|  |
| --- |
| **REGISTRATION REPORT**  **Part B**  Section 6  Mammalian Toxicology  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 May 2024  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). |
| May 2024 | The dossier was updated based on comments from the evaluating entity |
| October 2024 | Version evaluated by zRNS PL |

Table of Contents

[6 Mammalian Toxicology (KCP 7) 5](#_Toc175133137)

[6.1 Summary 5](#_Toc175133138)

[6.2 Toxicological Information on Active Substance(s) 8](#_Toc175133139)

[6.3 Toxicological Evaluation of Plant Protection Product 8](#_Toc175133140)

[6.4 Toxicological Evaluation of Groundwater Metabolites 9](#_Toc175133141)

[6.5 Dermal Absorption (KCP 7.3) 9](#_Toc175133142)

[6.6 Exposure Assessment of Plant Protection Product (KCP 7.2) 10](#_Toc175133143)

[6.6.1 Selection of critical use(s) and justification 10](#_Toc175133144)

[6.6.2 Operator exposure (KCP 7.2.1) 10](#_Toc175133145)

[6.6.2.1 Estimation of operator exposure 11](#_Toc175133146)

[6.6.2.2 Measurement of operator exposure 12](#_Toc175133147)

[6.6.3 Worker exposure (KCP 7.2.3) 12](#_Toc175133148)

[6.6.3.1 Estimation of worker exposure 12](#_Toc175133149)

[6.6.3.2 Refinement of generic DFR value (KCP 7.2) 13](#_Toc175133150)

[6.6.3.3 Measurement of worker exposure 13](#_Toc175133151)

[6.6.4 Resident and bystander exposure (KCP 7.2.2) 13](#_Toc175133152)

[6.6.4.1 Estimation of resident and bystander exposure 14](#_Toc175133153)

[6.6.4.2 Measurement of resident and/or bystander exposure 15](#_Toc175133154)

[6.6.5 Combined exposure 15](#_Toc175133155)

[6.6.5.1 Exposure assessment of Spiroxamine and Prothioconazole in ULTRACENT 460 EC 15](#_Toc175133156)

[Appendix 1 Lists of data considered in support of the evaluation 18](#_Toc175133157)

[Appendix 2 Detailed evaluation of the studies relied upon 20](#_Toc175133158)

[A 2.1 Statement on bridging possibilities 20](#_Toc175133159)

[A 2.2 Acute oral toxicity (KCP 7.1.1) 20](#_Toc175133160)

[A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2) 21](#_Toc175133161)

[A 2.4 Acute inhalation toxicity (KCP 7.1.3) 21](#_Toc175133162)

[A 2.5 Skin irritation (KCP 7.1.4) 22](#_Toc175133163)

[A 2.6 Eye irritation (KCP 7.1.5) 23](#_Toc175133164)

[A 2.7 Skin sensitisation (KCP 7.1.6) 24](#_Toc175133165)

[A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7) 25](#_Toc175133166)

[A 2.9 Data on co-formulants (KCP 7.4) 25](#_Toc175133167)

[A 2.9.1 The information submitted is acceptable.Material safety data sheet for each co-formulant 25](#_Toc175133168)

[A 2.9.2 Available toxicological data for each co-formulant 26](#_Toc175133169)

[A 2.10 Studies on dermal absorption (KCP 7.3) 26](#_Toc175133170)

[A 2.11 Other/Special Studies 26](#_Toc175133171)

[Appendix 3 Exposure calculations (EFSA OPEX v1.0.2) 27](#_Toc175133172)

[A 3.1 Field crops, Operator&Worker (Inspection, irrigation) exposure calculations 27](#_Toc175133173)

[A 3.2 Field crops, Resident exposure calculations, 10m buffer, 50% drift reduction 27](#_Toc175133174)

[~~A 3.3~~ ~~Operator exposure calculations (KCP 7.2.1.1)~~ 27](#_Toc175133175)

[~~A 3.4~~ ~~Worker exposure calculations (KCP 7.2.3.1)~~ 27](#_Toc175133176)

[~~A 3.5~~ ~~Resident and bystander exposure calculations (KCP 7.2.2.1)~~ 27](#_Toc175133177)

[~~A 3.6~~ ~~Combined exposure calculations for prothioconazole and spiroxamine~~ 27](#_Toc175133178)

[Appendix 4 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1) 28](#_Toc175133179)

# Mammalian Toxicology (KCP 7)

## Summary

Table 6.1‑1: Information on ULTRACENT 460 EC \*

|  |  |
| --- | --- |
| Product name and code | ULTRACENT 460 EC |
| Formulation type | Emulsifiable concentrate [EC] |
| Active substance(s) (incl. content) | prothioconazole; 160 g/L  spiroxamine; 300 g/L |
| Function | fungicide |
| Product already evaluated as the ‘representative formulation’ during the approval of the active substance(s) | No |
| Product previously evaluated in another MS according to Uniform Principles | No |

