germany 1994  0016-94 RA-2004/94 400165 | Winter wheat | -- | 375 | 300 |  | 2 | BBCH 69 | green m.  straw  grain | 0.11  6.6  5.4  4.0  < 0.05  < 0.05 | | *-*  *-*  *[0.92]*  *-*  *[<0.012]* | 0  0  35  42  35  42 |  |
| KIIA 6.3.1/02  N-EU Germany 1994  0018-94 RA-2004/94 400181 | Winter wheat | -- | 375 | 300 |  | 2 | BBCH 71 | green m.  straw  grain | 0.56  3.2  7.5  7.6  < 0.05  < 0.05 | | *-*  *-*  *-*  *[1.29] [<0.012]* | 0  0  35  42  35  42 |  |
| KIIA 6.3.1/02  N-EU N-France 1994  0194/94 RA-2004/94 401943 | Winter wheat | -- | 375 | 300 |  | 2 | BBCH 69 | green m.  straw  ear  grain | 0.32  3.8  1.2  2.0  2.4  1.6  0.34  0.54  <0.05 | | *-*  *-*  *-*  *-*  *[0.41]*  *-*  *-*  *-*  *[<0.012]* | 0  0  14  28  35  52  28  35  52 |  |

a factors of 0.23 (grain) and 0.17 (straw) for conversion of total residues to parent spiroxamine according to Table B. 7.6-1. Target PHI residue values underlined

**Analysis of parent spiroxamine only**

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/05: Anonymous (1992) HWG 1608 & KWG 4168; 417 EC; winter barley and winter wheat; Germany; BBA 0640-90, PF 3742, M-010809-01-2 |
| Guideline(s): | Yes  IVA Guideline, Residue Trials, Parts 1A and 1B |
| Deviations: | No |
| GLP: | No |
| Acceptability: | The study is considered as supplemental information (RAR 2017) |

and

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/06: Heinemann O (1999) Determination of residues of KWG 4168 & ICI A 5504 400 SE in/on spring barley and winter wheat following spray application in Germany, Sweden and Great Britain RA-2002/97, M-010782-01-1 |
| Guideline(s): | Yes  According to EC guidance document 7029/VI/95 rev.5: Appendix B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable (RAR 2017) |

and

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/07: Heinemann O & Elke K (2001) Determination of residues of JAU 6476-desthio & KWG 4168 on spring wheat following spray application of JAU 6476 & KWG 4168 460 EC in Great Britain, France, Germany and Italy RA-2092/00, M-087669-01-1 |
| Guideline(s): | Yes  According to EC guidance document 7029/VI/95 rev.5: Appendix B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable (RAR 2017) |

and

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/08: Freitag T & Wolter A (2006) Determination of the residues of JAU 6476, tebuconazole and KWG 4168 in/on winter wheat after spraying of JAU 6476 & HWG 1608 & KWG 4168 (450 EC) in the field in northern France, Germany, United Kingdom and Sweden RA-2574/05, M-271973-01-1 |
| Guideline(s): | Yes  According to EC guidance document 7029/VI/95 rev.5: Appendix B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable (RAR 2017) |

and

|  |  |
| --- | --- |
| Report | KIIA 6.3.1/10: Schoening R, Erler S (2008) Determination of the residues of BYF 00587, JAU 6476 and KWG 4168 in/on winter wheat and spring wheat after spraying of BYF 00587 & JAU 6476 & KWG 4168 (400 EC) in the field in northern France, the Netherlands, the United Kingdom and Germany RA-2040/07 M-271989-02-1 |
| Guideline(s): | Yes  According to EC guidance document 7029/VI/95 rev.5: Appendix B |
| Deviations: | No |
| GLP: | Yes |
| Acceptability: | The study is considered acceptable (RAR 2017) |

Fourteen GLP and 1 non-GLP trials are available for northern Europe, where spiroxamine was applied twice to wheat according to the cGAP with different comparable formulations (SE, EC, different co-formulants). The growth stage at the last application was BBCH 69.

Samples were analysed with different methods for parent spiroxamine only. Either Method 00506 (incl. supplement E001), method 00709 or method 01013/M001.

The LOQ for all methods and matrices is 0.05 mg/kg except for method 01013/M001, where the LOQ is 0.01 mg/kg (all matrices). All methods are evaluated in Part B.5

All samples were stored for not more than 15 months under deep-freeze conditions. Storage stability is therefore covered by the appropriate studies.

**Summary of residue data from supervised field trials in wheat (Northern Europe) analysed for parent spiroxamine only**

| Trial No./  Location/  EU zone/  Year | Commodity/ Variety | Date of  1.Sowing or planting  2.Flowering  3. Harvest | Application rate per treatment | | | Dates of treatment or no. of treatments and last date | Growth stage at last treatment or date | Portion analyzed | Residues (mg/kg) | | | PHI (days) | Details on trial |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| g a.s./ ha | Water (l/ha) | g a.s./hl | Spiroxamine | | |
|  | (a) | (b) |  |  |  | (c) |  |  | Parent spirox only | | Total residue of Spirox [*calculated*]a or measured | (d) | (e) |
| KIIA 6.3.1/10  RA-2040/07 R 2007 0444 5 (0444-07) GLP: yes 2007  Netherlands NL-1681 ND Zwaagdijk-Oost (NoordHolland) (N-EU) | Wheat, spring Baldus | -- | 375 | - | 125 | 2 | BBCH 69 | Green m  Grain  straw | 0.39  4.3  0.03  0.01  0.24  0.24 | | *-*  *-*  *[0.13]*  *-*  *[1.41]*  *-* | 0  0  35  62  35  61 |  |
|  |  | -- | 3 |  |  |  |  |  |  |  |  |  |  |
| KIIA 6.3.1/10  RA-2040/07 R 2007 0523 9 (0523-07) GLP: yes 2007  United Kingdom GB-IP21 4BQ Thrande-ston / Diss (Norfolk) (N-EU) | Wheat, spring Belvoir | -- | 375 | - | 125 | 2 | BBCH 69 | Green m  Ear  Rest of plant  Grain  Straw | 0.47  3.2  0.03  0.32  <0.01  0.39 | | *-*  *-*  *-*  *-*  *[<0.04]*  *[2.29]* | 0  0  35  35  73  73 |  |
| KIIA 6.3.1/10  RA-2040/07 R 2007 0524 7 (0524-07) GLP: yes 2007  Germany D-51399 Burscheid (Nordrhein-Westfalen) (N-EU) | Wheat, spring Thasos | -- | 375 | - | 125 | 2 | BBCH 69 | Green m  Grain  straw | 1.3  7.2  0.02  0.01  0.70  0.55 | | *-*  *-*  *[0.09]*  *-*  *[4.12]*  *-* | 0  0  35  56  35  56 |  |
| KIIA 6.3.1/10  RA-2040/07 R 2007 0443 7 (0443-07) GLP: yes 2007  France F-37120 Braslou (Centre) (N-EU) | Wheat, winter Mendel | -- | 375 | - | 125 | 2 | BBCH 69 | Green m  Ear  Rest of plant  Grain  Straw | 0.48  6.0  0.09  0.56  <0.01  0.50 | | *-*  *-*  *-*  *-*  *[<0.04]*  *[2.94]* | 0  0  35  35  44  44 |  |
| KIIA 6.3.1/08  RA-2573/05 R 2005 0470 5 (0470-05) GLP: yes 2005  France F-95710 Chaussy (Ile-de-France) (N-EU) | Wheat, winter PR 22 | -- | 313 | - | 104 | 2 | BBCH 69 | Green m  Grain  straw | 0.69  4.6  0.46  0.31  <0.05  0.47 | | *-*  *-*  *-*  *-*  *[<0.22]*  *[2.76]* | 0  0  28  35  42  42 |  |
| KIIA 6.3.1/08  RA-2573/05 R 2005 0471 3 (0471-05) GLP: yes 2005  Germany D-51377 Leverkusen (NordrheinWestfalen) (N-EU) | Wheat, winter Batis | -- | 313 | - | 104 | 2 | BBCH 69 | Green m  Grain  straw | 6.6  0.36  <0.05  0.69 | | *-*  *-*  *[<0.22]*  *[4.06]* | 0  35  52  52 |  |
| KIIA 6.3.1/08  RA-2573/05 R 2005 0803 4 (0803-05) GLP: yes 2005  United Kingdom GB-SG8 8SS Royston (Hertford-shire) (N-EU) | Wheat, winter Einstein | -- | 313 | - | 104 | 2 | BBCH 69 | Green m  Grain  straw | 4.3  0.79  <0.05  1.1 | | *-*  *-*  *[<0.22]*  *[6.47]* | 0  35  50  50 |  |
| KIIA 6.3.1/08  RA-2573/05 R 2005 0804 2 (0804-05) GLP: yes 2005  Sweden S-SE-225 92 Lund (Malmoe) (N-EU | Wheat, winter Ritmo | -- | 313 | - | 104 | 2 | BBCH 69 | Green m  Grain  straw | 5.9  0.78  <0.05  1.1 | | *-*  *-*  *[<0.22]*  *[6.47]* | 0  35  54  54 |  |
| KIIA 6.3.1/07  RA-2092/00 R 2000 0081 2 (0081-00) GLP: yes 2000  United Kingdom GB-IP31 3SH Thurston, Bury St. Edmunds (EFDS) (N-EU) | Wheat, spring Chablis | -- | 375 | - | 125 | 2 | BBCH 69 | Ear  Rest of plant  Grain  straw | 3.9  0.18  0.13  11  1.3  0.95  <0.05  <0.05  0.69  0.32 | | *-*  *-*  *-*  *-*  *-*  *-*  *[<0.22]*  *-*  *[4.06]*  *-* | 0  28  35  0  28  35  42  56  42  56 |  |
| KIIA 6.3.1/07  RA-2092/00 R 2000 0430 3 (0430-00) GLP: yes 2000  Germany D-51399 Burscheid, Versuchsgut Höfchen (N-EU) | Wheat, spring Lavett | -- | 375 | - | 125 | 2 | BBCH 69 | Ear  Rest of plant  Grain  straw | 6.2  0.42  0.20  0.12  6.8  1.0  0.97  0.71  <0.05  0.31 | | *-*  *-*  *-*  *-*  *-*  *-*  *-*  *-*  *[<0.22]*  *[1.82]* | *0*  *28*  *35*  *42*  *0*  *28*  *35*  *42*  *58*  *58* |  |
| KIIA 6.3.1/07  RA-2092/00  R 2000 0431 1 (0431-00) GLP: yes 2000  Germany D-40789 Monheim, Laacherhof (N-EU) | Wheat, spring Lavett | -- | 375 | - | 125 | 2 | BBCH 69 | Ear  Rest of plant  Grain  straw | 6.5  0.32  0.17  10  1.9  0.77  <0.05  <0.05  1.2  0.70 | | *-*  *-*  *-*  *-*  *-*  *-*  *[<0.22]*  *-*  *[7.06]*  *-* | 0  28  35  0  28  35  41  49  41  49 |  |
| KIIA 6.3.1/07  RA-2092/00 R 2000 0433 8 (0433-00) GLP: yes 2000  France F-27700 Fresne L'Archeveque (N-EU) | Wheat, spring Furio | -- | 375 | - | 125 | 2 | BBCH 69 | Ear  Rest of plant  Grain  straw | 3.8  0.25  5.2  0.53  <0.05  <0.05  0.40  0.27 | | *-*  *-*  *-*  *-*  *[<0.22]*  *-*  *{2.35]*  *-* | 0  28  0  28  35  42  35  42 |  |
| KIIA 6.3.1/06  RA-2002/97 70381/8 (0381-97) GLP: yes 1997  Sweden S-24593 Staffanstorp St.Uppäkra (N-EU) | Wheat, winter Ritmo | -- | 400 | - | 130 | 2 | BBCH 69 | Green m  Ear  Grain  straw | 5.9  0.34  <0.05  0.81  0.41 | | *-*  *-*  *<0.05\*\**  *-*  *-* | 0  35  45  35  45 |  |
| KIIA 6.3.1/06  RA-2002/97 70383/4 (0383-97) GLP: yes 1997  Sweden S-24591 Staffanstorp Korn-heddinge (N-EU) | Wheat, winter Ritmo | -- | 400 | - | 130 | 2 | BBCH 69 | Green m  Ear  Grain  straw | 7.8  0.27  <0.05  0.99  0.81 | | *-*  *-*  *<0.05\*\**  *-*  *-* | 0  35  43  35  43 |  |
| KIIA 6.3.1/05  PF 3742 00640/8 (0640-90)\*\*\*  GLP: no 1990  Germany D-51399 Burscheid, Versuchsgut Höfchen (N-EU) | Wheat, winter Apollo | -- | 375 | - | 125 | 2 | BBCH 61 | Green m  Ear  Grain\*\*\*  Straw\*\*\* | 4.0  1.5  0.78  0.23  0.17  <0.05  1.1  0.74 | | *-*  *-*  *-*  *-*  *-*  *-*  *-*  *-* | 0  14  8  28  35  57  35  57 |  |

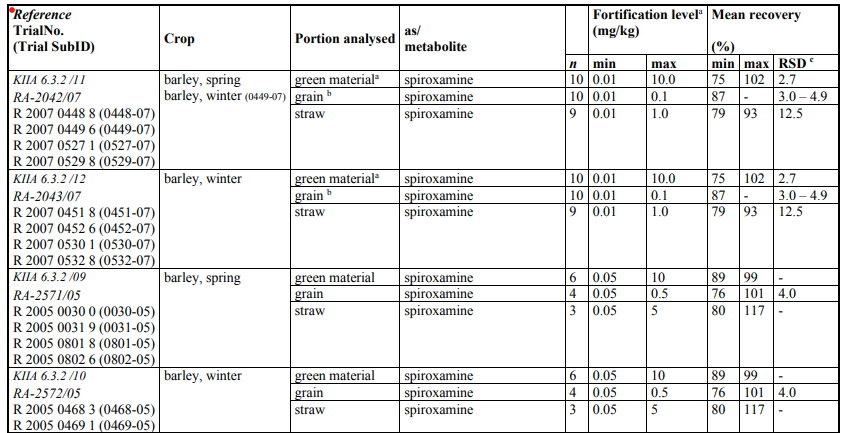
a factors of 1/0.23 (grain) and 1/0.17 (straw) for conversion of parent spiroxamine to total residues

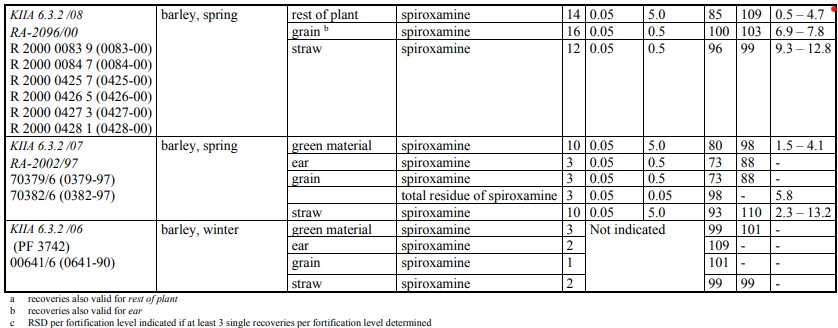
\*\* total residue determined as 4-t-butyl-cyclohexanone and expressed in spiroxamine equivalent