\* Information on the detailed composition of ULTRACENT 460 EC can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1‑2: Justified proposals for classification and labelling for ULTRACENT 460 EC according to Regulation (EC) No 1272/2008

|  |  |
| --- | --- |
| Hazard class(es), categories | Acute tox. 4, H302+H332  Skin Irrit. 2, H315  Eye Irrit. 2, H319  STOT SE 3, H335  Repr. 2, H361d  STOT RE 2, H373  Aquatic Acute 1, H400  Aquatic Chronic 1, H410 |
| Hazard pictograms or Code(s) for hazard pictogram(s) | **GHS07,** **GHS08, GHS09** |
| Signal word | **Warning** |
| Hazard statement(s) | **H302+H332, H315, H319, H335, H361d, H373,** H400**, H410** |
| Precautionary statement(s) | **P260, P280, P304+P340, P305+P351+P338, P308+P311, P391, P410** |
| Additional labelling phrases | **To avoid risks to man and the environment, comply with the instructions for use. [EUH401]** |
|  | **Contains spiroxamine. May produce an allergic reaction. [EUH208]** |

**zRMS**:

As it have been demonstrated in confidential part C of this report the composition of ULTRACENT 460 EC is comparable with composition of the product INPUT 460 EC, for which toxicological data are no longer protected, therefore in line with article 34 of Regulation (EC) No 1107/2009: “Applicants shall be exempted from supplying the test and study reports referred to in Article 33(3) where the Member State to which an application is made has the test and study reports concerned and …that any data protection period has expired.” Based on these data it is confirmed that ULTRACENT 460 EC should be classified as:

Acute tox. 4, H302+H332

Skin Irrit. 2, H315

Eye Irrit. 2, H319

STOT SE 3, H335

Repr. 2, H361d

STOT RE 2, H373

Aquatic Acute 1, H400

Aquatic Chronic 1, H410

EUH208 - Contains spiroxamine. May produce an allergic reaction.

Table 6.1‑3: Summary of risk assessment for operators, workers, residents and bystanders for ULTRACENT 460 EC

|  | Result | PPE / Risk mitigation measures |
| --- | --- | --- |
| Operators | Acceptable | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |
| Workers | Acceptable | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |
| Residents | Acceptable | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |
| Bystanders | Acceptable | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |

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.

*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 applicant, Bayer Sp. z o.o., submitted the results of toxicological tests accepted for the preparation of the assessment and report on the harmfulness to humans and animals of INPUT 460 EC. The estimated exposure to the plant protection product for the operator, worker and bystanders does not indicate a health risk for these groups of workers.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and residents/bystanders is presented in the following table.

Table 6.1‑4 Critical uses and overall conclusion of exposure assessment

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Use-No.\* | Crops and situation (e.g. growth stage of crop) | F, Fn, Fpn G, Gn, Gpn or I \*\* | Application | | Application rate | | PHI (d) | Remarks:   (e.g. safener/synergist (L/ha))  critical gap for operator, worker, resident or bystander exposure based on [Exposure model] | Acceptability of exposure assessment | | | |
| Method / Kind  (incl. application technique \*\*\* | Max. number (min. interval between applications)  a) per use  b) per crop/ season | Max. application rate  kg as/ha   a) a.s. 1 b) a.s. 2 | Water L/ha  min / max | Operator | Worker | Residents | Bystander |
| 1 | Wheat (winter) | F | Spraying | 1. 1 2. 1 | 1. 0.12 kg prothioconazole/ha + 0.225 kg spiroxamine/ha 2. 0.12 kg prothioconazole/ha + 0.225 kg spiroxamine/ha | 200 - 400 | 35 | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |  |  |  |  |
| 2 | Wheat (winter) | F | Spraying | 1. 1 2. 1 | 1. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha 2. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha | 200 - 400 | 35 | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |  |  |  |  |
| 3 | Wheat (winter and spring) | F | Spraying | 1. 1 2. 1 | 1. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha 2. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha | 200 - 400 | 35 | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |  |  |  |  |
| 4 | Barley (winter and spring) | F | Spraying | 1. 1 2. 1 | 1. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha 2. 0.16 kg prothioconazole/ha + 0.3 kg spiroxamine/ha | 200 - 400 | 35 | Reference to the unprotected data and dossier in support of INPUT 460 EC (R-61/2011, authorization holder Bayer AG). |  |  |  |  |

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

\*\* 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

\*\*\* e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 “Acceptability of exposure assessment”

|  |  |
| --- | --- |
| A | Exposure acceptable without PPE / risk mitigation measures |
| R | Further refinement and/or risk mitigation measures required |
| N | Exposure not acceptable/ Evaluation not possible |

## Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in Table 6.2‑1.

Table 6.2‑1: Information on active substance(s)

|  | Prothioconazole | Spiroxamine |
| --- | --- | --- |
| Common Name | Prothioconazole | Spiroxamine |
| CAS-No. | 178928-70-6 | 118134-30-8 |
| Classification and proposed labelling | | |
| With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended) | Hazard classes (s), categories: Aquatic Chronic 2  Code(s) for hazard pictogram(s): GHS09  Signal word: none  Hazard statement(s): H411  Precautionary statement(s): P273 | Hazard classes (s), categories: Acute Tox. 4 (oral); Acute tox. 4 (inhalation); Acute tox. 4 (dermal); Skin Irrit. 2; Skin Sens. 1; Aquatic Acute 1; Aquatic Chronic 1  Code(s) for hazard pictogram(s): GHS07; GHS09  Signal word: Warning  Hazard statement(s): H302+H312+H332, H315, H317, H410  Precautionary statement(s): P273, P280, P301+P312+P330, P302+P352+P2312, P204+P240+P312 |
| Additional C&L proposal | none | none |
| Agreed EU endpoints | | |
| AOEL systemic | 0.2 mg/kg bw/d | 0.015 mg/kg bw/d |
| Reference | EFSA Scientific Report (2007) 106, 1-98 | EFSA Journal  2010;8(9)1719 |
| Conditions to take into account/critical areas of concern with regard to toxicology | | |
| According to SANCO documents | Member States should pay particular attention to the operator safety in spray applications. Conditions of use should include adequate protective measures; | Member States should pay particular attention to the risk to operators and workers and shall ensure that conditions of use include the  application of adequate personal protective equipment; |

## Toxicological Evaluation of Plant Protection Product

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.