\*\*\* non-GLP residue trial only used as supplemental information

Target PHI residue values underlined

Procedural recoveries for spiroxamine in barley matrices





* + 1. Magnitude of residues in livestock

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Livestock feeding studies

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Distribution of the residue in peel/pulp

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + - 1. Processing studies on a core set of representative processes

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Magnitude of residues in representative succeeding crops

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

* + 1. Other/Special Studies

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

1. Pesticide Residue Intake Model (PRIMo)

Prothioconazole

Input data

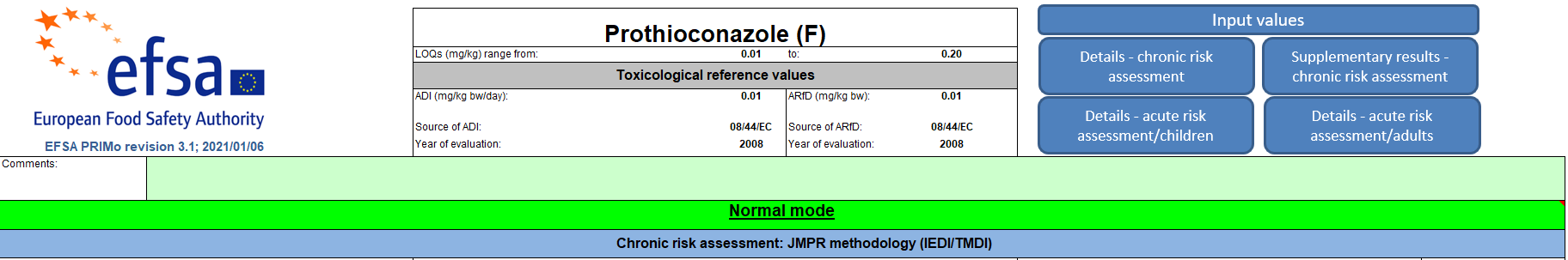
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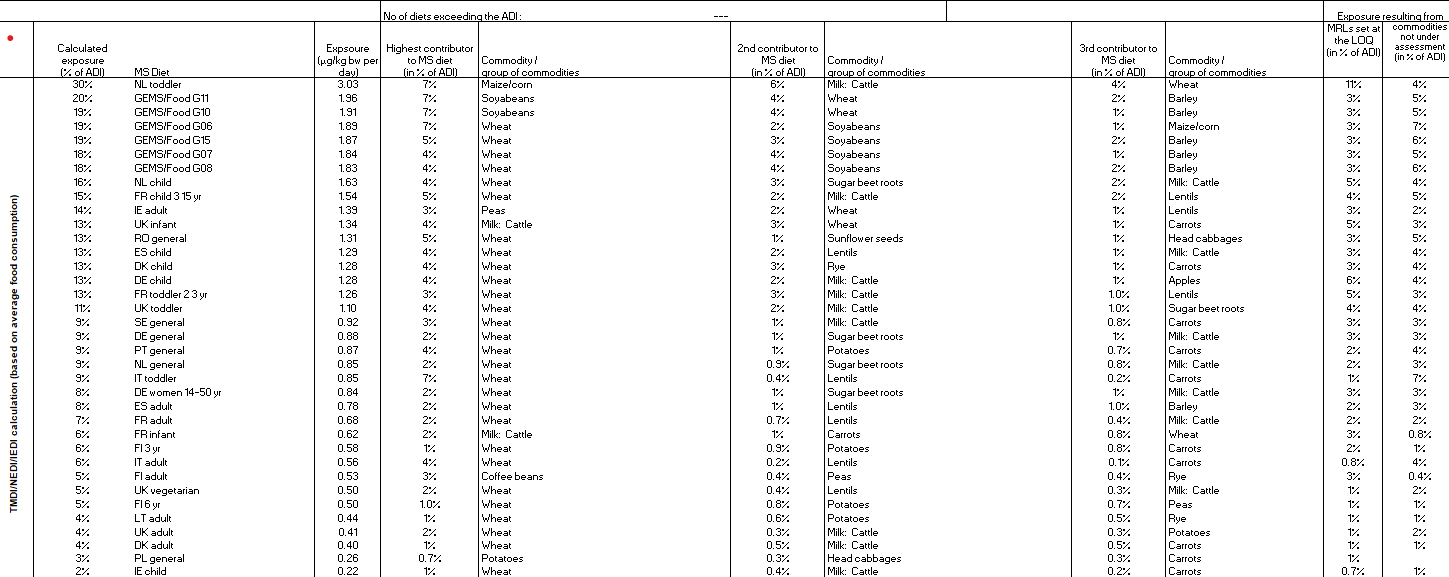
[Source: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg\_code=EN&pest\_res\_id\_list=365]



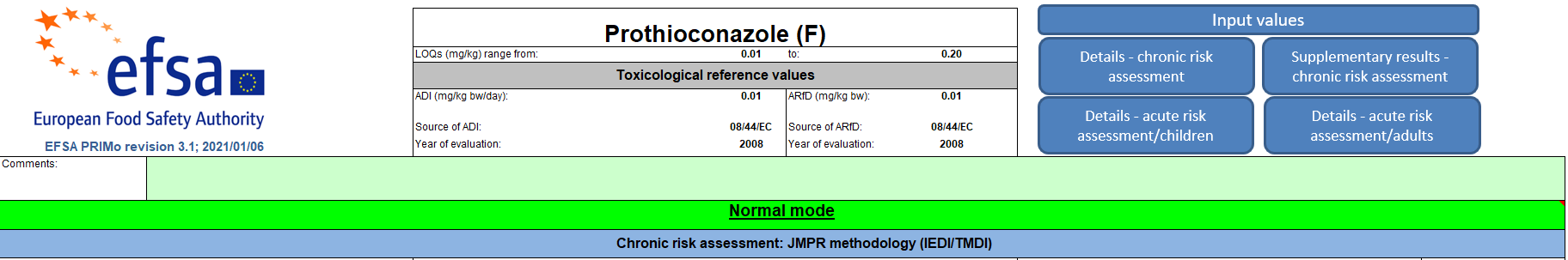
* 1. TMDI calculations

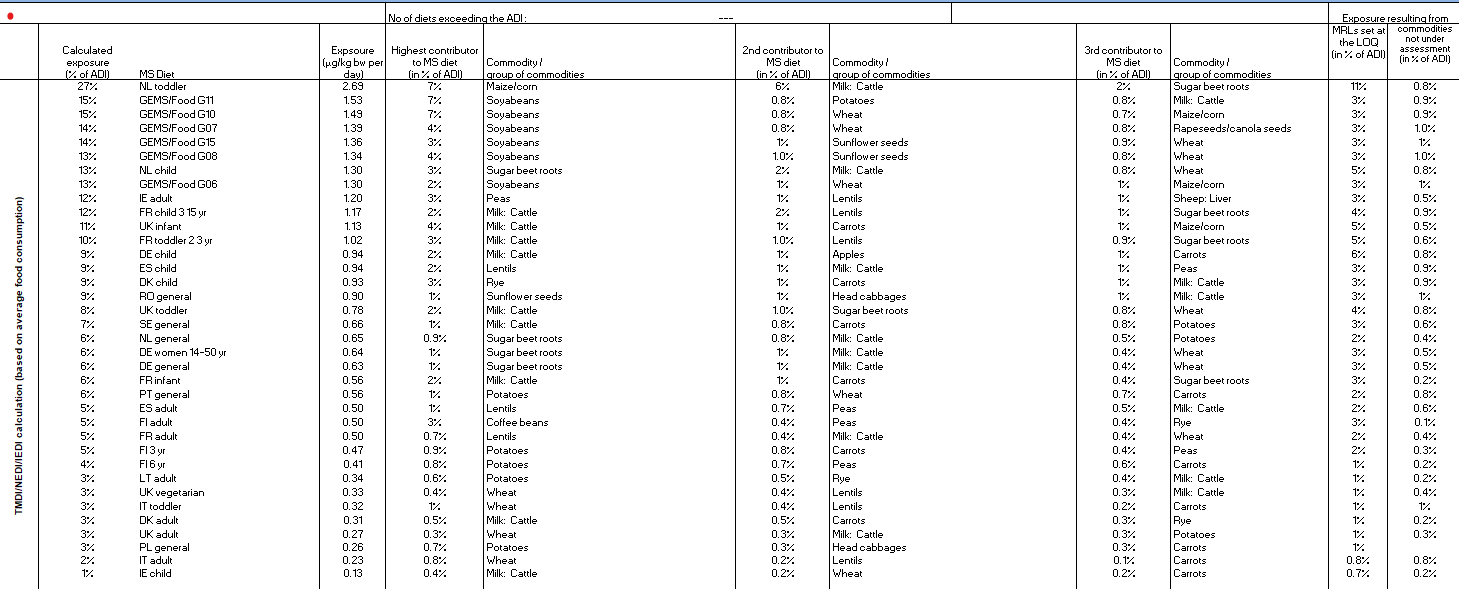
TMDI – Based on current MRLs of the active substance prothioconazole





* 1. IEDI calculations



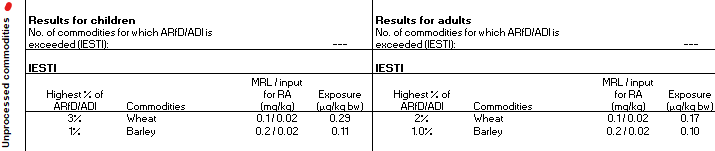


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* 1. IESTI calculations - Raw commodities

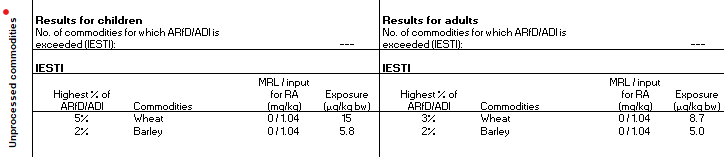
prothioconazole-desthio





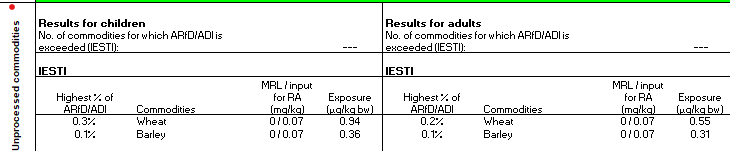
TA





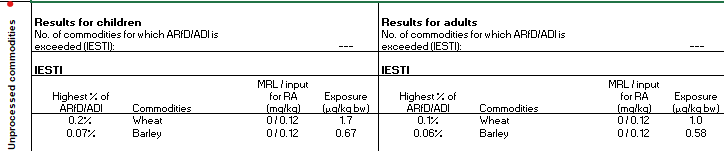
TLA





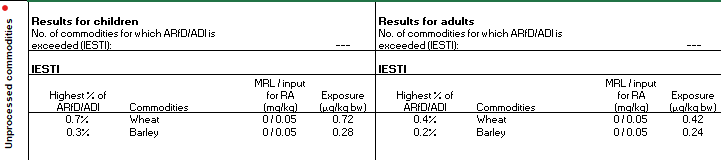
TAA





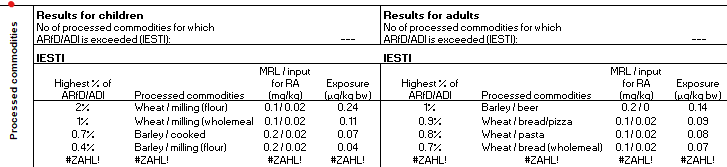
1,2,4-triazole





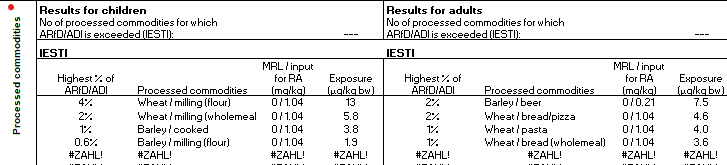
* 1. IESTI calculations - Processed commodities

prothioconazole-desthio

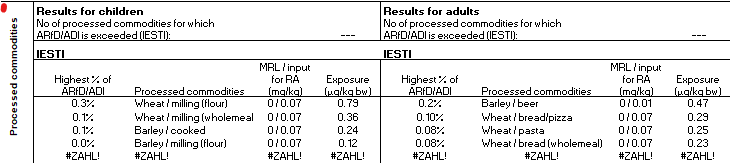
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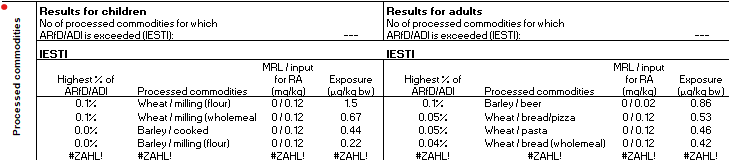
TLA





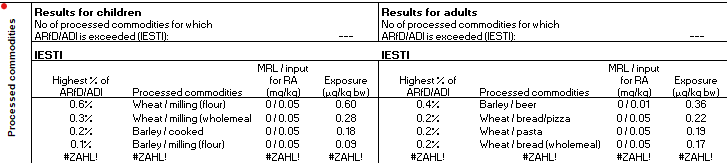
TAA





1,2,4-triazole



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**TDMs Data:**



The PRIMos should be pasted as visible pics, not unopenable Excel icons.

Spiroxamine

Input data

Input table of the current MRLs of spiroxamine (Regulation (EU) No 2016/452) downloaded on 2023/06/07:

[Source: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg\_code=EN&pest\_res\_id\_list=206]