*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:*

Summary of acute toxicity test results for the formulation:

|  |  |  |  |
| --- | --- | --- | --- |
| **Test** | **Species** | **Result** | **Reference** |
| Oral toxicity LD50 (mg/kg) | Rat (F) | > 5000 mg/kg bw | N/A, 2001 |
| Dermal toxicity LD50 (mg/kg) | Rat (M+F) | > 4000 mg/kg bw |  |
| N/A, 2001 |
|  |
| Inhalation toxicity LC50 (mg/m3) | Rat (M+F) | ~ 2212 mg/m3 |  |
| N/A, 2002 |
|  |
| Skin irritation test | Rabbit (M) | Irritating (R38) |  |
| N/A, 2001 |
|  |
| Eye irritation test | Rabbit (M) | Irritating (R36) |  |
| N/A, 2001 |
|  |
| Sensitisation test (M&K test) | Guinea pig | Not sensitising | N/A, 2004 |

## Toxicological Evaluation of Groundwater Metabolites

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.

## Dermal Absorption (KCP 7.3)

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.

*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:*

Dermal absorption for spiroxamine (KWG 4168) under in vivo conditions was assessed according to the guidelines of Directive 91/414/EC. Under the conditions of this study, the absorption for spiroxamine (KWG 4168) and the working fluid was determined to be 4% and 18.5%, respectively. Dermal absorption for prothioconazole (JAU 6476 - desthio) was assessed in an in vivo study on Rhesus Macaque monkeys "A study to determine the dermal absorption of [14C]SXX 0665 in SC480 formulation when administered dermally to male rhesus monkeys" and was set at 20%.

Conclusions:

The information presented on the in vivo dermal absorption of spiroxamine, prothioconazole and prothioconazole-desthio from the working solution are acceptable.

## Exposure Assessment of Plant Protection Product (KCP 7.2)

~~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.~~

Table 6.6‑1: Product information and toxicological reference values used for exposure assessment

|  |  |  |  |
| --- | --- | --- | --- |
| Product name and code | ULTRACENT 460 EC | | |
| Formulation type | EC | | |
| Category | Fungicide | | |
| Active substance(s) (incl. content) | **Spiroxamine**  300 g/L | **Prothioconazole**  160 g/L | Prothioconazole-desthio  (conversion factor 60% from parent) |
| AOEL systemic | 0.015 mg/kg bw/d | 0.2 mg/kg bw/d | 0.01 mg/kg bw/d |
| Inhalation absorption | 100% | 100% | 100% |
| Oral absorption | 100% | 100% | 100% |
| Dermal absorption | Concentrate: 4%  Dilution: 18.5% | Concentrate: 25%  Dilution: 70% (Default) | Concentrate: 0%  Dilution: 20% |

### Selection of critical use(s) and justification

~~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.~~

In exposure studies, it has been noted that complete conversion of prothioconazole to prothioconazole-desthio has not been observed, with a maximum conversion rate of approximately 60% (DAR Vol. 3, Annex B.6.14, UK 2004). Additionally, estimated conversion rates from prothioconazole to prothioconazole-desthio in soil fall within the range of 47.6% to 57.1% (RAR Vol. 3, CA Section B.8). Minimal degradation of the parent substance has been observed in water. Therefore, a conservative conversion rate of 60% has been utilized for combined risk assessment.

### Operator exposure (KCP 7.2.1)

~~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.~~

*~~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 operator exposure assessment was carried out using a model recommended by the European Union: the BBA model. The model used two scenarios taking into account the absence and use of individual protective measures. Due to the irritant properties of the plant protection product, protective gloves and a plastic visor to protect the face were recommended as standard.~~

~~The estimation performed according to the BBA model showed an acceptable exposure below the AOEL (0.5 mg/kg bw) for prothioconazole (JAU 6476) and below the AOEL (0.024 mg/kg bw) for spiroxamine (KWG 4168), in all scenarios and with the proposed application method.~~

~~Conclusions:~~

~~The models used are acceptable.~~

~~The result of this estimation allows us to conclude that the recommended range and mode of application of the product does not pose a risk and does not require specific individual protection measures.~~

#### Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of ULTRACENT 460 EC according to the critical use(s) is presented in Table 6.6‑2. The outcome of the estimation is presented in and Table 6.6‑3 (longer term exposure). Detailed calculations are in Appendix 3.

For both active substances, no acute acceptable operator exposure value (AAOEL, RVAAS) has been set on EU-level until now. Thus, no acute exposure calculations have been conducted: According to Commission Guidance Document SANTE-10832-2015 rev. 1.7 (24.01.2017), no acute operator exposure assessments can be performed with the OPEX model where no AAOEL has been set.