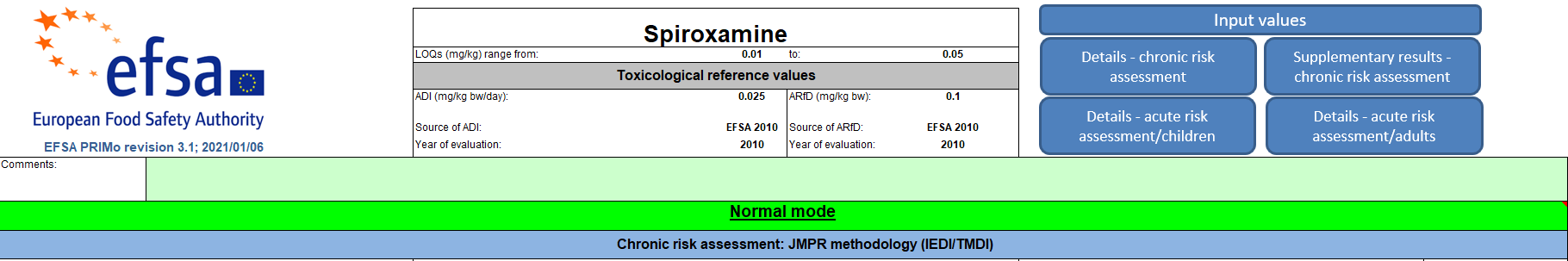


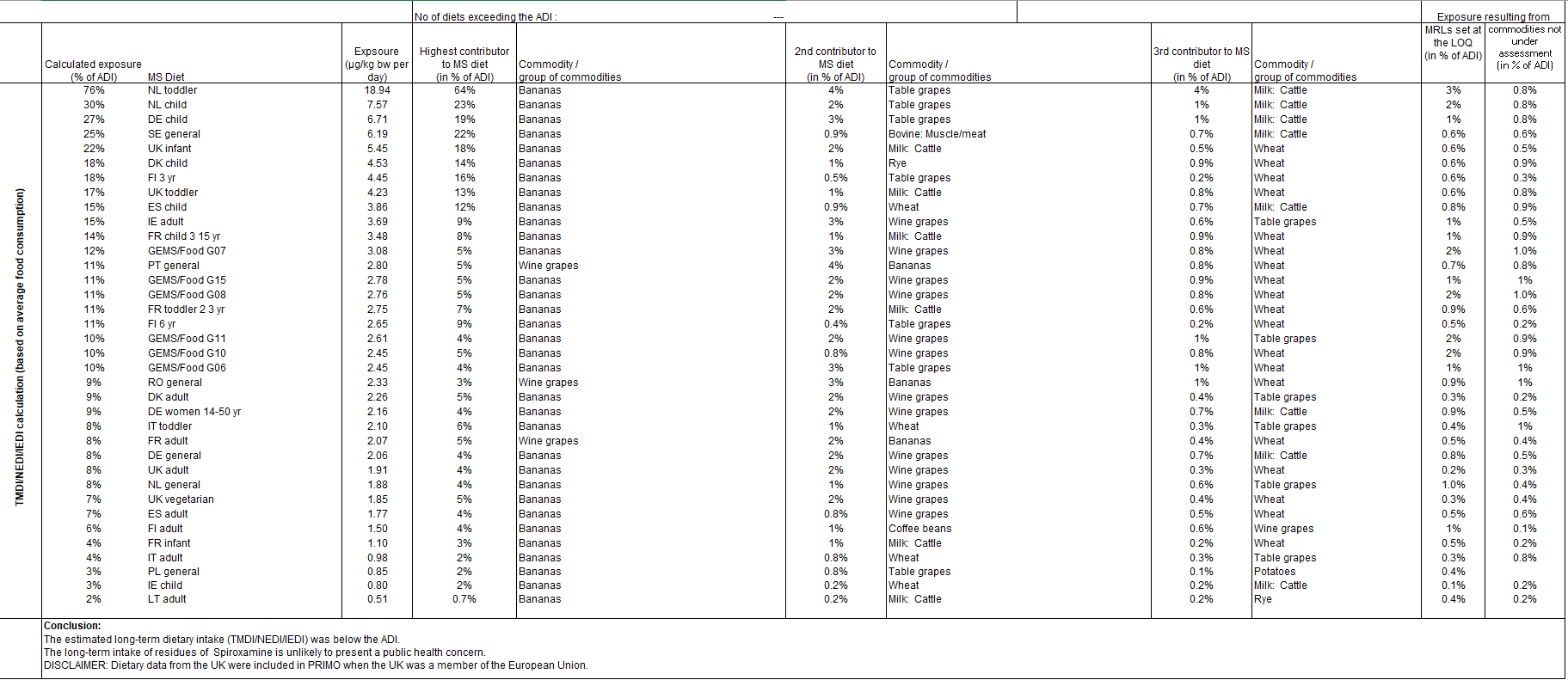
|  |  |  |
| --- | --- | --- |
|  |  | **Spiroxamine (sum of isomers) (R) (A)  Reg. (EU) No 2016/452 Annex II** |
| **Code number** | **Groups and examples of individual products to which the MRLs apply (a)** | **Current** |
| 100000 | FRUITS, FRESH or FROZEN; TREE NUTS |  |
| 110000 | Citrus fruits | 0.01\* |
| 110010 | Grapefruits | 0.01\* |
| 110020 | Oranges | 0.01\* |
| 110030 | Lemons | 0.01\* |
| 110040 | Limes | 0.01\* |
| 110050 | Mandarins | 0.01\* |
| 110990 | Others (2) | 0.01\* |
| 120000 | Tree nuts | 0.05\* |
| 120010 | Almonds | 0.05\* |
| 120020 | Brazil nuts | 0.05\* |
| 120030 | Cashew nuts | 0.05\* |
| 120040 | Chestnuts | 0.05\* |
| 120050 | Coconuts | 0.05\* |
| 120060 | Hazelnuts/cobnuts | 0.05\* |
| 120070 | Macadamias | 0.05\* |
| 120080 | Pecans | 0.05\* |
| 120090 | Pine nut kernels | 0.05\* |
| 120100 | Pistachios | 0.05\* |
| 120110 | Walnuts | 0.05\* |
| 120990 | Others (2) | 0.05\* |
| 130000 | Pome fruits | 0.01\* |
| 130010 | Apples | 0.01\* |
| 130020 | Pears | 0.01\* |
| 130030 | Quinces | 0.01\* |
| 130040 | Medlars | 0.01\* |
| 130050 | Loquats/Japanese medlars | 0.01\* |
| 130990 | Others (2) | 0.01\* |
| 140000 | Stone fruits | 0.01\* |
| 140010 | Apricots | 0.01\* |

| **Code number** | **Groups and examples of individual products to which the MRLs apply (a)** | **Current** |
| --- | --- | --- |
| 140020 | Cherries (sweet) | 0.01\* |
| 140030 | Peaches | 0.01\* |
| 140040 | Plums | 0.01\* |
| 140990 | Others (2) | 0.01\* |
| 150000 | Berries and small fruits |  |
| 151000 | (a) grapes |  |
| 151010 | Table grapes | 0.6 |
| 151020 | Wine grapes | 0.5 |
| 152000 | (b) strawberries | 0.01\* |
| 153000 | (c) cane fruits | 0.01\* |
| 153010 | Blackberries | 0.01\* |
| 153020 | Dewberries | 0.01\* |
| 153030 | Raspberries (red and yellow) | 0.01\* |
| 153990 | Others (2) | 0.01\* |
| 154000 | (d) other small fruits and berries | 0.01\* |
| 154010 | Blueberries | 0.01\* |
| 154020 | Cranberries | 0.01\* |
| 154030 | Currants (black, red and white) | 0.01\* |
| 154040 | Gooseberries (green, red and yellow) | 0.01\* |
| 154050 | Rose hips | 0.01\* |
| 154060 | Mulberries (black and white) | 0.01\* |
| 154070 | Azaroles/Mediterranean medlars | 0.01\* |
| 154080 | Elderberries | 0.01\* |
| 154990 | Others (2) | 0.01\* |
| 160000 | Miscellaneous fruitswith |  |
| 161000 | (a) edible peel | 0.01\* |
| 161010 | Dates | 0.01\* |
| 161020 | Figs | 0.01\* |
| 161030 | Table olives | 0.01\* |
| 161040 | Kumquats | 0.01\* |
| 161050 | Carambolas | 0.01\* |
| 161060 | Kaki/Japanese persimmons | 0.01\* |
| 161070 | Jambuls/jambolans | 0.01\* |
| 161990 | Others (2) | 0.01\* |
| 162000 | (b) inedible peel, small | 0.01\* |
| 162010 | Kiwi fruits (green, red, yellow) | 0.01\* |
| 162020 | Litchis/lychees | 0.01\* |
| 162030 | Passionfruits/maracujas | 0.01\* |
| 162040 | Prickly pears/cactus fruits | 0.01\* |
| 162050 | Star apples/cainitos | 0.01\* |
| 162060 | American persimmons/Virginia kaki | 0.01\* |
| 162990 | Others (2) | 0.01\* |
| 163000 | (c) inedible peel, large |  |
| 163010 | Avocados | 0.01\* |
| 163020 | Bananas | 3 |
| 163030 | Mangoes | 0.01\* |
| 163040 | Papayas | 0.01\* |
| 163050 | Granate apples/pomegranates | 0.01\* |
| 163060 | Cherimoyas | 0.01\* |
| 163070 | Guavas | 0.01\* |
| 163080 | Pineapples | 0.01\* |
| 163090 | Breadfruits | 0.01\* |
| 163100 | Durians | 0.01\* |
| 163110 | Soursops/guanabanas | 0.01\* |
| 163990 | Others (2) | 0.01\* |
| 200000 | VEGETABLES, FRESH or FROZEN |  |
| 210000 | Root and tuber vegetables | 0.01\* |
| 211000 | (a) potatoes | 0.01\* |
| 212000 | (b) tropical root and tuber vegetables | 0.01\* |
| 212010 | Cassava roots/manioc | 0.01\* |
| 212020 | Sweet potatoes | 0.01\* |
| 212030 | Yams | 0.01\* |
| 212040 | Arrowroots | 0.01\* |
| 212990 | Others (2) | 0.01\* |
| 213000 | (c) other root and tuber vegetables except sugar beets | 0.01\* |
| 213010 | Beetroots | 0.01\* |
| 213020 | Carrots | 0.01\* |
| 213030 | Celeriacs/turnip rooted celeries | 0.01\* |
| 213040 | Horseradishes | 0.01\* |
| 213050 | Jerusalem artichokes | 0.01\* |
| 213060 | Parsnips | 0.01\* |
| 213070 | Parsley roots/Hamburg roots parsley | 0.01\* |
| 213080 | Radishes | 0.01\* |
| 213090 | Salsifies | 0.01\* |
| 213100 | Swedes/rutabagas | 0.01\* |
| 213110 | Turnips | 0.01\* |
| 213990 | Others (2) | 0.01\* |
| 220000 | Bulb vegetables | 0.01\* |
| 220010 | Garlic | 0.01\* |
| 220020 | Onions | 0.01\* |
| 220030 | Shallots | 0.01\* |
| 220040 | Spring onions/green onions and Welsh onions | 0.01\* |
| 220990 | Others (2) | 0.01\* |
| 230000 | Fruiting vegetables | 0.01\* |
| 231000 | (a) Solanaceae and Malvaceae | 0.01\* |
| 231010 | Tomatoes | 0.01\* |
| 231020 | Sweet peppers/bell peppers | 0.01\* |
| 231030 | Aubergines/eggplants | 0.01\* |
| 231040 | Okra/lady's fingers | 0.01\* |
| 231990 | Others (2) | 0.01\* |
| 232000 | (b) cucurbits with edible peel | 0.01\* |
| 232010 | Cucumbers | 0.01\* |
| 232020 | Gherkins | 0.01\* |
| 232030 | Courgettes | 0.01\* |
| 232990 | Others (2) | 0.01\* |
| 233000 | (c) cucurbits with inedible peel | 0.01\* |
| 233010 | Melons | 0.01\* |
| 233020 | Pumpkins | 0.01\* |
| 233030 | Watermelons | 0.01\* |
| 233990 | Others (2) | 0.01\* |
| 234000 | (d) sweet corn | 0.01\* |
| 239000 | (e) other fruiting vegetables | 0.01\* |
| 240000 | Brassica vegetables(excluding brassica roots and brassica baby leaf crops) | 0.01\* |
| 241000 | (a) flowering brassica | 0.01\* |
| 241010 | Broccoli | 0.01\* |
| 241020 | Cauliflowers | 0.01\* |
| 241990 | Others (2) | 0.01\* |
| 242000 | (b) head brassica | 0.01\* |
| 242010 | Brussels sprouts | 0.01\* |
| 242020 | Head cabbages | 0.01\* |
| 242990 | Others (2) | 0.01\* |
| 243000 | (c) leafy brassica | 0.01\* |
| 243010 | Chinese cabbages/pe-tsai | 0.01\* |
| 243020 | Kales | 0.01\* |
| 243990 | Others (2) | 0.01\* |
| 244000 | (d) kohlrabies | 0.01\* |
| 250000 | Leaf vegetables, herbs and edible flowers |  |
| 251000 | (a) lettuces and salad plants | 0.01\* |
| 251010 | Lamb's lettuces/corn salads | 0.01\* |
| 251020 | Lettuces | 0.01\* |
| 251030 | Escaroles/broad-leaved endives | 0.01\* |
| 251040 | Cresses and other sprouts and shoots | 0.01\* |
| 251050 | Land cresses | 0.01\* |
| 251060 | Roman rocket/rucola | 0.01\* |
| 251070 | Red mustards | 0.01\* |
| 251080 | Baby leaf crops (including brassica species) | 0.01\* |
| 251990 | Others (2) | 0.01\* |
| 252000 | (b) spinaches and similar leaves | 0.01\* |
| 252010 | Spinaches | 0.01\* |
| 252020 | Purslanes | 0.01\* |
| 252030 | Chards/beet leaves | 0.01\* |
| 252990 | Others (2) | 0.01\* |
| 253000 | (c) grape leaves and similar species | 0.01\* |
| 254000 | (d) watercresses | 0.01\* |
| 255000 | (e) witloofs/Belgian endives | 0.01\* |
| 256000 | (f) herbs and edible flowers | 0.02\* |
| 256010 | Chervil | 0.02\* |
| 256020 | Chives | 0.02\* |
| 256030 | Celery leaves | 0.02\* |
| 256040 | Parsley | 0.02\* |
| 256050 | Sage | 0.02\* |
| 256060 | Rosemary | 0.02\* |
| 256070 | Thyme | 0.02\* |
| 256080 | Basil and edible flowers | 0.02\* |
| 256090 | Laurel/bay leaves | 0.02\* |
| 256100 | Tarragon | 0.02\* |
| 256990 | Others (2) | 0.02\* |
| 260000 | Legume vegetables | 0.01\* |
| 260010 | Beans (with pods) | 0.01\* |
| 260020 | Beans (without pods) | 0.01\* |
| 260030 | Peas (with pods) | 0.01\* |
| 260040 | Peas (without pods) | 0.01\* |
| 260050 | Lentils | 0.01\* |
| 260990 | Others (2) | 0.01\* |
| 270000 | Stem vegetables | 0.01\* |
| 270010 | Asparagus | 0.01\* |
| 270020 | Cardoons | 0.01\* |
| 270030 | Celeries | 0.01\* |
| 270040 | Florence fennels | 0.01\* |
| 270050 | Globe artichokes | 0.01\* |
| 270060 | Leeks | 0.01\* |
| 270070 | Rhubarbs | 0.01\* |
| 270080 | Bamboo shoots | 0.01\* |
| 270090 | Palm hearts | 0.01\* |
| 270990 | Others (2) | 0.01\* |