Table 6.6‑2: Exposure models for intended uses

|  |  |
| --- | --- |
| Critical use(s) | Use 1-4: Field crops (max. 1x 1.0 L product/ha) |
| Model(s) | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032.  EFSA OPEX version 1.0.2 |

Table 6.6‑3: Estimated operator exposure (longer term exposure)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Spiroxamine | | Prothioconazole | | Prothioconazole-desthio | | Combined  (hazard index) |
| Model data | Level of PPE | Total absorbed dose  (mg/kg/day) | % of systemic AOEL | Total absorbed dose  (mg/kg/day) | % of systemic AOEL | Total absorbed dose  (mg/kg/day) | % of systemic AOEL |
| Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile  Crop density: Normal | | | | | | | | |
| Application rate | | 1x 0.3 kg a.i./ha | | 1x 0.064 kg a.i./ha | | 1x 0.0871 kg a.i./ha\*\* | |  |
| **Spray application**  (AOEM**;** 75th percentile)  Body weight: 60 kg | Work wear\* + protected hands  M/L and + Work wear A | 0.008 | 55.3 | 0.008 | 4 | 0.0024 | 23.7 | 0.83 |

\* arms, body and legs covered

\*\* based on a 60% conversion rate with molecular weight correction factor of 0.907

**zRMS**:

***The assumption of 60% conversion from the parent prothioconazole to the metabolite prothioconazole-desthio is acceptable***

**Operators.** As a result of application product ULTRACENT 460 EC at dose of 1L/ha in line with GAP the exposure of operator wearing work wear covering body, arms and legs during M/L and A and protective gloves doing M/L calculated with the EFSA AOEM 2022 amounted for spiroxamine 55.3% of respective AOEL, to prothioconazole 4% of AOEL and to Prothioconazole-desthio 23.7% of respective AOEL. Combined Hazard index was below 1. Therefore, the application of a product ULTRACENT 460 EC does not pose an unacceptable risk to the health of operator using tractor-mounted/trailed boom sprayer without drift reduction technology for application of the product at dose of 1L/ha in line with its intended use within good agricultural practice providing that he is wearing a work wear (with arms, body and legs covered) during M/L and A, and protective gloves during M/L. It is noted that the product is classified as Skin Irrit. 2 and Eye Irrit 2 thus the operator should wear a work wear covering arms, body and legs during mixing/loading and application, protective gloves, eye protection/face protection during mixing/loading operations or when directly contacting surface of equipment contaminated with concentrated product.

#### Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and consideration of the above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

### Worker exposure (KCP 7.2.3)

~~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.~~

*~~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:~~*

~~Due to the fact that the assessed product is only applied to cereal crops where practically no manual agro-technical treatments are used, there is no basis for conducting an exposure estimation for agricultural workers.~~

~~Conclusions:~~

~~The justification provided is acceptable.~~

#### Estimation of worker exposure

Table 6.6‑4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with ULTRACENT 460 EC according to the critical uses. Outcome of the estimation is presented in Table 6.6‑5 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6‑4: Exposure models for intended uses

|  |  |
| --- | --- |
| Critical use(s) | Use 1-4: Field crops (max. 1x 1.0 L product/ha) |
| Model(s) | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032.  EFSA OPEX version 1.0.2 |

Table 6.6‑5: Estimated worker exposure (longer term exposure)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Model data | Level of PPE | Spiroxamine | | Prothioconazole | | Prothioconazole-desthio | |
| Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL |
| Inspection, irrigation / Outdoor  Work rate: 2 hours/day,  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha | | Dermal absorption: 18.5 % | | Dermal absorption: 75% | | Dermal absorption: 20% | |
| Number of applications and application rate | | 1x 0.3 kg a.i./ha | | 1x 0.064 kg a.i./ha | | 1x 0.0871 kg a.i./ha\* | |
| Body weight:  60 kg | Potential  TC: 12500 cm2/person/h | 0.07 | **463** | 0.06 | 30 | 0.02 | **218** |
| Work wear (arms, body  and legs covered)  TC: 1400 cm2/person/h | 0.008 | 51.8 | 0.007 | 3.4 | 0.002 | 24.4 |
| Work wear (arms, body  and legs covered) and  gloves  TC: 1250 cm2/person/h | 0.007 | 46.3 | 0.006 | 3 | 0.002 | 21.8 |

\* based on a 60% conversion rate with molecular weight correction factor of 0.907

**zRMS**:

The estimation of exposure of worker wearing a work wear (with arms, body and legs covered) to both active substances of a product ULTRACENT 460 EC applied on a field of cereals at dose of 1.0 L product/ha, using tractor-mounted/trailed boom sprayer without drift reduction technology, calculated with the EFSA AOEM 2022 demonstrates that a potential exposure of worker and an exposure of worker wearing a work wear (with arms, body and legs covered) is equal respectively for spiroxamine 51.8 % of respective AOEL, to prothioconazole 3.4% of AOEL and to Prothioconazole-desthio 24.4% of respective AOEL.

The sum of exposures of worker wearing a work wear (with arms, body and legs covered) to both active substances and to metabolite Prothioconazole-desthio expressed as percent-age of their AOELs (51.8 % + 3.4 % + 24.4%) is below 100%, therefore the application of product ULTRACENT 460 EC does not pose an unacceptable risk to the health of worker wearing a work wear (with arms, body and legs covered) entering for 2hrs inspection a field of cereals treated with a product ULTRACENT 460 EC according to its intended use on cereals within good agricultural practice.

#### Refinement of generic DFR value (KCP 7.2)

Not required.

#### Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

### Resident and bystander exposure (KCP 7.2.2)

~~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.~~

*~~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:~~*

~~Bystander exposure calculated using the Ganzelmeier drift model, and Lloyd's and Bell's data, was less than 1% for the calculated AOELs for prothioconazole and spiroxamine, and therefore, in line with the label recommendations and in accordance with GAP principles, there is no risk of bystander exposure.~~

~~Conclusions:~~

~~The information and justification provided is acceptable.~~

#### Estimation of resident and bystander exposure

Table 6.6‑6 shows the exposure model(s) used for estimation of resident and bystander exposure to spiroxamine, prothioconazole and its metabolite prothioconazole-desthio. The outcome of the estimation is presented in Table 6.6‑8 (acute) and Table 6.6‑7 (longer term resident exposure). Detailed calculations are in Appendix 3.

Table 6.6‑6: Exposure models for intended uses

|  |  |
| --- | --- |
| Critical use(s) | Use 1-4: Field crops (max. 1x 1.0 L product/ha) |
| Model(s) | Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2022;20(1):7032.  EFSA OPEX version 1.0.2 |

Table 6.6‑7: Estimated resident exposure (longer term exposure)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Spiroxamine | | Prothioconazole | | Prothioconazole-desthio | |
| Model data |  | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL |
| Field crops/Outdoor/Downward spraying/Vehicle-mounted  Buffer zone: 10 m  Drift reduction technology: yes, 50%  DT50: 30 days  DFR: 3 µg/cm2/kg a.s./ha | | Dermal absorption: 18.5 % | | Dermal absorption: 75% | | Dermal absorption: 20% | |
| Number of applications and application rate | | 1x 0.3 kg a.i./ha | | 1x 0.064 kg a.i./ha | | 1x 0.0871 kg a.i./ha\* | |
| Resident child  Body weight:  10 kg | Drift (75th perc.) | 0.002 | 13.6 | 0.002 | 0.9 | 0.0006 | 6.4 |
| Vapour (75th perc.) | 0.0008 | 5.3 | 0.0008 | 0.4 | 0.0008 | 8 |
| Deposits (75th perc.) | 0.0001 | 0.8 | 9e-05 | 0.04 | 4e-05 | 0.4 |
| Re-entry (75th perc.) | 0.009 | 62.4 | 0.008 | 4.1 | 0.003 | 29.4 |
| **Sum (mean)** | 0.01 | 63.4 | 0.008 | 4.2 | 0.004 | 35.3 |
| Resident adult  Body weight:  60 kg | Drift (75th perc.) | 0.0004 | 2.5 | 0.0003 | 0.2 | 0.0001 | 1.2 |
| Vapour (75th perc.) | 0.0003 | 1.8 | 0.0003 | 0.1 | 0.0003 | 2.7 |
| Deposits (75th perc.) | 4e-05 | 0.3 | 4e-05 | 0.02 | 1e-05 | 0.1 |
| Re-entry (75th perc.) | 0.005 | 34.7 | 0.005 | 2.3 | 0.002 | 16.3 |
| **Sum (mean)** | 0.005 | 31.1 | 0.004 | 2 | 0.002 | 16.5 |

\* based on a 60% conversion rate with molecular weight correction factor of 0.907

Table 6.6‑8: Estimated bystander exposure (acute exposure)

In absence of acute endpoints, the exposure for the bystander cannot be fully analysed. Nonetheless, bystander exposure is covered by resident exposure assessment.

**zRMS**:

The exposure estimation of resident (adult and child) to both active substances of a product ULTRACENT 460 EC applied on a field of cereals at dose of 1.0 L product/ha, using tractor-mounted/trailed boom sprayer with drift reduction technology, and 10 m not spray buffer zone calculated with the EFSA AOEM 2022 demonstrates that such a exposure for child and adult resident is equal respectively for spiroxamine to 63.4% and to 31.1 % of AOEL, and for prothioconazole to 4.2 % and to 2.0 % of AOEL for Prothioconazole, and to Prothioconazole-desthio an environmental metabolite of Prothioconazole to 35.3 and 16.5 % of AOEL The combined exposures of adult or child resident to both active substances and to metabolite Prothioconazole-desthio expressed as hazard index equal respectively 1 for child resident and 0.5 for adult resident thus the application of product ULTRACENT 460 EC does not pose an unacceptable risk to the health of adult and child resident for its intended use on cereals within good agricultural practice under condition of using risk management measures such as drift reduction technology (50%) and 10 m buffer zone not spread with a product. It is highly probable that the exposures of residents have been considerably overestimated since a default dermal absorption values were used for Prothioconazole, while in fact its absorption could be at least two times smaller. Also the dermal absorption value of 20% for Prothioconazole-desthio has been used based on results of old study, and its real absorption is most probably lower.

No bystander acute exposure estimation for spiroxamine and for Prothioconazole is required since no acute acceptable operator exposure value (AAOEL) has be set for any of these active substances nor for metabolite Prothioconazole-desthio. Therefore, as indicated in the EU guidance (SANTE-10832-2015 rev. 1.7; 24 January 2017), no unacceptable risk is expected for bystanders due to short-term single exposure to spiroxamine and to Prothioconazole, and to metabolite Prothioconazole-desthio as a result of application of a product ULTRACENT 460 EC with accordance with intended use within good agricultural practice.