| 280000 | Fungi, mosses and lichens | 0.01\* |
| 280010 | Cultivated fungi | 0.01\* |
| 280020 | Wild fungi | 0.01\* |
| 280990 | Mosses and lichens | 0.01\* |
| 290000 | Algae and prokaryotes organisms | 0.01\* |
| 300000 | PULSES | 0.01\* |
| 300010 | Beans | 0.01\* |
| 300020 | Lentils | 0.01\* |
| 300030 | Peas | 0.01\* |
| 300040 | Lupins/lupini beans | 0.01\* |
| 300990 | Others (2) | 0.01\* |
| 400000 | OILSEEDS AND OIL FRUITS | 0.05\* |
| 401000 | Oilseeds | 0.05\* |
| 401010 | Linseeds | 0.05\* |
| 401020 | Peanuts/groundnuts | 0.05\* |
| 401030 | Poppy seeds | 0.05\* |
| 401040 | Sesame seeds | 0.05\* |
| 401050 | Sunflower seeds | 0.05\* |
| 401060 | Rapeseeds/canola seeds | 0.05\* |
| 401070 | Soyabeans | 0.05\* |
| 401080 | Mustard seeds | 0.05\* |
| 401090 | Cotton seeds | 0.05\* |
| 401100 | Pumpkin seeds | 0.05\* |
| 401110 | Safflower seeds | 0.05\* |
| 401120 | Borage seeds | 0.05\* |
| 401130 | Gold of pleasure seeds | 0.05\* |
| 401140 | Hemp seeds | 0.05\* |
| 401150 | Castor beans | 0.05\* |
| 401990 | Others (2) | 0.05\* |
| 402000 | Oil fruits | 0.05\* |
| 402010 | Olives for oil production | 0.05\* |
| 402020 | Oil palms kernels | 0.05\* |
| 402030 | Oil palms fruits | 0.05\* |
| 402040 | Kapok | 0.05\* |
| 402990 | Others (2) | 0.05\* |
| 500000 | CEREALS |  |
| 500010 | Barley | 0.05 |
| 500020 | Buckwheat and other pseudocereals | 0.01\* |
| 500030 | Maize/corn | 0.01\* |
| 500040 | Common millet/proso millet | 0.01\* |
| 500050 | Oat | 0.05 |
| 500060 | Rice | 0.01\* |
| 500070 | Rye | 0.05 |
| 500080 | Sorghum | 0.01\* |
| 500090 | Wheat | 0.05 |
| 500990 | Others (2) | 0.01\* |
| 600000 | TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS | 0.05\* |
| 610000 | Teas | 0.05\* |
| 620000 | Coffee beans | 0.05\* |
| 630000 | Herbal infusions from | 0.05\* |
| 631000 | (a) flowers | 0.05\* |
| 631010 | Chamomile | 0.05\* |
| 631020 | Hibiscus/roselle | 0.05\* |
| 631030 | Rose | 0.05\* |
| 631040 | Jasmine | 0.05\* |
| 631050 | Lime/linden | 0.05\* |
| 631990 | Others (2) | 0.05\* |
| 632000 | (b) leaves and herbs | 0.05\* |
| 632010 | Strawberry | 0.05\* |
| 632020 | Rooibos | 0.05\* |
| 632030 | Mate/maté | 0.05\* |
| 632990 | Others (2) | 0.05\* |
| 633000 | (c) roots | 0.05\* |
| 633010 | Valerian | 0.05\* |
| 633020 | Ginseng | 0.05\* |
| 633990 | Others (2) | 0.05\* |
| 639000 | (d) any other parts of the plant | 0.05\* |
| 640000 | Cocoa beans | 0.05\* |
| 650000 | Carobs/Saint John's breads | 0.05\* |
| 700000 | HOPS | 0.05\* |
| 800000 | SPICES |  |
| 810000 | Seed spices | 0.05\* |
| 810010 | Anise/aniseed | 0.05\* |
| 810020 | Black caraway/black cumin | 0.05\* |
| 810030 | Celery | 0.05\* |
| 810040 | Coriander | 0.05\* |
| 810050 | Cumin | 0.05\* |
| 810060 | Dill | 0.05\* |
| 810070 | Fennel | 0.05\* |
| 810080 | Fenugreek | 0.05\* |
| 810090 | Nutmeg | 0.05\* |
| 810990 | Others (2) | 0.05\* |
| 820000 | Fruit spices | 0.05\* |
| 820010 | Allspice/pimento | 0.05\* |
| 820020 | Sichuan pepper | 0.05\* |
| 820030 | Caraway | 0.05\* |
| 820040 | Cardamom | 0.05\* |
| 820050 | Juniper berry | 0.05\* |
| 820060 | Peppercorn (black, green and white) | 0.05\* |
| 820070 | Vanilla | 0.05\* |
| 820080 | Tamarind | 0.05\* |
| 820990 | Others (2) | 0.05\* |
| 830000 | Bark spices | 0.05\* |
| 830010 | Cinnamon | 0.05\* |
| 830990 | Others (2) | 0.05\* |
| 840000 | Root and rhizome spices |  |
| 840010 | Liquorice | 0.05\* |
| 840020 | Ginger (10) | 0.05\* |
| 840030 | Turmeric/curcuma |  |
| 840040 | Horseradish (11) | 0.05\* |
| 840990 | Others (2) | 0.05\* |
| 850000 | Bud spices | 0.05\* |
| 850010 | Cloves | 0.05\* |
| 850020 | Capers | 0.05\* |
| 850990 | Others (2) | 0.05\* |
| 860000 | Flower pistil spices | 0.05\* |
| 860010 | Saffron | 0.05\* |
| 860990 | Others (2) | 0.05\* |
| 870000 | Aril spices | 0.05\* |
| 870010 | Mace | 0.05\* |
| 870990 | Others (2) | 0.01\* |
| 900000 | SUGAR PLANTS | 0.01\* |
| 900010 | Sugar beet roots | 0.01\* |
| 900020 | Sugar canes | 0.01\* |
| 900030 | Chicory roots | 0.01\* |
| 900990 | Others (2) |  |
| 1000000 | PRODUCTS OF ANIMAL ORIGIN -TERRESTRIAL ANIMALS |  |
| 1010000 | Commodities from | 0.02\* |
| 1011000 | (a) swine | 0.02\* |
| 1011010 | Muscle | 0.02\* |
| 1011020 | Fat | 0.02\* |
| 1011030 | Liver | 0.02\* |
| 1011040 | Kidney | 0.02\* |
| 1011050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1011990 | Others (2) |  |
| 1012000 | (b) bovine | 0.03 |
| 1012010 | Muscle | 0.05 |
| 1012020 | Fat | 0.3 |
| 1012030 | Liver | 0.15 |
| 1012040 | Kidney | 0.3 |
| 1012050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1012990 | Others (2) |  |
| 1013000 | (c) sheep | 0.03 |
| 1013010 | Muscle | 0.05 |
| 1013020 | Fat | 0.3 |
| 1013030 | Liver | 0.15 |
| 1013040 | Kidney | 0.3 |
| 1013050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1013990 | Others (2) |  |
| 1014000 | d) goat | 0.03 |
| 1014010 | Muscle | 0.05 |
| 1014020 | Fat | 0.3 |
| 1014030 | Liver | 0.15 |
| 1014040 | Kidney | 0.3 |
| 1014050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1014990 | Others (2) |  |
| 1015000 | (e) equine | 0.03 |
| 1015010 | Muscle | 0.05 |
| 1015020 | Fat | 0.3 |
| 1015030 | Liver | 0.15 |
| 1015040 | Kidney | 0.3 |
| 1015050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1015990 | Others (2) |  |
| 1016000 | (f) poultry | 0.05 |
| 1016010 | Muscle | 0.05 |
| 1016020 | Fat | 0.2 |
| 1016030 | Liver | 0.02\* |
| 1016040 | Kidney | 0.2 |
| 1016050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1016990 | Others (2) |  |
| 1017000 | (g) other farmed terrestrial animals | 0.03 |
| 1017010 | Muscle | 0.05 |
| 1017020 | Fat | 0.3 |
| 1017030 | Liver | 0.15 |
| 1017040 | Kidney | 0.3 |
| 1017050 | Edible offals (other than liver and kidney) | 0.02\* |
| 1017990 | Others (2) | 0.015 |
| 1020000 | Milk | 0.015 |
| 1020010 | Cattle | 0.015 |
| 1020020 | Sheep | 0.015 |
| 1020030 | Goat | 0.015 |
| 1020040 | Horse | 0.015 |
| 1020990 | Others (2) | 0.05 |
| 1030000 | Birds eggs | 0.05 |
| 1030010 | Chicken | 0.05 |
| 1030020 | Duck | 0.05 |
| 1030030 | Geese | 0.05 |
| 1030040 | Quail | 0.05 |
| 1030990 | Others (2) | 0.05\* |
| 1040000 | Honey and other apiculture products (7) | 0.02\* |
| 1050000 | Amphibians and Reptiles | 0.02\* |
| 1060000 | Terrestrial invertebrate animals | 0.02\* |
| 1070000 | Wild terrestrial vertebrate animals |  |
| 1100000 | PRODUCTS OF ANIMAL ORIGIN - FISH, FISHPRODUCTS AND ANY OTHER MARINE AND FRESHWATER FOOD PRODUCTS (8) |  |
| 1200000 | PRODUCTS OR PART OF PRODUCTS EXCLUSIVELY USED FOR ANIMAL FEED PRODUCTION (8) |  |
| 1300000 | PROCESSED FOOD PRODUCTS (9) |  |