#### Measurement of resident and/or bystander exposure

Since the resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for spiroxamine, prothioconazole and its metabolite will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures (10 m spray buffer in combination with drift reducing technology), a study to provide measurements of resident/bystander exposure was not necessary and was therefore not performed.

### Combined exposure

~~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.~~

The product is a mixture of two active substances.

#### Exposure assessment of Spiroxamine and Prothioconazole in ULTRACENT 460 EC

Note: The combined toxicological effect of these active substances has not been investigated with regard to repeated dose toxicity.

At the first tier, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity. Initially, the individual Hazard Quotients (HQ) are calculated for all active substances in the PPP by assessing the exposure according to appropriate models and dividing the individual exposure levels by the respective systemic AOEL. This is equivalent to the predicted exposure as % of systemic AOEL from e.g. Table 6.6‑3 converted to decimal. The Hazard Index (HI) is the sum of the individual HQs.

Table 6.6‑9: Risk assessment from combined exposure (long-term exposure)

| Application scenario | Active ingredient | Estimated exposure / AOEL (HQ) |
| --- | --- | --- |
| Operators – Vehicle-mounted | Spiroxamine | 0.550 |
| Prothioconazole | 0.040 |
| Prothioconazole-desthio | 0.237 |
| **Cumulative risk operators (HI)** | **0.827** |
| Workers – inspection, irrigation  incl. workwear | Spiroxamine | 0.518 |
| Prothioconazole | 0.034 |
| Prothioconazole-desthio | 0.244 |
| **Cumulative risk workers (HI)** | **0.8** |
| Resident - child | Spiroxamine |  |
| Drift | 0.137 |
| Vapour | 0.053 |
| Deposits | 0.008 |
| Re-entry | 0.624 |
| Sum of all pathways | 0.634 |
| Prothioconazole |  |
| Drift | 0.009 |
| Vapour | 0.004 |
| Deposits | 0.0004 |
| Re-entry | 0.041 |
| Sum of all pathways | 0.042 |
| Prothioconazole-desthio |  |
| Drift | 0.064 |
| Vapour | 0.080 |
| Deposits | 0.004 |
| Re-entry | 0.294 |
| Sum of all pathways | 0.353 |
| **Cumulative risk resident – child (HI)** |  |
| Drift | 0.20 |
| Vapour | 0.10 |
| Deposits | 0.01 |
| Re-entry | 1.0 |
| **Sum of all pathways** | **1.0** |
| Resident - adult | Spiroxamine |  |
| Drift | 0.025 |
| Vapour | 0.018 |
| Deposits | 0.003 |
| Re-entry | 0.347 |
| Sum of all pathways | 0.311 |
| Prothioconazole |  |
| Drift | 0.002 |
| Vapour | 0.001 |
| Deposits | 0.0002 |
| Re-entry | 0.023 |
| Sum of all pathways | 0.020 |
| Prothioconazole-desthio |  |
| Drift | 0.012 |
| Vapour | 0.027 |
| Deposits | 0.001 |
| Re-entry | 0.163 |
| Sum of all pathways | 0.165 |
| **Cumulative risk resident – adult (HI)** |  |
| Drift | 0.04 |
| Vapour | 0.05 |
| Deposits | 0.004 |
| Re-entry | 0.5 |
| **Sum of all pathways** | **0.5** |

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

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 XXXX), 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 |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

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

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

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

List of data relied on 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 |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

1. Detailed evaluation of the studies relied upon
   1. Statement on bridging possibilities

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. Acute oral toxicity (KCP 7.1.1)

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.

*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:*

Acute oral toxicity study (report no. 31561), "Study for acute oral toxicity in Rats". Performed by XXXX, unpublished report.

The study was conducted in accordance with the guidelines: OECD Guidelines N° 423 "Acute Toxic Class Method" adopted 17th December 2001 and Directive 67/548/EEC Annex IV B, B1.tris (27 June 1967) and EPA OPPTS 870.1100 - 712-C-98-190), (August 1998) according to GLP principles.

Note: The study used a commercial product diluted in deionised water administered as a single dose by gastric probe. Observation was carried out for 14 consecutive days.

Acute oral toxicity, male and female rats:

|  |  |  |  |
| --- | --- | --- | --- |
| **Dose (mg/kg)** | **Number of dead animals/clinical signs/n=3** | **Duration of symptoms/time of death** | **Mortality**  **[%]** |
| males | | | |
| 200 | 0/0/3 | -- | 0 |
| 500 | 0/3/3 | -- | 0 |
| females | | | |
| 200 | 0/0/3 | -- | 0 |
| 500 | 0/3/3 | -- | 0 |
| 2000 | 3/3/3 | 10min-2 days/2h- 2days | 100 |

Conclusions:

The study is acceptable.

Under the conditions of the experiment, the LD50 dose for the plant protection product INPUT 460 EC [code 06920/00459(0019)] is 500 < LD50 < 2000 mg/kg b.w. The tested formulation is to be classified as Acute tox. 4 with the phrase H302.

* 1. Acute percutaneous (dermal) toxicity (KCP 7.1.2)

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.

*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:*

Acute dermal toxicity study (report no. 31562), 2001 "Study of acute dermal toxicity in rats". Performed by XXXX, unpublished report.

The study was conducted in accordance with the guidelines: OECD Guidelines No. 402 (24 February 1987), EC Directive 67/548/EEC Annex V, B3 (27 June 1967), EPA OPPTS 870.1200 - 712-C-98-192, (August 1998) according to GLP principles. The test substance diluted in water was applied to the shaved skin of the dorsum and flanks of Wistar rats. The observation was carried out for 15 consecutive days.

Acute dermal toxicity male/female rats:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Dose (mg/kg)** | **Number of dead animals/clinical signs/n=3** | | **Duration of symptoms/time of death** | **Mortality**  **[%]** |
|  | | males | |  |
| 4000 | 0/5/5 |  | 2d-8d | 0 |
|  | | females | |  |
| 4000 | 0/5/5 |  | 2d-8d | 0 |

Conclusions:

The study is acceptable.

Under the conditions of the experiment, the LD50 dose for the plant protection product INPUT 460 EC [code 06920/00459(0019)] is >4000 mg/kg b.w. (F + M).

* 1. Acute inhalation toxicity (KCP 7.1.3)

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.

*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:*

Acute inhalation toxicity study (report no. 31735), "Study on acute inhalation toxicity in rats according to OECD 403". Performed by XXXX, unpublished report.

The study was conducted in accordance with: OECD Guidelines No. 403 (24 February 1987), EC Directive 92/69/EEC, EPA OPPTS 870.1300 - 712-C-98-192, (August 1998) according to GLP principles. Two groups of Wistar rats were exposed by the intranasal route to an aqueous aerosol of the test substance (aerosol particle size of 1.3-1.4 µm indicates high respirability) with concentrations of 1018 and 4805 mg/m3 for 4 hours. After exposure, animals were observed for 14 consecutive days.

Acute inhalation toxicity male/female rats:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **Dose (mg/m3 air) analytical concentration** | **Number of dead animals/ clinical symptoms /n=5** | **Duration of symptoms/time of death** | **Mortality**  **[%]** |
| males | | | | |
| 1 | 0 | 0/0/5 | -- | 0 |
| 2 | 1018 | 0/5/5 | 0d-5d | 0 |
| 3 | 4805 | 4/2/5 | 0d-14d | 80 |
| females | | | | |
| 1 | 0 | 0/0/5 | -- | 0 |
| 2 | 1018 | 0/5/5 | 0d-5d | 0 |
| 3 | 4805 | 5/3/5 | 0d | 100 |

Conclusions:

The study is acceptable.

Under the conditions of the experiment conducted, the LC50 dose for the plant protection product INPUT 460 EC [code 06920/00459(0019)] is ~2212 mg/m3 b.w. (F + M). The tested formulation should be classified as Acute tox. 4 with the phrase H332.

* 1. Skin irritation (KCP 7.1.4)

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.

*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:*

Acute toxicity test: skin irritation (report no. R 8083).

"Acute skin irritation test (patch test) of JAU 6476 160 EC & KWG 4168 300 in rabbits". Performed by XXXX, unpublished report.

The test was conducted in accordance with the guidelines: OECD Guidelines No. 404 (24 April 2002), EC Directive 67/548/EEC Part B, No. B4 (1967), EPA OPPTS 870.2500 - 712-C-98¬195 (1998) according to GLP principles. The test substance was applied to the shaved skin (dorsal part) of 3 Himalayan rabbits (males). Observation was carried out at 1, 24, 48, 72 hours and from 4 to 14 days after the end of exposure.

Acute toxicity- dermal irritation - undiluted test substance (Exposure time: 4 hours), 3 rabbits, females.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Draize scale | | | | | | | | | |
| Duration of exposure | | 4 hours | | | | | | | |  | |
| Observation time | | 1 hour | | 24 hours | | 48 hours | | 72 hours | | 4 days-13 days | |
| Animal no. | Body weight | E\* | O\* | E | O | E | O | E | O | E | O |
| 1 | --g | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| 2 | -- g | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| 3 | -- g | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |

\*E = Erythema (redness), O = Oedema (swelling)

Conclusions:

The study is acceptable.

Under the conditions of the experiment, the tested plant protection product INPUT 460 EC [code 06920/00459(0019)] showed skin irritant properties. The test formulation should be classified as Skin Irrit. 2 with the phrase H315.

* 1. Eye irritation (KCP 7.1.5)

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.

*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:*

Acute toxicity study: eye irritation (report no. R 8084).

Acute eye irritation study of JAU 6476 160 EC & KWG 4168 300 by instillation into conjunctival sac of rabbits". Performed by XXXX, unpublished report.

The study was conducted in accordance with the guidelines: OECD Guidelines N° 405 (April 24, 2002), EC Directive 67/548/EEC Part B, No.B5 EPA OPPTS 870.2400 (712-C-98-195) according to GLP principles. A test substance of 0.1 ml was injected into the conjunctival sac of the right eye of 3 Himalayan rabbits (males). Observation was carried out at 1, 24, 48, 72 hours and from 4 to 20 days after the end of exposure.