* 1. TMDI calculations

TMDI – Based on current MRLs of the active substance spiroxamine





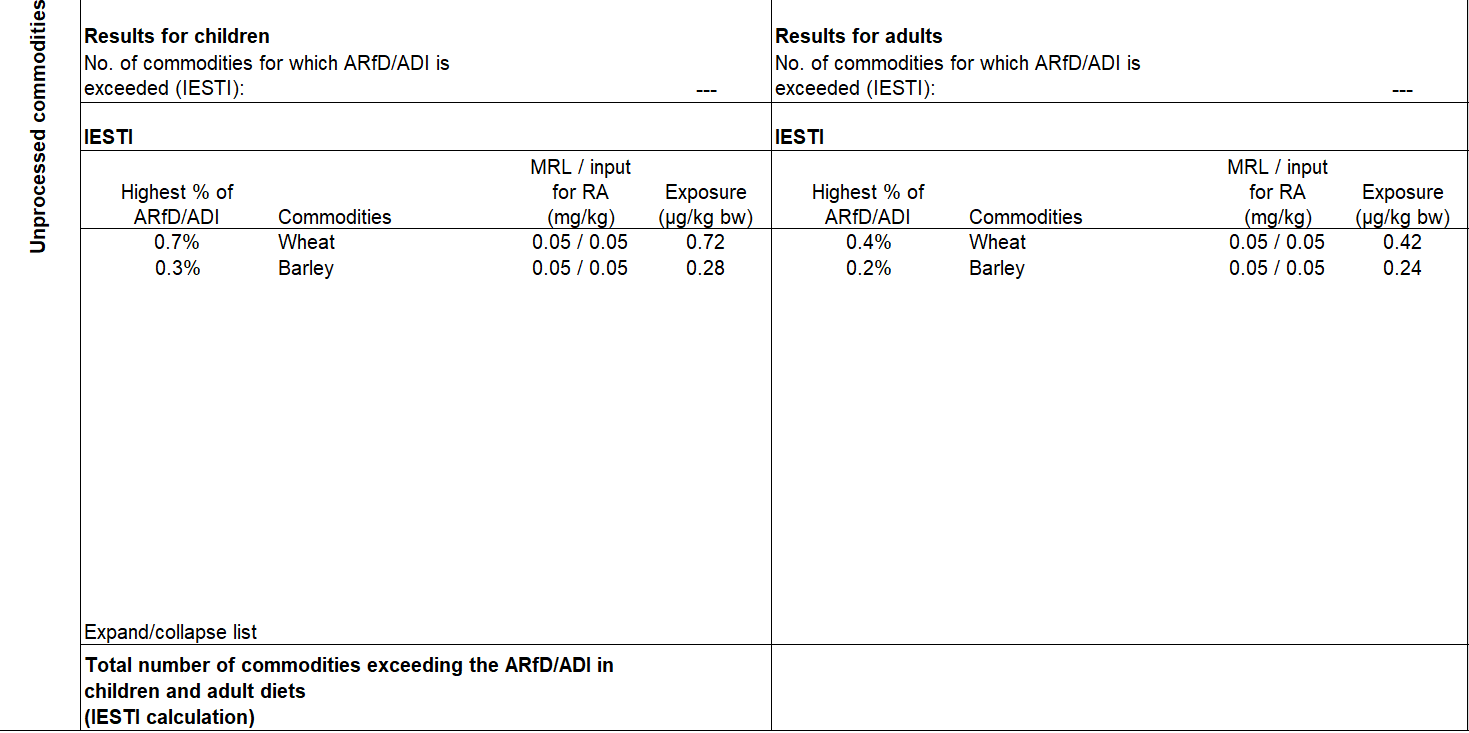
* 1. IEDI calculations

Not relevant. The TMDI does not exceed the threshold value of 100 % ADI.

* 1. IESTI calculations - Raw commodities

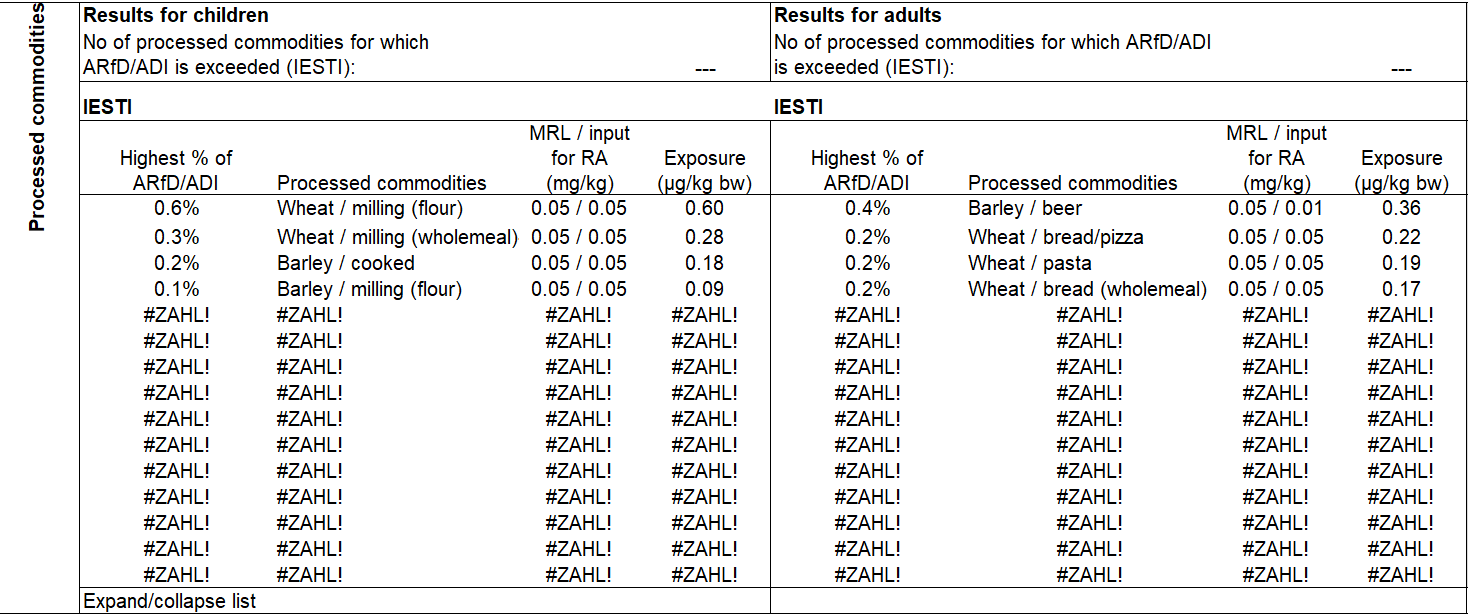
IESTI – Based on current MRLs of the active substance spiroxamine





* 1. IESTI calculations - Processed commodities

IESTI – Based on current MRLs of the active substance spiroxamine

1. Additional information provided by the applicant

No data is submitted in support of the application for authorization of ULTRACENT 460 EC. Reference is made to the unprotected data and dossier of INPUT 460 EC (R-61/2011, authorization holder Bayer AG), in accordance with Article 34 of Regulation 1107/2009/EC. It was not considered necessary to submit additional data and the evaluator is referred to the registration report of INPUT 460 EC.

1. The main metabolite in treated crops, prothioconazole-desthio, is considered relevant and was used as the basis for the consumer risk assessment as it is more toxic than parent prothioconazole. Therefore, an ADI and ARfD were established for the metabolite. (Source: Updated SANCO/3923 /07 – final) [↑](#footnote-ref-1)