Acute toxicity: eye irritation (rabbit)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Animal 1 | | | | | | | | |
| Observation time | 1h | 24h | 48h | 72h | day  7 | day  14 | day  20 | mean  (24-48-72h) |
| Degree of corneal opacity | 0 | 3 | 3 | 2 | 2 | 1 | 0 | 2.6 |
| iris | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 |
| Conjunctival redness | 1 | 3 | 3 | 1 | 1 | 0 | 0 | 2.3 |
| Conjunctival congestion | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 1.3 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Animal 2 | | | | | | | | |
| Observation time | 1h | 24h | 48h | 72h | day  7 | day  14 | day  20 | mean  (24-48-72h) |
| Degree of corneal opacity | 0 | 3 | 3 | 2 | 1 | -- | -- | 2.6 |
| iris | 0 | 1 | 1 | 1 | 1 | -- | -- | 1 |
| Conjunctival redness | 1 | 3 | 2 | 2 | 1 | -- | -- | 2.3 |
| Conjunctival congestion | 1 | 2 | 2 | 1 | 0 | -- | -- | 1.6 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Animal 3 | | | | | | | | |
| Observation time | 1h | 24h | 48h | 72h | day  7 | day  14 | day  20 | mean  (24-48-72h) |
| Degree of corneal opacity | 0 | 3 | 3 | 2 | 1 | 1 | -- | 2.6 |
| iris | 0 | 1 | 1 | 1 | 1 | 0 | -- | 1 |
| Conjunctival redness | 1 | 2 | 1 | 1 | 1 | 0 | -- | 1.3 |
| Conjunctival congestion | 1 | 3 | 2 | 1 | 0 | 0 | -- | 2 |

Conclusions:

The study is acceptable.

Under the conditions of the experiment, the test plant protection product INPUT 460 EC [code 06920/00459(0019)] showed eye irritation properties. The tested formulation should be classified as Eye Irrit. 2 with the phrase H319.

* 1. Skin sensitisation (KCP 7.1.6)

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.

*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:*

Acute toxicity study: sensitisation (report no. 32072), "Study for the Skin Sensitization Effect in Guinea Pigs (guinea pig maximization test according Magnusson and Kligmann)". Performed by XXXX, unpublished report.

The study was conducted in accordance with the guidelines: OECD Guidelines N° 406, 12 May 1981, adopted 17th July 1992, EC Directive 96/54/EEC Method B6 (30 July 1996), EPA OPPTS 870.2600 - 712-C-03-197, (March 2003) according to GLP principles.

Note: The commercial product in undiluted form was used for the study. The study was conducted on a group of 30 female guinea pigs (20 individuals in the test group and 10 in the control group). A 3% solution was used and did not cause a sensitisation reaction.

Sensitisation test (M&K) guinea pig

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Sex** | **Animal number** | **Control group**  **Test patch** | | **Control patch** | |
| **48 hours** | **72 hours** | **48 hours** | **72 hours** |
| Males | 01 | 0 | 0 | 0 | 0 |
|  | 02 | 0 | 0 | 0 | 0 |
|  | 03 | 0 | 0 | 0 | 0 |
|  | 04 | + | + | + | + |
|  | 05 | 0 | 0 | 0 | 0 |
|  | 06 | 0 | 0 | 0 | 0 |
|  | 07 | 0 | 0 | 0 | 0 |
|  | 08 | 0 | 0 | 0 | 0 |
|  | 09 | 0 | 0 | 0 | 0 |
|  | 10 | 0 | 0 | 0 | 0 |
|  |  | Test group | | | |
| Females | 11 | 0 | 0 | 0 | 0 |
|  | 12 | 0 | 0 | 0 | 0 |
|  | 13 | 0 | 0 | 0 | 0 |
|  | 14 | 0 | 0 | 0 | 0 |
|  | 15 | 0 | 0 | 0 | 0 |
|  | 16 | 0 | 0 | 0 | 0 |
|  | 17 | 0 | 0 | 0 | 0 |
|  | 18 | 0 | 0 | 0 | 0 |
|  | 19 | 0 | 0 | 0 | 0 |
|  | 20 | 0 | 0 | 0 | 0 |
|  | 21 | 0 | 0 | 0 | 0 |
|  | 22 | 0 | 0 | 0 | 0 |
|  | 23 | + | + | + | + |
|  | 24 | 0 | 0 | 0 | 0 |
|  | 25 | 0 | 0 | 0 | 0 |
|  | 26 | 0 | 0 | 0 | 0 |
|  | 27 | 0 | 0 | 0 | 0 |
|  | 28 | 0 | 0 | 0 | 0 |
|  | 29 | 0 | 0 | 0 | 0 |
|  | 30 | 0 | 0 | 0 | 0 |

Conclusions:

The test is acceptable.

Under the conditions of the experiment, the plant protection product INPUT 460 EC [code 06920/00459(0019)] tested did not show sensitising properties to guinea pig skin.

* 1. Supplementary studies for combinations of plant protection products (KCP 7.1.7)

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. Data on co-formulants (KCP 7.4)

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

The applicant has submitted Safety Data Sheets for the product and the active substance, drawn up in accordance with the Regulation of the Minister of Health.

Conclusions:

* + 1. The information submitted is acceptable.Material safety data sheet for each co-formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

* + 1. Available toxicological data for each co-formulant

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. Studies on dermal absorption (KCP 7.3)

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. Exposure calculations (EFSA OPEX v1.0.2)
   1. Field crops, Operator&Worker (Inspection, irrigation) exposure calculations



* 1. Field crops, Resident exposure calculations, 10m buffer, 50% drift reduction



* 1. ~~Operator exposure calculations (KCP 7.2.1.1)~~

~~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. ~~Worker exposure calculations (KCP 7.2.3.1)~~

~~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. ~~Resident and bystander exposure calculations (KCP 7.2.2.1)~~

~~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. ~~Combined exposure calculations for prothioconazole and spiroxamine~~

~~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. Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)

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.